A D D E N D A

CALIFORNIA TUMOR TISSUE REGISTRY

FORTY-SIXTH SEMI-ANNUAL SLIDE SEMINAR

ON

TUMORS OF THE ESOPHAGUS

AND GASTRO-INTESTINAL TRACT

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SUNDAY, DECEMBER 8, 1968
9:00 A.M. - 5:30 P. M.

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DECEMBER 8, 1968 - CASE NO. 1

ACCESSION NO. 15599

MODERATOR'S DIAGNOSIS: VILLOUS TUMOR OF THE SIGMOID

HISTORY:

This 54 year old white male entered the hospital with complaint of lower abdominal pain for six months without weight loss or gastrointestinal bleeding.

DISCUSSION:

Under low magnification the lesion is composed of long, slender projections that appear to spring almost directly from the mucosa. In some areas one is able to see gland formations, but generally the villous pattern dominates. In contrast to the normal colonic epithelium, one sees nuclear stratification, diminution of the number of goblet cells and a number of normal mitotic figures. In occasional areas there is an intricate glandular pattern that raises the question of malignant neoplasm. In the stalk of the sections one finds what appears to be invasion by neoplastic epithelium. However, if one pays close attention to this epithelium it appears to be strikingly similar to that of the overlying villous adenoma. In one cut of a lesion such as this, one should not hasten to the diagnosis of invasiveness until step-sections have been made through the block and additional sections submitted of the lesion. In most instances, this turns out to be pseudo invasion representing infoldings of epithelium. This villous tumor presents relatively few atypicalities other than the previously mentioned glandular intricacies. By our definition of "carcinoma in situ" in such a lesion, we search for gland formations that are complex with the appearance of glands forming within glands and the nuclear atypicalities so often associated with carcinoma. If such a focus is found, this is designated as carcinoma in situ. In general we have not based our diagnoses of carcinoma in situ in villous tumors only on the nuclear alterations.

The implications of the diagnosis of villous tumor are well known, that is, approximately 30%-50% of villous tumors may contain a focus that can be designated as malignant. Invasive carcinoma is found in about 24%; the larger the lesion the greater the possibility of an invasive component. If a malignant area is noted in a villous adenoma, then its behavior is similar to that of a carcinoma occurring de novo in the colon. That is if it is carcinoma in situ, it will rarely, if ever, be the source of metastases. If the carcinoma has invaded into the stalk or beyond, then it takes on the characteristics of carcinomas under similar circumstances. One might ponder if all villous tumors are not malignant when confronted with the frequency with which villous adenomas demonstrate malignant foci. One reason for considering them

all malignant, if one were so inclined, can be found in the growth rates that have been demonstrated by serial barium enema studies. These studies indicate that the growth rate is similar to that of carcinoma of the large bowel.

Villous tumors often present a difficult biopsy problem for the surgeon. As they are often large lesions, the periphery of the lesion is subjected to biopsy and at times several biopsies and diagnosis of villous tumor is made. In reality a carcinoma may be situated in the center of the lesion. Careful physical examination of the lesion if within reach of the finger may give more information than random biopsies. If the lesion is fixed, ulcerated, or has firm areas within it, then the chances of its having carcinoma are very high. If possible, biopsies from the center of the lesion are suggested.

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ACCESSION NO. 17341

MODERATOR'S DIAGNOSIS: HYPERTROPHIC GASTRITIS

HISTORY:

The patient was first admitted to the hospital in August 1967 because of progressive swelling of the legs and shortness of breath of two weeks' duration. A hypochromic anemia was present. Transfusions and digitalization were administered resulting in marked improvement. He was readmitted for re-evaluation on January 28, 1968.

DISCUSSION:

Clinically this patient has findings that suggest the possibility of hypertrophic gastritis. The patient presents with edema and has laboratory findings of hypoproteinemia with a total protein of 4.2 g%. Patients having these findings including the radiographic alterations described are commonly designated as having Menetrier's disease. One value in this patient's laboratory examination does not fit entirely with the disease: the reported normal gastric acidity. Classically, these patients have hypoproteinemia, and hypo or anacidity. The serum protein alterations are not constant, but generally the changes in the gastric acidity have been.

The histologic sections from this patient's stomach demonstrate a remarkably thickened mucosa that on the slide measures up to 7 mm. The normal gastric mucosa varies between .6 and 1.1 mm. Without knowing the exact sites from which the tissue sections were taken, one cannot make precise statements about the pathological findings. However it is evident that the surface of the gastric mucosa is somewhat papillary and the epithelium shows goblet cell alteration reminiscent of small bowel epithelium. Chronic inflammatory cells and edema are seen. In several areas great dilatation of glands is noted. Deeper in the mucosa one notes that in none of the sections are there a normal number of parietal cells. If any of these or all of these sections represent the body of the stomach, one would have to say there is a definite decrease in the parietal cells in 1 or 2 of the sections, and an absence of parietal cells in the remainder of the sections. The above observations correlate with the clinical observation of loss of protein and decreased formation of acid.

Other hypertrophic gastridides are known. Among these is hypertrophic hypersecretory gastropathy. In this lesion there is hypersecretion of gastric hydrochloric acid, pepsin and mucoproteins. The radiographic findings are similar to those seen in giant hypertrophic gastritis. The lesion differs however, in that there is no significant loss in serum protein. Histologically there are differences also in

that there is hyperplasia of the glandular portion of the gastric mucosa with no evident loss in the parietal cell mass. This lesion has also been designated as hypertrophic glandular gastritis by Schindler. The findings in Zollinger-Ellison syndrome of the gastric mucosa are similar to those in hypertrophic glandular gastritis.

One of the outstanding histological alterations in hypertrophic gastritis is the loss of or diminution of the parietal cell mass. It has been demonstrated that the parietal cell mass in the normal gastric mucosa varies from site to site with the largest number of parietal cells being located in the mid-portion of the body of the stomach. Lesser numbers are encountered at the proximal and distal ends of the stomach with relatively few in the antrum. The parietal cell mass varies with diseases being approximately three times greater in the patient with a duodenal ulcer when compared to normal, and in patients with Zollinger-Ellison syndrome the parietal cell mass is approximately ten times normal.

There has been considerable discussion concerning the relationship between giant hypertrophic gastritis and carcinoma of the stomach. There have been reports of carcinomas associated with this lesion. However, many observers feel that there is no statistically significant relationship between this form of gastritis and carcinoma.

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DECEMBER 8, 1968 - CASE NO. 3

ACCESSION NO. 15782

MODERATOR'S DIAGNOSIS: ADENOCARCINOMA OF THE STOMACH

HISTORY:

This 55 year old caucasian male was admitted to the hospital with a lesser curvature ulcer which had failed to resolve over a four week fall.

DISCUSSION:

This carcinoma of the stomach illustrates several interesting histological features. It is a poorly differentiated adenocarcinoma that forms only a few recognizable glands. Under the low magnification it is noted that the advancing borders of the lesion are smooth, and rounded, often referred to as "pushing" borders. Also, numerous inflammatory cells are mixed with the lesion and at its borders. These cells impart a bluish discoloration to the slide. This has been referred to by Steiner and Associates as the "blue cell cancer." At the edges of the lesion, the gastric mucosa exhibits metaplastic changes that resemble small intestinal epithelium along with atypical hyperplastic alterations.

Before discussing the histological features mentioned above, a classification of carcinoma of the stomach would seem to be in order. A recent classification by Remine is based upon gross configuration and is as follows: Ulcerative polypoid, infiltrative, superficial and mucinous. A classification suggested by Lauren consists of two categories: an intestinal type and a diffuse type. Grading of the lesion has also been considered important by many people with Broder's grading system being one of the more popular. Some have considered this to be extremely important in predicting the prognosis of the lesion. Others such as Lauren, et al, have found that the Broder's classification was of little use, considering the fact that the lesions were often of mixed differentiation. Carcinomas of the stomach have also been staged using a modified Duke's classification ranging from A to B1, B2 and C. These describe progressively invasive lesions with A being the most superficial and C being one associated with metastases. All of the various classifications have made attempts to relate the lesion to the expected prognosis. For example, under Remine's classification the superficial carcinomas have an excellent prognosis whereas the diffusely infiltrative lesions have a rather poor prognosis. In Lauren, et al, classification, the intestinal types of carcinoma of the stomach have a considerably better prognosis than do the diffuse types.

A histological feature other than grading and histologic type that has a bearing on prognosis is judgement as to whether a lesion has a

pushing or an infiltrating margin. Carcinomas that have a pushing margin as demonstrated by this case a 5 year survival of patients can be expected to be approximately 50%. If the margins are infiltrative, the 5 year survival is around 12%. It has also been observed that if there is degeneration of tumor at the borders of the margin, this likewise is an indication of a better prognosis than if this alteration is absent. Many pathological factors are involved in the prognosis of carcinoma of the stomach. Of considerable importance of course, is the presence or absence of regional node involvement. Approximately 60% of resected gastric carcinomas will have positive lymph nodes. Of those that have negative lymph nodes, again 50% five year survival can be expected, and if the nodes are positive the survival rate is 20% or less. The size of the lesion, the location of the lesion in the stomach, whether the carcinoma has invaded through the gastric wall, whether it involves adjacent organs, whether the nerve sheaths and blood vessels are invaded, all are factors in prognosis of gastric carcinoma.

The ultimate in the determination of success of treatment depends upon comparison of treated, that is resected gastric carcinomas, with those patients who have non-resectable gastric carcinomas. In a rather large group of untreated gastric carcinomas, at the Mayo Clinic, it was noted that 90% of the patients were dead within 12 months of the diagnosis and only 2% were alive at 5 years, and 1% had 10 years. This can then be compared with resected lesions in which under favorable circumstances one can expect a 50% five year survival. Even in the patients who have positive lymph nodes as has been mentioned above, the 5 year survival is considerably better than in the non-treated group. Thus one can ascribe success to the surgical forms of therapy even though the success in a sense is rather limited.

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DECEMBER 8, 1968 - CASE NO. 4

ACCESSION 17490

MODERATOR'S DIAGNOSIS: ENDOMETRIOSIS OF SIGMOID

HISTORY:

The patient was a 42 year old woman admitted to the hospital because of intermittent constipation that was related to her menstrual periods. She was a gravida 3 para 3. There had been no history of melena or of blood in the stools. Dyspareunia or intermenstrual bleeding had not been noticed.

DISCUSSION:

The histological section demonstrates a characteristic pattern of endometriosis. The epithelial component closely resembles endometrial epithelium and is focally ciliated. Of importance is the demonstration of stroma, and in this slide stroma is easily seen. A few glands are dilated and contain fresh blood. The overlying colonic mucosa appears normal. Unless one is aware of the possibility of endometriosis involving large or small bowel, it is conceivable that a mistaken diagnosis of adenocarcinoma might be made on frozen section. However, on frozen section if one searches for it, the stromal component of endometriosis is often identifiable. The surgeon encountering endometriosis of the bowel may consider the lesion to be a neoplasm from its gross appearance as it frequently is firm, nodular, and the wall of the bowel appears to be thickened. The thickness of the bowel is due to hypertrophy of the smooth muscle in the presence of the endometriosis. If the endometrial component involves or abutts upon the muscularis mucosae, it will also demonstrate muscular hypertrophy. Involvement of the large bowel usually is serosal or in the muscularis propria. Less commonly are the submucosa or mucosa involved.

Endometriosis is common, occurring in 10-20% of women. In intestinal endometriosis the distribution is as follows: rectum and sigmoid, 72%; rectovaginal system, 13%; small intestine, 7%; cecum, 4%; and appendix, 3%. The lesion can be clinically suspected, as the patients often have rectal pain during the menstrual period and occasionally experience rectal bleeding. As one might expect, the lesion is found most commonly in women in the pre-menopausal ages, however, well-documented examples have been demonstrated in patients well beyond the menopause. An age range of 16 to 83 has been reported.

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DECEMBER 8, 1968 - CASE NO. 5

ACCESSION NO. 17491

MODERATOR'S DIAGNOSIS: BENIGN NON-CHROMAFFIN PARAGANGLIOMA

HISTORY:

The patient, a 56 year old woman, had experienced weakness and exertional dyspnea one month prior to admission to the hospital. A past family history and systemic review were not remarkable. Examination by her physician indicated that she was anemic and she was treated with oral iron. After two weeks no improvement was noted and she was given transfusions.

DISCUSSION:

The sections of the polypoid lesion of the duodenum demonstrate 2 histological components to the lesion. There are nests of cells that have an epithelial appearance. These are surrounded by a spindle cell stroma which in some areas is dominant and bears a resemblance to neurofibroma. The epithelial nests of cells resemble those seen in a carotid body tumor. Within some of these tumor units one may see large cells with rather dense eosinophilic cytoplasm that resemble ganglion cells. The spindle cells are not specific and bear some resemblance to smooth muscle although this could not be borne out with the Masson-trichrome stain. As can be seen, the lesion does involve the muscularis of the duodenum and in some areas the suggestion might be made that the lesion arises from the muscularis. However, with the two cell patterns present and a demonstration of neurites with the Bodian stain it was felt that this lesion represents a benign non-chromaffin paraganglioma of the duodenum. A fine review of this lesion was made by Taylor and Helwig in 1962. One of the questions that arises in a discussion of this lesion is the differentiation from ganglioneuroma. Similar lesions have been described in the literature as ganglioneuromas. However, in this lesion we do have the cell nests that resemble those in the tumors of the chemoreceptors and we have little evidence to support that these are ganglion cells. Another problem is the lack of evidence to support the fact that there is paraganglionic tissue in the duodenal area. However, in other species evidence of abdominal chemoreceptors related to the celiac and other sympathetic ganglia have been demonstrated.

Of the patients reported, the average age has been 52 years and the major symptom from this lesion has been gastrointestinal bleeding. Some of the patients have complained of pain suggestive of a peptic ulcer. Grossly most of the lesions have been pedunculated, however some of them have been described as being sessile. The lesions have ranged in size from 1 to 3 cm. Evidence of vascular, nerve or nodal involvement has not been seen, and these lesions have been considered to be benign.

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DECEMBER 8, 1968 - CASE NO. 6

ACCESSION NO. 17495

MODERATOR'S DIAGNOSIS: LEIOMYOSARCOMA OF SMALL INTESTINE

HISTORY:

This 46 year old woman was admitted to the Methodist Hospital on March 7, 1968 with a long complex history involving the following: In November 1966, patient had anemia with weakness. A duodenal ulceration was demonstrated on upper gastrointestinal series. The anemia responded to transfusions. In March 1967 an anemia workup revealed a normal upper G.I. series and a barium enema. The latter, however, disclosed diverticulosis. In June 1967, the patient began to experience left flank pain with a mass and fever which was presumed to be pyelonephritis. In February 1968, the anemia recurred; abdominal bloating, distension and epigastric pain developed which radiated to the back and an irregular right abdominal mass was perceived for the first time. A workup in another hospital included a percutaneous biopsy of the liver which disclosed malignancy, primary site undetermined. The past history revealed that the patient had a total abdominal hysterectomy and bilateral salpino-oophorectomy in 1955.

DISCUSSION:

This lesion has a rather unusal pattern in that it appears to be producing a large quantity of mucin, and indeed mucin is demonstrable with the Alcian blue stain. The cells of the neoplasm tend to form small cords and nests separated by the mucinous material. Under higher magnification the cells have a spindle appearance, and one may imagine that myofibrils are present. At the edge of the lesion where identifiable smooth muscle is seen, a transition between this and the neoplastic cells can be noted. The nuclei of the tumor cells are large, and nucleoli are reasonably prominent but mitotic figures are not common. Our first encounter with this case was by needle biopsy of the liver in which the small tumor strands were found with the cells being somewhat rounded. We were unable to make a specific diagnosis, but we suggested the possibility of a sarcoma, although carcinoma could not be ruled out.

Of the benign lesions of the small bowel, leiomyoma is listed by most authors as the most common. Of primary malignant lesions of the small bowel, adenocarcinoma is the most common with leiomyosarcomas as the second most common malignant tumor. They are most frequently seen in the jejunum and ileum. Patients with a leiomyosarcoma of the small bowel frequently present because of gastrointestinal bleeding. Signs and symptoms of intestinal obstruction secondary to intussuception are clinical manifestations of leiomyosarcoma. If these lesions metastasize, they generally go via the bloodstream, ending up in

the liver or the lungs. It has been stated by Starr and Dockerty that if these lesions are resectable that one can expect a 50% five year survival.

One of the problems in diagnosis of the smooth muscle tumors wherever they may appear is the distinction between the benign and the malignant. The major criterion that has been used other than evidence of metastases is the presence of mitotic activity. It is recognized that mitotic figures may be seen in what are considered to be benign or malignant smooth muscle tumors. The important observation seems to be the quantity of mitotic activity. In other organs this has been in the neighborhood of one mitotic figure/high power field. Whether the same criteria may be applied to small bowel smooth muscle tumors I am unable to say with certainty. In the case at hand, it is apparent that mitotic figures are few, but the patient does have a malignant lesion as evidenced by proved metastases to the liver.

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ACCESSION NO. 17494

MODERATOR'S DIAGNOSIS: HEMANGIOMA OF THE RECTUM

HISTORY:

The patient, a 45 year old man, was admitted to the hospital because of diarrhea and vomiting that had occurred one week prior to admission. This had left him feeling unusually weak and anorexic. For the past several years he had noted rectal bleeding. This had been intermittent and never severe. Three years ago he had had an unknown type of rectal operation for rectal bleeding. For a brief period of time after the operation the bleeding had stopped, but soon recurred again. His family history and systemic review were not remarkable.

DISCUSSION:

The sections of this lesion demonstrate a hemangioma in which all layers of the bowel wall and the perirectal fat are involved. Several of the large vessels are thrombosed, with focal calcification in a few of the thrombi. The major component of the lesion appears to be large venous spaces, some of which have a somewhat intricate pattern. This lesion may be classified as a cavernous hemangioma or perhaps better, a vascular malformation.

The finding of calcified or partly calcified thrombi in the vessels correlates with the roentgenographic findings of numerous phleboliths seen on the plain film of the abdomen. This roentgenographic finding is helpful in the diagnosis of hemangiomas of the intestinal tract. Patients with this lesion most often present because of bleeding which may have resulted in a rather severe anemia. In addition, the lesions may enlarge to cause narrowing of the bowel lumen and occasional instances of intussusception and volvulus of the large bowel have occurred on the basis of a hemangioma.

Hemangiomas are distributed throughout the gastrointestinal tract with those involving the large bowel representing approximately 15% of such lesions. In occasional cases, the hemangiomatous involvement may be diffuse or at least involve multiple sites. Also, hemangiomas may be associated with similar lesions in other organs, such as the liver, other parts of the gastrointestinal tract, or the skin. The treatment of these lesions depends considerably upon the extent and the site of involvement. Local excision is effective in small localized angiomas, whereas larger resections may be required to alleviate symptoms in the more diffuse hemangiomas.

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DECEMBER 8, 1968 - CASE NO. 8

ACCESSION NO. 17493

MODERATOR'S DIANGOSIS: GRANULAR CELL MYOBLASTOMA OF THE ESOPHAGUS

HISTORY:

The patient was a 42 year old woman who had a 2 weeks history of dysphagia. There were no other symptoms.

DISCUSSION:

This lesion is well known, although the location is rare. This is one of approximately six known cases of granular cell myoblastoma known to have occurred in the esophagus. Histologically this lesion lies dominantly in the muscularis although at one point it extends up to the epithelium at a point where the epithelium is superficially ulcerated. The cells that compose the lesion are characteristic of granular cell myoblastoma as seen at any other site. The cells appear to be densely acidophilic, granular with indistinct cytoplasmic boundaries and fairly uniform nuclei. The cells appear to infiltrate the muscularis.

Granular cell myoblastomas have been reported to occur in nearly all areas of the body, including all parts of the alimentary tract.

The histogenesis of this lesion remains an enigma, although there are indications that the lesion may take its origin from Schwann cells. Most observers at this time would feel that the lesion is not of muscular origin. An indication of the uncertainty of its origin is seen in the reference to it in the second edition of the AFIP fascicle, Tumors of the Soft Tissues, that lists the lesion as a "granular cell tumor". In our own studies of granular cell myoblastomas we have been unable to identify with certainty an origin from Schwann cells. In a few light microscopic sections of granular cell myoblastomas from the skin we have seen granular cells within nerve twigs. Whether this indicates an origin from the nerve or secondary involvement of the nerves remains unknown. In a study of the granules we found that they are not mitochondria although they did bear some resemblance to lysosomes. However, histochemical staining did not indicate in our studies that these granules were in fact lysosomes. They remain unidentified.

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DECEMBER 8, 1968 - CASE NO. 9

ACCESSION NO. 17492

MODERATOR'S DIAGNOSIS: DIFFUSE NODULAR HYPERPLASIA OF BRUNNER'S GLANDS

HISTORY:

This patient had a long history of gastrointestinal complaints, chiefly diarrhea, which she experienced since adolescence. On January 2, 1962, she presented with a history of onset of nausea, vomiting and deep seated epigastric pain. She was thought clinically to have a duodenal obstruction, at which time operation revealed diffusely enlarged, "rubbery, firm" pancreas with marked edema of the duodenum and antral portion of the stomach. Circa two years later she developed extrahepatic obstruction and an exploratory laparotomy revealed a circumferential enlargement of the 2nd and 3rd portion of the duodenum. The first three portions of the duodenum were resected.

DISCUSSION:

Histologically and grossly this lesion demonstrates a diffuse hyperplasia of Brunner's glands. The glands are confined to the submucosal area of the section and are fairly uniform in their appearance as are the individual cells. There seems to be no indication that this is a malignant neoplasm. Tumors of Brunner's gland origin are uncommon. They have been divided into various morphological categories by Feyrter: circumscribed nodular hyperplasia, diffuse nodular hyperplasia, and polypoid lesions. Of these morphological varieties, the polypoid is the most commonly seen. Apparently, malignant neoplasms arising from Brunner glands are rare if at all existent. Two examples have been reported, and these are considered to be of uncertain origin.

The most common symptoms associated with lesions of Brunner's glands have been bleeding and obstruction. Associated with obstruction has been intussuception of duodenum into jejunum as a result of a polypoid Brunner's gland adenoma. Patients may also complain of epigastric distress, vomiting, occasional weight loss, and diarrhea.

The function of Brunner glands remains somewhat obscure, although it has been demonstrated that the glands do secrete an alkaline fluid containing mucin. It is felt that the main function is protection of the duodenal epithelium from the effect of the gastric acid.

Whether the Brunner gland lesions are true neoplasms or represent hamartomas is questionable. Many observers feel they represent hamartomatous lesions on the basis of the findings that can be demonstrated in the present case, that is thin arms of smooth muscle wending their way through the hyperplastic glands. This has been considered analagous to the alterations seen in Peutz-Jegher's polyps. Also in this case, we find Paneth cells

in the Brunner's gland. This has also been considered an indication of a hamartomatous origin in that Paneth cells are normally found at the bottom of the duodenal crypts and as Brunner's glands appear in the 6th month of fetal life, as massive epithelial ingrowths in the duodenal crypts, it is felt that this adds weight to the theory of their being hamartomatous.

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DECEMBER 8, 1968 - CASE NO. 10

ACCESSION NO. 15299

MODERATOR'S DIAGNOSIS: DEGENERATING LEIOMYOMA? LEIOMYOBLASTOMA?

HISTORY:

Patient had been well until October 1966 when she had onset of gastric difficulties, postprandial pain in epigastric region and gradual increase in size of her abdomen. Mother died of gastric carcinoma and also had carcinoma of the breast. Gastro-intestinal series revealed prepyloric gastric lesion, therefore she was admitted to the hospital on November 20, 1966 for an exploratory laparotomy. Patient had had no endometrial problems, no bleeding and pap smear was negative 4 months ago.

DISCUSSION:

The sections present a rather interesting lesion. Grossly the lesion is described as an intramural mass of the stomach in a patient who also had disseminated endometrial carcinoma. Thus the first histological problem would be to decide whether this could represent adenocarcinoma metastatic to the stomach. Not having seen the slides from the endometrial carcinoma, one would surmise that it was considerably different from the lesion at hand. Interspersed, one finds cells in a rather myxoid background. These cells are not particularly pleomorphic, and mitotic figures are rare. In several areas one is able to demonstrate what appears to be a transition between recognizable smooth muscle cells and the lesional cells. Most of the cells in the lesion are not spindled; in some areas the cells have a rounded appearance with a clear zone about the nucleus. This clear zone may actually represent a colorless cytoplasm. An epithelial component in this lesion is not recognizable.

This lesion was submitted as a hamartoma of the stomach. The few references that we have been able to find concerning such a lesion of the stomach have indicated that hamartomas are generally combinations of smooth muscle and an epithelial element; these are most probably a heterotopic pancreas. Rare teratomas composed of varied elements have been recorded. Using this little information as a straw, I would suggest that this lesion does not represent a hamartoma. Our feelings concerning this lesion have revolved around a leiomyoblastoma or degenerating leiomyoma. It is true that the nuclei and cells of this lesion are not particularly bizarre. However, leiomyoblastomas do have a variety of patterns, and the pattern that is seen here may represent one of those in which the cells are not bizarre. Generally the lesions are composed entirely of the abnormal smooth muscle cells, but there have been descriptions made which indicate that one may find small streamers of lesional cells in the surrounding smooth muscle. Perhaps this is such a case.

The gross configuation of this lesion would compare favorably with those described for other leiomyoblastomas, that is they are intramural lesions and resemble to some degree leiomyomas. They may or may not be ulcerated. Also of interest in these lesions is that a variety of histological diagnoses have been made on the basis of the peculiar patterns. These diagnoses have ranged from chondroma to carcinoma to a wide variety of sarcomatous lesions. In the majority of instances leiomyoblastomas are benign in their behavior. Occasional lesions have been described with metastases and histologically these have not differed from the others except that there has been an increased mitotic rate. In Stout's review of 69 leiomyoblastomas, 2 of the patients developed metastases. Thus it was seen that this is not an entirely benign lesion, and the prognosis in most instances must be guarded, especially when the mitotic rate is increased.

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DECEMBER 8, 1968 - CASE NO. 11

ACCESSION NO. 17363

MODERATOR'S DIAGNOSIS: INFLAMMATORY FIBROID POLYP

HISTORY:

This patient was admitted to the hospital on January 17, 1968, with the complaints of intermittent abdominal pain and vomiting for approximately six weeks duration. Recurring attacks of abdominal distention had been relieved by vomiting and rest in bed. Attacks had become more severe and there had been a loss of weight.

DISCUSSION:

Histologically, this polypoid lesion of the ileum is known by a number of names: inflammatory fibroid polyp, eosinophilic gastroenteritis, eosinophilic infiltration of the gastrointestinal tract, eosinophilic granuloma, inflammatory pseudotumors. The lesion that we have for study is characterized by its polypoid nature and associated with surface ulceration. The overlying small bowel mucosa is abnormal in that it is heavily infiltrated with eosinophils and appears to be atrophic. The major body of the lesion lies in the submucosa, and these appear to be isolated bundles of smooth muscle within it. The background cells seem to be fibroblasts and there are numerous small vessels. The dominant inflammatory cell is the eosinophil, with a scattering of other inflammatory cells. Multinucleated cells are not seen. An occasional small vessel has eosinophils within its walls. Vascular necrosis is not observed.

The etiology of lesions of this type remains unknown. There have been numerous areas of speculation, including foreign body reaction, local reaction of the gastrointestinal tract to allergens, reaction to parasites, fungi or bacteria. A number of the patients do have an accompanying eosinophilia, particularly those that have a diffuse eosinophilic gastroenteritis. Histologically in a few of the cases, there has been an associated vasculitis, and occasionally vascular necrosis. This, accompained by an occasional history of allergy, has suggested that allergy forms the basis for a number of these lesions, if not for most of them.

A classification of this lesion has been given by Ureles and is as follows:

Class I - Diffuse eosinophilic gastroenteritis

Group A - Polyenteric
Group B - Monoenteric
Group C - Regional

Class II - Circumscribed eosinophilic infiltrative granuloma

Group A - Regional
Group B - Polypoid

The patients in each of the two major classifications are generally in different age groups. In Class I, a number of the patients have a history of an allergy. Except for rare examples this lesion is seen in adults, although a similar lesion has been described in a 2 year old child with the findings of intussuception.

Concerning the lesion in the seminar set, there has been a suggestion that this fibroid type of polyp is neurogenic in nature. In a histological study, Goldman and Friedman felt that the fibroid polyp of the stomach demonstrated neural proliferations similar to the appendicial neural hyperplasia.

Treatment of this lesion, particularly of the Class I or diffuse variety, has been either surgical or with corticosteroids. Remissions have been successfully induced with the use of corticosteroids. With the localized form or the Class II type of lesion, surgical removal has proved to be definitive.

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DECEMBER 8, 1968 - CASE NO. 12

ACCESSION NO. 11917

MODERATOR'S DIAGNOSIS: MALIGNANT LYMPHOMA OF THE INTESTINES

Small cleaved follicle pattern
Poorly differentiated lymphocytic lymphoma

HISTORY:

The terminal admission for this 61 year old Caucasian male was on October 20, 1961, when he was admitted for rectal bleeding of several months' duration, culminating in an average cup full of bright red blood being passed with each bowel movement. There was a questionable recent weight loss.

DISCUSSION:

These four cases present various configurations of intestinal lymphomas. The first case is unusual in that there are multiple polypoid lesions of the small and large bowels. Histologically the lesions of this case appear to be well differentiated lymphocytic lymphoma. One of the sections has a nodular pattern, still maintaining its well differentiated characteristics. Separate foci of involvement of the intestinal tract in malignant lymphoma is common, seen in approximately 10% of cases. However, multiple polypoid lesions as demonstrated in this patient's intestine are unusual, but have been described.

Grossly the other three lesions present features which are often seen in malignant lymphomas of the intestines, that is they are commonly ulcerated and associated with a thickened bowel wall. One of the lesions circumscribed the bowel wall; the others were associated with ulcerations. In Case 21 we have an example of a polypoid lymphoma associated with ulcerated lymphomas in the same segment of bowel. It is assumed that the clinical manifestations in these patients ruled out the possibilty of the intestinal lymphomas being part of a disseminated process. It is known that approximately 35% of patients dying of malignant lymphoma will have involvement of the gastrointestinal tract. Thus it is important that patients with an apparently isolated gastrointestinal lymphoma be examined carefully for other evidences of lymphoma or leukemia. Histologically the lesions in the multiple polypoid lymphomas of the bowel demonstrate two histological patterns: 1) a well differentiated lymphosarcoma; and 2) a nodular lymphoma of the well differentiated lymphocytic type. Case 17 illustrates a poorly differentiated lymphocytic lymphoma that involves the full thickness of the bowel wall.

Two patterns are seen in Case 21, one being a malignant lymphoma of the histiocytic type (reticulum cell sarcoma) blending into a second pattern resembling Hodgkin's disease. Considering that the major portion of the tumor tissue on the slide appears to be a reticulum cell sarcoma, one wonders if the pleomorphic areas are not a variety of

reticulum cell sarcoma. It is true that a number of the cells bear a close resemblance to Reed-Sternberg cells lending a difficult histological decision. Considering what is present, however, I would wonder if this isn't a malignant lymphoma of the pleomorphic histiocytic type that has been described by Rappaport (AFIP Fascicle). Areas such as are seen in this slide have been designated as Hodgkin's sarcoma. This indicates the difficulty of differentiating Hodgkin's disease from this pleomorphic variety of reticulum cell sarcoma. Case 22 has the histological features of a Hodgkin's disease. Several characteristic Reed-Sternberg cells are noted. The surface of the lesion is ulcerated, resulting in numerous inflammatory cells in the superficial area of the lesion. Deeper in the lesion one finds a mixed inflammatory infiltrate with numerous eosinophils. A background of neoplastic reticuloendothelial cells mixed with lymphocytes is noted.

Of the malignant lymphomas of the gastrointestinal tract, lymphosarcoma and reticulum cell sarcoma are the most common varieties. Hodgkin's disease is seen less frequently, and the nodular lymphomas are considered rare. In most series, lymphomas of the gastrointestinal tract, are infrequent at either extremity of the tract, that is uncommon in the stomach and large bowel when compared to the small bowel. The lymphomas of the stomach are more common than are those of the large bowel. In the small bowel lymphomas are less frequent in the upper small intestine, becoming more frequent towards the distal portions.

Although there is not a hard and fast correlation between the histological type of malignant lymphoma and prognosis, there is a generally accepted observation that patients having reticulum cell sarcoma do rather poorly compared to those that have a well differentiated lymphosarcoma. The overall treatment results are somewhat varied; those of the stomach have already been mentioned. In the small bowel and large bowel they vary from 0% in some series to as high as 60+% in others. In a recent review of large intestinal lymphomas, it was noted that if lymphoma involves the large intestine as part of a disseminated disease, only a rare patient survives 5 years. In contrast, those patients with lymphoma confined to the large intestine have a 55% chance for 5 year survival and a 50% chance for a 10 year survival. It has been observed that if the lymph nodes are demonstrated to be positive for lymphoma, the survival rate is decreased by about 50%.

One lesion occurring in the rectum that might be confused with lymphosarcoma is the lymphoid polyp or as some refer to them, pseudolymphomas. These lesions may appear as polypoid masses, and if large may be confused with lymphosarcoma. Histologically the features that distinguish these from malignant lymphoma are similar to those discussed under lymphoid pseudotumors of the stomach. Follow-up of lymphoid

polyps indicates that these lesions do not transform into lymphosarcoma.

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Lukes, Collins Non-Hodgkin's Lymphomas
Brit J of Med 1972

DECEMBER 8, 1968 - CASE NO. 13

ACCESSION NO. 17396

MODERATOR'S DIAGNOSIS: SQUAMOUS CELL CARCINOMA OF THE STOMACH

HISTORY:

The patient was admitted to the hospital on April 1, 1968 for a multitude of varied gastrointestinal complaints, including weight loss, anorexia, abdominal pain and abdominal distention, present for at least the past six months. An outside upper gastrointestinal series showed a probable infiltrating gastric neoplasm extending to the distal end of the esophagus.

DISCUSSION:

The slides are an example of an unusual and rare carcinoma of the stomach. This appears to be a pure squamous cell carcinoma of the stomach. Many pathologists have been wary of the diagnosis of squamous cell carcinoma, considering such lesions to be invasive from the esophagus. But, in cases with the lesion located away from the esophagus, say at the pylorus, primary squamous cell carcinoma is acceptable. In the event the lesion is associated with pancreatic involvement, again one has to consider that squamous carcinomas or adenoacanthomas of the pancreas do occur, and thus the possibility of invasion from a pancreatic lesion has to be considered. With these considerations a few acceptable cases of gastric squamous cell carcinoma have been reported. The majority have been located in the distal half of the stomach, with an occasional one in the proximal half. The same is true of the adenoacanthomas of the stomach. Grossly, the lesions are similar to and indistinguishable from adenocarcinomas of the stomach. But histologically one finds an easily recognizable squamous carcinoma and, in the case of adenoacanthoma, a glandular component. Keratinizing masses and individual cell keratinization are seen along with the recognizable intercellular bridges. In the mixed lesions, one may find mucin-secreting cells, glands, or signet ring cells.

One might wonder about the origin of squamous cell carcinoma of the stomach. Experimentally these lesions have been produced by various carcinogenic agents. In the human, squamous islands have been described along the lesser curvature, these islands being separated from the esophageal mucosa. In addition, occasional instances of squamous metaplasia of the epithelium have been described. Thus it might be that squamous carcinomas originate from either metaplasia or ectopic squamous epithelium. Rare squamous papillomas of the stomach have been described, one in which there was massive papillomatosis of the stomach; whether these rare lesions undergo malignant transformation is not known.

Clinically these lesions present symptoms that are similar to those of adenocarcinoma of the stomach. In the recently reported series of Boswell and Helwig, the patient's age at which the lesions were diagnosed was slightly younger than with adenocarcinoma of the stomach. In the follow-up it appears that the results of treatment are similar to those of other carcinomas of the stomach.

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DECEMBER 8, 1968 - CASE NO. 14
CASE NO. 15
ACCESSION NO. 10882

#14

MODERATOR'S DIAGNOSIS: LYMPHOID PSEUDOTUMOR AND MALIGNANT LYMPHOMA OF THE STOMACH - Immunoblastic sarcoma (IBS) - ?plasmacytoid vs large nonCleaved follicular cell lymphoma - Diffuse Histiocytic Lymphoma (Rappaport)

HISTORY:

The onset of symptoms of vomiting and epigastric distress occurred in June 1959. On June 1, 1959, an upper gastrointestinal series revealed a filling defect in the distal stomach. The patient improved on ulcer management, and two days later an upper gastrointestinal series was interpreted as showing marked improvement. One month after the first gastrointestinal series the films were reported "normal." The patient had no more symptoms of specific nature, but complained that "he just felt that his stomach was not right." In March, 1960, there was vomiting but no pain. An upper gastrointestinal series revealed a filling defect similar to that seen in June 1959. There was no decided clinical improvement after this, but in two or three weeks a repeat gastrointestinal series revealed an area suspicious of a polyp of the antrum of the greater curvature near the pylorus.

DISCUSSION:

Histologically, the sections of the lesion in Case 14 have features that suggest that this lesion may best be classified as a lymphoid pseudotumor. The major histological feature is that of germinal centers in an otherwise rather monotonous lymphoid infiltration of the mucosa and submucosa. The important pathological problem in this case is the distinction between a benign and a malignant tumor of lymphoid origin. Several features have been described that are considered to be helpful; among them are the demonstration of secondary centers in the lymphoid tissue, the polymorphic infiltrate which usually includes plasma cells and eosinophils, and the association of scar tissue with the lymphoid infiltration. This case has the first two features, but scar tissue is rather minimal. The lymphoid component of this lesion appears to be composed of cells that are for-the-most-part mature lymphocytes. If we contrast this lesion with the slides from Case 15, we notice a striking difference between the major cell components. In the latter case, the cells are immature, considerably larger than those in Case 14, and impart a rather monotonous pattern to the gastric wall. There is a mixed inflammatory infiltrate in Case 15; this may well be due to the fact that surface ulceration is present. There is considerably more scarring in the slides from Case 15 that in those of Case 14. This may well be related to the operative procedure that was carried out some 8 years before. In Case 15, we see that the lesional tissue involves the full thickness of the gastric wall; this in itself is not specific for a malignant neoplasm, as full thickness involvement of the gastric wall of pseudo tumors may be seen. The second lesion in this patient is a malignant lymphoma, a reticulum cell sarcoma.

From information that I have, the slides from Case 14 were seen by a number of pathologists, the majority of whom consider it to be a malignant lymphoma. Distinction between lymphoma and pseudotumor is difficult to make in many instances. In this case, there are several areas in which there is a fairly pure infiltration of lymphocytes. This could well lend itself to a diagnosis of lymphosarcoma. However, the presence of distinct secondary centers within the lesional tissue plus the mixed inflammatory infiltrate should lead one to consider strongly the possibility of a lymphoid pseudotumor. The interesting problem in this case is the appearance of the second lesion which to me is a malignant lymphoma. Could this have arisen on the basis of a pre-existing benign lymphoid tumor? This would be one possibility; another would be that the first lesion was indeed a lymphoma and over the period of years had gradually evolved into one that is obviously so. A third possibility would be that this patient has 2 lesions; one benign 8 years previously, and in the interim a second lesion, a malignant one has appeared. My own choice of the possibilities would be the third.

Lymphoid pseudotumors clinically, radiographically and pathologically mimic malignant lymphomas of the stomach. It is only with careful histologic examination that one is able to delineate these two lesions. In general, patients who have lymphoid pseudotumors are younger than those that have a primary lymphoma of the stomach. The symptoms may be entirely similar and the gross characteristics may be very much the same. Primary lymphomas of the stomach are nearly always ulcerated whereas some of the pseudotumors may not be. Gastroscopically and radiographically the pseudotumors are often regarded as carcinomas of the stomach. Grossly, lymphomas of the stomach are frequently divided into four patterns: ulcerative, polypoid, diffuse, and giant rugal hypertrophy. The majority of primary lymphomas of the stomach involve the distal one-half. This same is true of lymphoid pseudotumors. The majority of primary lymphomas of the stomach are lymphosarcomas with a lesser number being reticulum cell sarcoma and rarely Hodgkin's disease.

In previous years it has been regarded that the prognosis of primary lymphosarcoma of the stomach was good, certainly exceeding that of carcinoma of the stomach. But in recent years the reviews in which the lymphoid pseudotumors have been excluded, it has been observed that the prognosis is rather poor, hardly exceeding that which would be expected for carcinoma of the stomach. In fact, in Jacob's series he had one survivor among 15 cases, all of which were histologically typed as reticulum cell sarcoma. Patients who have had a diagnosis of lymphoid pseudotumor have not died of this disease, or of lymphoma. Thus the clinical behavior of the lesion lends credence to the histological designation of this as a benign lesion.

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ACCESSION NO. 10882

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DECEMBER 8, 1968 - CASE NO.16

ACCESSION NO. 17581

MODERATOR'S DIAGNOSIS: MALIGNANT MELANOMA IN THE SMALL BOWEL

HISTORY:

The patient was in the usual state of health until approximately 2 months ago at which time he began to feel progressively fatigued. He sought the services of a physician approximately six weeks ago.

DISCUSSION:

This lesion has all the histological characteristics of a heavily pigmented malignant melanoma. The surface is ulcerated and the lesion appears to be permeating the mucosa, and the mucosal and submucosal lymphatic channels. The entire thickness of the bowel wall is involved in one area.

The main problem in this case is whether one can arrive at a decision as to whether the lesion is primary or metastatic. For all practical purposes most observers consider that a lesion such as this is metastatic unless proved otherwise. If primary melanomas do arise in the gastrointestinal tract, it must be a rare event. A few such cases have been reported in JAMA, primary malignant melanoma of the stomach occurred in a patient who was described as having numerous nevi in all skin areas of the body. An axillary node contained metastatic melanoma. The lesion was diagnosed by gastroscopic biopsy, the patient died, and an autopsy was not obtained. Because a malignant melanoma is not found on the skin does not necessarily exclude skin as a primary site. It has been demonstrated that malignant melanomas of the skin may undergo spontaneous regression. This phenomenon may account for some of the malignant melanomas that are said to arise in unusual locations. Malignant melanomas have been reported to involve the rectum, but the question arises, was the primary site in the anus? If melanoma does occur primarily in the intestinal tract, then one must wonder about the origin of the cells. Some have suggested the transformation of mucous glands into melanocytes. This has been described in the oral cavity. Others have suggested that there is a melanotic transformation of the nerve cells, for example those of Meissner's or Auerbach's plexi in the intestinal tract.

Metastatic tumors to the small intestine are uncommon, making up just a little more than 1% of metastases. However, of the metastases to the small intestine, those arising from melanomas make up approximately 25%. Thus in this case it is not possible to be dogmatic in stating that the lesion is primary or metastatic; however, the probabilities are high that this represents a metastatic melanoma to the small bowel.

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DECEMBER 8, 1968 - CASE NO. 17

ACCESSION NO. 15508

MODERATOR'S DIAGNOSIS: MALIGNANT LYMPHOMA OF THE INTESTINES

Small cleaved follicle center cell lymphoma
poorly differentiated lymphocytic

HISTORY:

Patient was in good health all of her life until the first part of 1966 at which time she noted the onset of vague, right lower quadrant pain, which she described as a "pulling sensation." This symptom persisted for approximately one year, during which time there was no associated anorexia, weight loss, diarrhea, melena, nausea, or vomiting. On January 3, 1967 the patient presented herself to her physician with more severe pain again localized in the right lower quadrant, and which now radiated to the right subscapular area and was associated with nausea and occasional episodes of vomiting. She was finally admitted to the hospital in February 1967.

DISCUSSION:

These four cases present various configurations of intestinal lymphomas. The first case is unusal in that there are multiple polypoid lesions of the small and large bowels. Histologically the lesions of this case appear to be well differentiated lymphocytic lymphoma. One of the sections has a nodular pattern, still maintaining its well differentiated characteristics. Separate foci of involvement of the intestinal tract in malignant lymphoma is common, seen in approximately 10% of cases. However, multiple polypoid lesions as demonstrated in this patient's intestine are unusual, but have been described.

Grossly the other three lesions present features which are often seen in malignant lymphomas of the intestines, that is they are commonly ulcerated and associated with a thickened bowel wall. One of the lesions circumscribed the bowel wall; the others were associated with ulcerations. In Case 21 we have an example of a polypoid lymphoma associated with ulcerated lymphomas in the same segment of bowel. It is assumed that the clinical manifestations in these patients ruled out the possibilty of the intestinal lymphomas being part of a disseminated process. It is known that approximately 35% of patients dying of malignant lymphoma will have involvement of the gastrointestinal tract. Thus it is important that patients with an apparently isolated gastrointestinal lymphoma be examined carefully for other evidences of lymphoma or leukemia. Histologically the lesions in the multiple polypoid lymphomas of the bowel demonstrate two histological patterns: 1) a well differentiated lymphosarcoma; and 2) a nodular lymphoma of the well differentiated lymphocytic type. Case 17 illustrates a poorly differentiated lymphocytic lymphoma that involves the full thickness of the bowel wall.

Two patterns are seen in Case 21, one being a malignant lymphoma

of the histiocytic type (reticulum cell sarcoma) blending into a second pattern resembling Hodgkin's disease. Considering that the major portion of the tumor tissue on the slide appears to be a reticulum cell sarcoma, one wonders if the pleomorphic areas are not a variety of reticulum cell sarcoma. It is true that a number of the cells bear a close resemblance to Reed-Sternberg cells lending a difficult histological decision. Considering what is present, however, I would wonder if this isn't a malignant lymphoma of the pleomorphic histiocytic type that has been described by Rappaport (AFIP Fascicle). Areas such as are seen in this slide have been designated as Hodgkin's sarcoma. This indicates the difficulty of differentiating Hodgkin's disease from this pleomorphic variety of reticulum cell sarcoma. Case 22 has the histological features of a Hodgkin's disease. Several characteristic Reed-Sternberg cells are noted. The surface of the lesion is ulcerated, resulting in numerous inflammatory cells in the superficial area of the lesion. Deeper in the lesion one finds a mixed inflammatory infiltrate with numerous eosinophils. A background of neoplastic reticuloendothelial cells mixed with lymphocytes is noted.

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Although there is not a hard and fast correlation between the histological type of malignant lymphoma and prognosis, there is a generally accepted observation that patients having reticulum cell sarcoma do rather poorly compared to those that have a well differentiated lymphosarcoma. The overall treatment results are somewhat varied; those of the stomach have already been mentioned. In the small bowel and large bowel they vary from 0% in some series to as high as 60+% in others. In a recent review of large intestinal lymphomas, it was noted that if lymphoma involves the large intestine as part of a disseminated disease, only a rare patient survives 5 years. In contrast, those patients with lymphoma confined to the large intestine have a 55% chance for 5 year survival and a 50% chance for a 10 year survival. It has been observed that if the lymph nodes are demonstrated to be positive for lymphoma, the survival rate is decreased by about 50%.

One lesion occurring in the rectum that might be confused with

lymphosarcoma is the lymphoid polyp or as some refer to them, pseudolymphomas. These lesions may appear as polypoid masses, and if large may be confused with lymphosarcoma. Histologically the features that distinguish these from malignant lymphoma are similar to those discussed under lymphoid pseudotumors of the stomach. Follow-up of lymphoid polyps indicates that these lesions do not transform into lymphosarcoma.

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DECEMBER 8, 1968 - CASE NO. 18

ACCESSION NO. 15506

MODERATOR'S DIAGNOSIS: ADENOCARCINOMA OF THE LARGE BOWEL AND A FIBROUS TUMOR OF THE MESENTERY.

HISTORY:

This 30 year old Caucasian male had been in good health all of his life with the exception of a partial colectomy which was performed in 1962 because of congenital polyposis. On March 9, 1967, the patient became ill with lower abdominal pain, which later became associated with fever, chills, and general malaise as well as occasional episodes of vomiting. The pain became more generalized and increased in severity, and the episodes of vomiting became frequent. There was no associated diarrhea, melena, anorexia or weight loss. Because of these symptoms, the patient was admitted to the hospital on March 12, 1967 with a fever of 102°.

DISCUSSION:

From the slides studied, the patient has two lesions, one an adenocarcinoma and the second a fibrous lesion of the mesentery. The carcinoma of the colon is fairly well differentiated with an infiltrative margin and a few mucinous areas. It does not differ from ordinary carcinomas of the large bowel. With a history of having a previous bowel resection for "congenital polyposis", and the fibrous lesions of the mesentery, one might consider the possibility of Gardner's syndrome. Only one of the small fragments of colonic mucosa attached to the carcinoma shows an atypical proliferative change of the glands. This area could represent an adenomatous polyp. Although most of the polyps described in Gardner's syndrome are considered to be adenomatous, one wonders if they differ from solitary adenomatous polyps. Our experience in examining numerous polyps and areas of normal-appearing colonic mucosa from a colon from a patient with familial polyposis indicated differences between solitary adenomatous polyps and polyposis. Grossly, many of them had multiple heads and presented small buddings from their stalks. Histologically an outstanding feature was the minute foci of epithelial alterations in what appeared to be the normal colonic mucosa. Occasionally individual colonic glands exhibited nuclear alterations that were abnormal. Whether these same findings would pertain to all cases of familial polyposis of Gardner's syndrome, we cannot say.

The mesenteric lesion does not appear to be an example of retractile mesenteritis. If it is, it must represent a healed phase as the lesion appears to be purely fibrous. In fact, it more closely resembles fibromatosis. In cases of retractile mesenteritis or mesenteric panniculitis, one finds evidence of damage to fat associated with an inflammatory infiltration along with fibrosis. The evidence of damaged fat is not present in the lesion that we have. It is conceivable that this

fibrous lesion does represent a healed inflammatory process, perhaps following the first abdominal operation. With the previous history of polyposis of the large bowel, the fibrous lesion of the mesentery and the adenocarcinoma, one might consider this a case of Gardner's syndrome. In addition to colonic polyps, such lesions as sebaceous cysts, osteomas, and various fibrous tumors have been described.

A major significance of Gardner's syndrome is the risk of developing a denocarcinoma of the bowel. To date this represents approximately 50% of the reported cases. Gardner's syndrome is considered to be a hereditary defect, being a non sex-linked dominant gene that theoretically could result in 50% of the offspring of an affected person having the syndrome of polyposis and the soft tissue or bony lesions.

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DECEMBER 8, 1968 - CASE NO. 19

ACCESSION NO. 17435

MODERATOR'S DIAGNOSIS: DIVERTICULUM AND POOLS OF MUCIN

HISTORY:

This 63 year-old single man was well until approximately 2 months ago when he began to notice a change of bowel habits toward loose frequent stools with some feeling of incomplete evacuation. On three different occasions he noted some bright red bleeding mixed in with his stool. He has had no heavy bleeding, or any other evidence of bowel disorder. His weight has remained relatively stable as has his appetite.

DISCUSSION:

Histologically the lesion presents as pools of mucin in the pericolonic tissues. The mucosa appears to be intact and does not demonstrate any unusual epithelial abnormalities. In one section there appears to be a wall of a diverticulum, as mucosa seems to descend through the muscularis propria. The mucinous masses are surrounded by connective tissue; there is no evident epithelial lining of these. A scattering of inflammatory cells are noted throughout and at the edge of the lesion's foci of more intense chronic inflammation. Occasional multinucleated giant cells are present and unidentifiable foreign material is seen. The muscularis propria was described as being hypertrophic on gross examination. This fits with the presence of diverticuli in this segment of the colon.

The pathological problem here lies in the proper identification of these mucinous masses. Do they represent a mucinous carcinoma, a colitis cystica profunda, or mucin that has been spilled from a diverticulum? Of the three possibilities, assuming that the lesion is primary at this site, the first seems the most unlikely, in that in the examination of four separate blocks, neoplastic epithelial cells were not found. In the mucinous carcinomas that we have seen, we have found neoplastic cells associated with the mucin. It is possible that one might find isolated pools of mucin in which neoplastic epithelial cells were not found. In the mucinous carcinomas that we have seen, we have found neoplastic cells associated with the mucin. It is possible that one might find isolated pools of mucin in which neoplastic cells would not be found, but with further sectioning these cells would be demonstrated. Colitis cystica profunda remains a possibility, however the majority of these lesions that have been solitary have involved the rectum. In addition, although one may find pools of mucin without an epithelial component, most are associated with an epithelial component that is non-neoplastic. The majority of the cysts in this disease lie in the

bowel wall. This leaves the last possibility that a diverticulum may have been obstructed, resulting in a mucocele. Since the mucin lies near what appears to be a diverticulum and is located in the extra colonic tissues, this latter possibility seems to be reasonable although evidence of residual mucocele is not seen. Thus unless other histological features have been discovered in further sectioning of this lesion, it would seem that this represents extravasation of mucin, presumably from a pre-existent diverticulum.

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DECEMBER 8, 1968 ACCESSION NO. 17559 (20)

MODERATOR'S DIAGNOSIS: TRANSITIONAL CLOACOGENIC CARCINOMA (BASALOID) OF THE ANUS

HISTORY:

Less than one month prior to admission to the hospital, the patient noted anal pain while having a bowel movement. Shorly thereafter, she noted slight bleeding with her bowel movements. She gave a history of constipation "all her life."

DISCUSSION:

Histologically this lesion involves the anal verge, as anal skin is evident on the sections. The lesion has a basal cell carcinoma appearance. The deep margins of the lesion are rounded, suggesting a pushing margin. In focal areas carcinoma-in-situ is noted and in part the lesion takes origin from the surface epithelium. The periphery of the tumor demonstrates peripheral palisading of the nuclei, imparting the appearance of basal cell carcinoma and thus the designation of basaloid carcinoma of the anus. In rare areas of this lesion, one is able to deomonstrate small foci of keratin. The lesional tissue displays a rather uniform cellularity without much pleomorphism. Mitotic figures are fairly common. The lesion must be distinguished from basal cell carcinoma; basal cell carcinomas occur in the perianal skin or at the anal verge. Basaloid carcinomas are located in the canal.

These lesions have been described under an array of names such as basal cell carcinoma, muco-epidermoid carcinoma, anal duct carcinoma, and cloacogenic carcinoma. The presently most popular names seem to be transitional cell carcinoma of the anus or transitional cloacogenic carcinoma of the anus. These tumors may arise at any site in the anal canal. Occasional lesions of the rectum have been ascribed to the fact that the anal ducts often ramify cephalad beneath the rectal mucosa. There are several histological features that have a bearing on the outcome of treatment. Among these features are the degree of differentiation; with the lesions that are most poorly differentiated having a very bad prognosis. These lesions closely resemble oat cell carcinomas of the lung. Small lesions, that is those that are less than 2 cm. in diameter, have a good prognosis when compared to the larger lesions. Those lesions having a pushing margin and particularly those with a heavy inflammatory infiltration about their advancing margins have a better prognosis than those without. Also of importance is the presence or absence of vascular invasion and the presence or absence of involvement of lymph nodes. The overall survival rate in the treatment of these lesions is near 50%. The survival varied according to the above mentioned gross and histologic criteria.

Of interest in these patients, clinically is the fact that 2/3 of these patients are women, whereas in squamous cell carcinoma although in some series women dominate, in most the sex distribution is nearly equal. Clinically these patients have symptoms that are similar to those of rectal carcinoma with bleeding being one of the commonest. Local recurrence has plagued a number of these patients, roughly 26% of those that have been treated have had local recurrence, usually in the perineum. Metastases are found most commonly in the liver, lungs, bones and lymph nodes.

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DECEMBER 8, 1968 - CASE NO. 21

ACCESSION NO. 17598

MODERATOR'S DIAGNOSIS: MALIGNANT LYMPHOMA OF THE INTESTINES

HISTORY:

This 67 year old Caucasian male was admitted to the hospital on April 4, 1967 having noted the onset of sharp left lower quadrant pain on the morning of admission which became diffuse with the development of chills and fever. He had been hospitalized previously in February 1967 because of lower abdominal cramps, weight loss and fever of unknown origin. The patient was treated conservatively initially with I.V. fluids, bed rest, nasogastric intubation, and chloromycetin. The abdominal symptoms subsided. It was felt that the most likely cause of the illness was an intra-abdominal neoplasm.

DISCUSSION:

These four cases present various configurations of intestinal lymphomas. The first case is unusual in that there are multiple polypoid lesions of the small and large bowels. Histologically the lesions of this case appear to be well differentiated lymphocytic lymphoma. One of the sections has a nodular pattern, still maintaining its well differentiated characteristics. Separate foci of involvement of the intestinal tract in malignant lymphoma is common, seen in approximately 10% of cases. However, multiple polypoid lesions as demonstrated in this patient's intestine are unusual, but have been described.

Grossly the other three lesions present features which are often seen in malignant lymphomas of the intestines, that is they are commonly ulcerated and associated with a thickened bowel wall. One of the lesions circumscribed the bowel wall; the others were associated with ulcerations. In Case 21 we have an example of a polypoid lymphoma associated with ulcerated lymphomas in the same segment of bowel. It is assumed that the clinical manifestations in these patients ruled out the possibilty of the intestinal lymphomas being part of a disseminated process. It is known that approximately 35% of patients dying of malignant lymphoma will have involvement of the gastrointestinal tract. Thus it is important that patients with an apparently isolated gastrointestinal lymphoma be examined carefully for other evidences of lymphoma or leukemia. Histologically the lesions in the multiple polypoid lymphomas of the bowel demonstrate two histological patterns: 1) a well differentiated lymphosarcoma; and 2) a nodular lymphoma of the well differentiated lymphocytic type. Case 17 illustrates a poorly differentiated lymphocytic lymphoma that involves the full thickness of the bowel wall.

Two patterns are seen in Case 21, one being a malignant lymphoma

of the histiocytic type (reticulum cell sarcoma) blending into a second pattern resembling Hodgkin's disease. Considering that the major portion of the tumor tissue on the slide appears to be a reticulum cell sarcoma, one wonders if the pleomorphic areas are not a variety of reticulum cell sarcoma. It is true that a number of the cells bear a close resemblance to Reed-Sternberg cells lending a difficult histological decision. Considering what is present, however, I would wonder if this isn't a malignant lymphoma of the pleomorphic histiocytic type that has been described by Rappaport (AFIP Fascicle). Areas such as are seen in this slide have been designated as Hodgkin's sarcoma. This indicates the difficulty of differentiating Hodgkin's disease from this pleomorphic variety of reticulum cell sarcoma. Case 22 has the histological features of a Hodgkin's disease. Several characteristic Reed-Sternberg cells are noted. The surface of the lesion is ulcerated, resulting in numerous inflammatory cells in the superficial area of the lesion. Deeper in the lesion one finds a mixed inflammatory infiltrate with numerous eosinophils. A background of neoplastic reticuloendothelial cells mixed with lymphocytes is noted.

Of the malignant lymphomas of the gastrointestinal tract, lymphosarcoma and reticulum cell sarcoma are the most common varieties. Hodgkin's disease is seen less frequently, and the nodular lymphomas are considered rare. In most series, lymphomas of the gastrointestinal tract, are infrequent at either extremity of the tract, that is uncommon in the stomach and large bowel when compared to the small bowel. The lymphomas of the stomach are more common than are those of the large bowel. In the small bowel lymphomas are less frequent in the upper small intestine, becoming more frequent towards the distal portions.

Although there is not a hard and fast correlation between the histological type of malignant lymphoma and prognosis, there is a generally accepted observation that patients having reticulum cell sarcoma do rather poorly compared to those that have a well differentiated lymphosarcoma. The overall treatment results are somewhat varied; those of the stomach have already been mentioned. In the small bowel and large bowel they vary from 0% in some series to as high as 60+% in others. In a recent review of large intestinal lymphomas, it was noted that if lymphoma involves the large intestine as part of a disseminated disease, only a rare patient survives 5 years. In contrast, those patients with lymphoma confined to the large intestine have a 55% chance for 5 year survival and a 50% chance for a 10 year survival. It has been observed that if the lymph nodes are demonstrated to be positive for lymphoma, the survival rate is decreased by about 50%.

One lesion occurring in the rectum that might be considered with lymphosarcoma is the lymphoid polyp or as some refer to them, pseudo-

lymphomas. These lesions may appear as polypoid masses, and if large may be confused with lymphosarcoma. Histologically the features that distinguish these from malignant lymphoma are similar to those discussed under lymphoid pseudotumors of the stomach. Follow-up of lymphoid polyps indicates that these lesions do not transform into lymphosarcoma.

REFERENCES:

1. Allen, A.W., Donaldson, G., Sniffen, R.C., and Goodale, F.: Primary Malignant Lymphoma of the Gastrointestinal Tract: Ann. Surg. 140:428, 1954.

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DECEMBER 8, 1968 - CASE NO. 22

ACCESSION NO. 12804

MODERATOR'S DIAGNOSIS: MALIGNANT LYMPHOMA OF THE INTESTINES

HISTORY:

This 76 year old female had been in good health until approximately five months ago when she noticed onset of difficulty in defecation with constipation. She resorted to cathartics. Two months previously she began to note appearance of bright red blood with defecation and with progressive narrowing of stool.

DISCUSSION:

These four cases present various configurations of intestinal lymphomas. The first case is unusual in that there are multiple polypoid lesions of the small and large bowels. Histologically the lesions of this case appear to be well differentiated lymphocytic lymphoma. One of the sections has a nodular pattern, still maintaining its well differentiated characteristics. Separate foci of involvement of the intestinal tract in malignant lymphoma is common, seen in approximately 10% of cases. However, multiple polypoid lesions as demonstrated in this patient's intestine are unusual, but have been described.

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DECEMBER 8, 1968 - CASE NO. 23

ACCESSION NO. 17693

MODERATOR'S DIAGNOSIS: MALAKOPLAKIA

HISTORY:

The patient was admitted to the hospital on September 17, 1968 with one month history of abdominal pain, diarrhea, and poor control of bowel movements, increased in severity past 24 hours prior to admission.

DISCUSSION:

Two lesions are seen in the section in the seminar set: one, a fairly well differentiated adenocarcinoma of the sigmoid, and the second a lesior that seems to be composed of large acidophilic granular cells. The latter is the most interesting of the two lesions. If one looks carefully at these granular cells, it soon becomes apparent that there are numerous basophilic inclusions within the cytoplasm. Under high magnification, the inclusions in some instances appear to be laminated. The rounded inclusions vary in the intensity of staining with hematoxylin. A combination of these hematoxylin stained bodies and the histiocytic cells causes one to consider the diagnosis of malakoplakia. Ordinarily one thinks of malakoplakia as a lesion of the urinary tract, and indeed the major number of cases that have been reported have involved the urinary bladder, renal pelvis, prostate or testis. Recently malakoplakia has been described as involving the intestine, the stomach, and the retroperitoneal areas. I have been unable to find any case associated with adenocarcinoma as this one is. However, there have been cases reported, one in the gastro-intestinal tract, and one in the urinary tract that resulted in the death of a patient from bleeding.

Histochemical studies have been carried out in an attempt to determine the nature of inclusion bodies commonly referred to as Michaelis-Gutmann bodies. By various staining techniques it has been demonstrated that these bodies include lipids, proteins, iron and calcium. The origin of these bodies also has been the subject of investigation and speculation. Some have considered these to be encrusted red blood cells, related to an E. coli infection. A recent study has suggested that the inclusion bodies are the result of release of massive amounts of a glycolipid from micro-organisms; the micro-organisms responsible are thought to be E. coli and aerogenes.

In the sections seen in the seminar set there are clusters of bacteria within the malakoplakic component of the lesion. From the history, it is stated that there was perforation of the sigmoid, so that it is possible that these bacteria are secondary invaders from the perforation. It is also interesting to speculate that perhaps the perforation, if it had

occurred some days before the operative procedure, may have been the inflammatory incident that incited the development of the malakoplakia.

The large cells that compose the lesion have been considered by many to be histiocytes, and others to be altered mast-cells. If these cells are mast-cells, some have suggested that the inclusion bodies are formed by the deposition of the various substances mentioned above on the granules of the mast-cell. Electron microscopic studies of malakoplakic lesions have indicated that the cells are histiocytes and that the inclusion may be formed from PAS positive cytoplasmic granules.

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DECEMBER 8, 1968 - CASE NO. 24

ACCESSION NO. 13761

MODERATOR'S DIAGNOSIS: CARCINOSARCOMA OF THE ESOPHAGUS

HISTORY:

This 71 year old Negro male was admitted to the hospital for the last time on April 12, 1964, because of increasing abdominal discomfort, anorexia, weight loss and vomiting.

DISCUSSION:

Histologically the lesion presents varied patterns, including poorly differentiated squamous cell carcinoma, an undifferentiated sarcomatous element, and areas suggestive of osteosarcoma. In numerous areas, calcified osteoid surrounded by malignant components are present. Elsewhere, an undifferentiated malignant stroma blends with a poorly differentiated squamous cell carcinoma. From a histological standpoint with the intimate intermingling of carcinomatous and sarcomatous elements, this lesion can be classified as a carcinosarcoma. Grossly the mass is described as a polypoid tumor projecting into the lumen of the esophagus at approximately the level of the bifurcation of the trachea. Most of the reported carcinosarcomas of the esophagus have been described as polypoid.

Carcinosarcomas tend to remain confined to the esophagus, occasionally invading locally and being associated with distant metastases. It is often speculated that the outcome of treatment of patients with these lesions should be good. However, most of the patients have succumbed, usually in the post-operative period. This may be due to the fact that the majority of these patients are elderly men. The metastases in the lesions have characteristically been the sarcomatous portions. This was demonstrated in this case in which the osteosarcoma and the undifferentiated sarcomatous elements metastasized, but the epithelial did not. The sarcomatous elements of the collected cases have been undifferentiated, but sometimes fibrosarcoma, leiomyosarcoma, and on rare occasions an osteosarcoma. The epithelial element has generally been a squamous cell carcinoma, although adenocarcinoma has been described.

A lesion that may be confused with a carcinosarcoma is a squamous cell carcinoma of the esophagus with a pseudosarcomatous component. It has generally been considered that pseudosarcomas are always associated with a squamous cell carcinoma. It is difficult from a histological standpoint to be certain that the sarcomatous element is not malignant. However in the majority of instances, the stromal component has been non-invasive. This being a point in favor of a stromal reaction to the presence of the carcinoma.

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DECEMBER 8, 1968

ACCESSION NO. 13906 (25)

MODERATOR'S DIAGNOSIS: CARCINOID OF THE RECTUM (Schistosomiasis in one set of slides)

HISTORY:

Patient was hospitalized in June 1964 for symptomatic hemorrhoids of 7 years duration.

DISCUSSION:

Histologically the slides present a pattern characteristic of carcinoid. One sees a variety of patterns, actually in which there are solid areas, cords, small masses, and in a few areas ribbons of cells, some of which are arranged in glandular patterns. The lesion seems to have provoked a fibrous reaction, and the muscularis mucosae appears to be hypertrophied with smooth muscle strands separating the tumor into varied sized compartments. The overlying mucosa appears essentially normal. As a biopsy specimen, the lesions are on occasion mistaken for adenocarcinomas of the rectum. The element causing this mistake is the glandular pattern such as in this case. But if one considers the location in the bowel wall, the ribbon-like pattern, the fibrous reaction, and at times the hypertrophy of the smooth muscle, one is not likely to make this mistake. Stains for argentaffin granules are not always helpful. The minority of carcinoids of the rectum are silver positive. Since it has been demonstrated that carcinoids may show evidences of mucus secretion, a mucin stain is not a guarantee that a given lesion is a carcinoid.

Rectal carcinoids seldom produce symptoms; occasional patients presented because of rectal bleeding or a change in bowel habits. In unusual situations the lesion has been large enough to cause constriction, with signs and symptoms of obstruction. By proctoscopic examination the lesion is often described as a mucosal nodule or polyp, and only occasionally has a carcinoid been described as yellow. The diagnosis is infrequently made by the person performing the proctoscopic examination. Rectal carcinoids may be located in any segemnt of the circumference of the rectum with the anterior wall being the commonest single site. Rarely the carcinoids will present as multiple tumors. The majority of carcinoids of the rectum are small, that is measuring less than 1 cm. in greatest dimension. Most will lie within the first 10 cm. of the rectum above the anal verge.

There has been considerable discussion in the literature concerning methods of treatment of this lesion. The treatment is usually predicated upon the size of the lesion. Those lesions measuring 1 cm. or less in diameter are considered to be adequately treated by local excision as only in rare circumstances have metastases been demonstrated from lesions of this size. There have been no deaths recorded as the result of metastases

from lesions of this size. In those lesions that measure 2 cm. or more in diameter an abdomino-perineal resection has often been the suggested form of therapy. There are a number of cases reported in which metastases have occurred from lesions of this size. The favorite site of metastases has been the regional lymph nodes and the liver. Despite the frequent metastases to the liver of the large carcinoids of the rectum, there are no recorded instances of the carcinoid syndrome associated with the lesion of the rectum.

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