A D D E N D A

TO THE

CALIFORNIA CANCER COMMISSION

SEMI-ANNUAL SLIDE CONFERENCE

ON

TUMORS OF THE GASTRO-INTESTINAL TRACT

MODERATOR:

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MAYO CLINIC
ROCHESTER, MINNESOTA

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CASE NO. 1 APRIL 14, 1962

ACCESSION NO. 11673

CONTRIBUTOR: Milton L. Bassis
Kaiser Foundation Hospital
San Francisco, California

(Epithelioma of the anus)

PATHOLOGY

My first section represents an attempt to arrive at a reasonable site of origin for the tumor in question. It depicts, in my opinion, malignant involvement of squamous epithelium. It is also to be noted, as the tumor cells stream away, they are much smaller than the cells which gave them birth. In the second slide, the small size of the cells is again emphasized, as is also what I like to call the squamous growth pattern in cellular islands and peninsulas. I interpret a scirrhous reaction in the stroma as a serious prognostic sign. In slide 3, individual cell keratinization is present, the cells are larger and the presence of anaplastic appearing giant cells places a Broders grade of IV on the lesion. Slide 4 may generate some bitter discussion, but I feel it discloses malignant replacement of anal glands much as we see occurring in the cervix with in situ cancers in that location. I do not believe that it represents a "collision" phenomenon.

My diagnosis, therefore, is grade IV squamous cell carcinoma with basaloid features, probably arising high in the anal canal.

DISCUSSION

Almost a hundred years ago, a Frenchman named Hermann described a zone of transitional epithelium, bridging the upper reaches of the anal canal, and he claimed that the cells were cloacal in origin. In 1956, Grinvalsky and Helwig did some A.F.I.P. promoting of this long forgotten patch of anal real estate, and they suggested that atypical cancers in this cryptogenic corner might be properly designated as "transitional cloacogenic carcinomas." Lone, Berg and Stearns of the Memorial, joined the van shortly thereafter and described basaloid tumors of the anus. They believed that these tumors carried a good prognosis. Wettosch, Woolner, and Jackman described seven highly malignant basaloid small cell neoplasms of the anal canal. Berg, Lone, and Stearns added to the growing "pile" by writing up a group of mucoepidermoid tumors of the anal canal.

Being personally a lumper rather than a splitter, I feel with Haythorn that so-called basal cell cancers of mucosal origin are non-cornifying, highly malignant neoplasma related to squamous cell carcinomas. The anal counterparts occur in the cervix as small cell squamous cell growths for which nobody postulates a transitional cell of origin. Squamous cell carcinomas and adenoacanthomas can be primary in the gallbladder - far removed from any squamocolumnar junctional zone.

The important fact to remember is that basal cell carcinomas can be primary in the skin around the anus. They are non-metastasizing tumors. Mucosal cancers which simulate basal cell carcinomas occur more proximally, they are more malignant cytologically with cells of a larger average size, and they are clinically dangerous growths.

In a recent survey of 109 cases of anal squamous cell carcinomas observed at our institution, about 15% were anaplastic growths of the type under discussion. They were for the most part found in women, they occurred high in the anal canal; the incidence of positive nodes and of liver involvement was higher than in the control group of ano-rectal neoplasms, and the five-year survivals were only 20% as compared with 50% for the entire series. (83% with nodes negative, 40% with nodes positive) Only one with positive inguinal nodes lived five years.

REFERENCE

Wittoesch, J. S., Woolner, L. B., & Jackson, R. J.: Basal Cell Epithelioma and Basaloid Lesions of the Anus. Surgery, Gynecology & Obstetrics, Vol. 104:75-80, Jan. 1957.

Grennell, R. S.: An Analysis of Forty-nine Cases of Squamous Cell Carcinomc of the Anus. Surgery, Gynecology & Obstetrics, Vol. 98:29-39, Jan. 1954.

CASE NO. 2 APRIL 14, 1962

ACCESSION NO. 11670

CONTRIBUTOR: Francis S. Buck
Los Angeles County Hospital
Los Angeles, California

(Carcinosarcoma of the esophagus)

PATHOLOGY

Grossly this tumor was polypoid and pedunculated - a feature observed in well over half of the recorded cases of its kind. Microscopically (slides) one observes poorly-differentiated squamous cell carcinomatous nests sharply delineated from a stroma of spindle cell elements. In areas (slide) the latter exhibit bizarre giant cell forms with eccentric nuclei and stringy masses of acidophilic cytoplasm. Strap forms are everywhere apparent and longitudinal striations are easy to find. Cross striations I was unable to demonstrate. In some areas (slide) the spindle cell component lies in a basophilic matrix reminiscent of young cartilage. Again, however, this is a matter of individual interpretation.

As to diagnosis, I believe that this lesion is what in the literature of some twenty-four cases has been called polypoid carcinosarcoma of the esophagus.

DISCUSSION

I am sure that we are all in agreement that this particular lesion is a highly malignant one. I am certain that the case is deserving of a report in the literature where it would join some 24 others of its own particular species. I am also certain that were this tumor observed in the uterus, there would be no quarrel with calling it a mesodermal mixed tumor with squamous cell carcinoma and rhabdomyosarcoma present.

However, we are here dealing with the esophagus, and unless one can prove that the stroma of the malignant squamous cell element contains cells with cross striations or is producing chondroid or osteoid, it is next to impossible to establish that it is in fact a carcinosarcoma. Eide of New Orleans succeeded in demonstrating cross striations in his tumor, using Mallory's phosphotungstic acid. Ackerman employed reticulum stains to establish that the pattern of reticulum in the stroma of these growths was that seen in sarcomas and not that observed in carcinomas. In the other cases, no serious attempts were made to place a non-epithelial tag on the supposed sarcomatous aspects of the growths. Saphir, of course, is a non-conformist who practically refuses to accept the diagnosis of carcinosarcoma. As for myself, I am perhaps biased because of the experience I have had with uterine carcinosarcomas. To me they are a true entity and I do not concern myself too much over whether they are collision composition or combination in type. I believe this tumor to be a true carcinosarcoma, while admitting that I am unable to prove my point to the satisfaction of the doubting Thomases. But I affirm that these polypoid growths of the esophagus with their 25% incidence of metastasis are different

grossly, microscopically, and biologically from the squamous cell growths from which, according to some, they are derived by a process of metaplastic "spindling." We should not wait until necropsy to diagnose them as has been done with 95% of cases reported in the literature. The 50% which are polypoid should lend themselves well to surgical resection.

REFERENCE

Pearlman, Samuel: So-called Carcinosarcoma of the Esophagus. Am. J. of Rhinology & Laryngology, Vol. 49:804-819, March 1940.

Bergman, Martin, Ackerman, L. and Kemler, L.: Carcinosarcoma of the Lung. Cancer, Vol. 4:919-929, 1951.

Stout, A. P. et al: A Case of Carcinosarcoma of the Esophagus. Am. J. of Roentgenology & Radium Therapy, Vol. 61:461-469, 1949.

CASE NO. 3 APRIL 14, 1962

ACCESSION NO. 11648

CONTRIBUTOR: Robert G. Fischer
Eden Hospital
Castro Valley, California

(Malignant lymphoma, lymphoblastic type, ileum)

PATHOLOGY

The first slide on this case shows a tumor of small dark staining cells. It has a very sharply delineated margin, it dissects under the mucosa and it ensheaths rather than invades the thin-walled vein shown in the lower portion of the lantern slide. Slide 2 shows how the tumor infiltrates among the smooth muscle fibers of the ileum. These gradually become replaced and disappear. The production of a characteristic aneurysmal dilatation of the ileum at the site of involvement is a rather distinctive effect produced by this type of tumor - perhaps exclusively. The third slide shows a population explosion of small dark cells having practically no cytoplasm surrounding their nuclei. The cells look like lymphocytes but the presence in each of a single large nucleolus marks them as lymphoblasts.

In my opinion, the growth is a malignant lymphoma of the small cell or lymphoblastic type.

DISCUSSION

Lymphosarcomatous involvement of the small intestine was first described in 1864 by Wallenberg. By 1892 Balzer was able to collect twelve cases from the literature. It was believed that the lesions were all secondary. In 1893 Kundrat separated leukemia from lymphosarcoma and demonstrated that the latter condition could commence in localized lymphoid aggregates such as are found in the lung and in the gastrointestinal tract. Raiford, Stout and others have brought to almost 400 the number of primary gastrointestinal lymphosarcomas.

The lesions are rare but in our series of 659 tumors of the small intestine, benign and malignant, no less than 55 were of the type under discussion. Forty-seven were surgical - and all of clinical significance; 8 were first discovered at necropsy.

The patients were usually young and five of them were children. Ninety-five per cent had gastrointestinal symptoms featuring colicky pain. The pain of acute peritonitis was rarely observed since the lesions do not tend to perforate. Likewise, because they appear to ensheath rather than invade blood vessels, significant anemia from blood loss was infrequent. In over half of the patients a mass was felt - this because the tumors were usually large. At operation the growths were more frequently ileal than jejunal and 25% of them arose from multiple centers. Resection was usually possible in spite of the tumor's large size because adhesions were absent. In several instances, however, peritoneal lymphoblastomatosis was present along with "Krukenberg tumors" in two patients.

Five-year survivals ran 30% with x-ray being of distinct benefit in those patients with positive nodes. Children and women with lympho of the small intestine did poorly and it is my impression that the outlook was worst in the reticulum cell type. Since most of the patients who died succumbed at home, we do not have accurate data respecting the incidence of terminal leukemia.

REFERENCE

Faulkner, James W., Dockerty, M. B.: Lymphosarcoma of the Small Intestine. Surgery, Gynecology and Obstetrics, Vol. 95:76-84, July 1952.

CASE NO. 4 APRIL 14, 1962

ACCESSION NO. 11472

CONTRIBUTOR: R. F. Hufner
Los Angeles, California

(Liposarcoma of mesentery)

PATHOLOGY

My first section shows about 90 per cent replacement of the fat of the mesentery by a cellular myxomatous process in which scattered giant cells are noted. In one of my slides a portion of the bowel wall was also included. It was not involved by tumor. For this reason I concluded that we were dealing with something which was indeed primary in the mesentery or in the retroperitoneum. In the second slide we note that the cell population consists of branching spindle elements in a background that has a bluish myxomatous appearance with hematoxylin. Again bizarre giant cells are noted. The fact that these giant cells are multinucleated makes us think more of liposarcoma than of rhabdomyosarcoma. In slide 3 the giant cells are observed to possess vacuolated nuclei and although I have no fat stains on this section, I am certain that the vacuoles would be filled with lipoid.

My diagnosis is liposarcoma.

DISCUSSION

It took me a long time to come to the understanding that myxomatous tumors exhibiting this mixture of branching spindle cells and vacuolated giant cells represented one form of malignancy in adipose connective tissue rather than fibromyxosarcoma. I was also slow in realizing that whereas lipomas of the distal portions of the extremities rarely exhibited malignant change, those situated near or on the trunk and especially those in the retroperitoneum and mesentery were more frequently malignant than benign. I had to encounter more than one recurrent lipoma with a mere scattering of giant cells before I realized that these giant elements very often represented malignant change in mesenchymal cells which were differentiating into adipose connective tissue. I now regard with grave suspicion any lipoma displaying these characteristics. I now carry out a very thorough sampling of large lipomatous tumors, because I am convinced that this is one benign tumor that is fairly prone to undergo malignant change. My personal experience with these tumors concerns the retroperitoneum rather than the mesentery. Of 43 lipomatous tumors studied, 28 were malignant and 15 were benign. We cured only one of the former group. Ackerman in his fascicle likewise reports a 50 per cent incidence of malignancy among lipomatous new growths of the mesentery.

The present lesion was apparently a double one. Multiple liposarcomas have been previously reported to involve the retroperitoneum.

REFERENCE

DeWeerd, J. W. and Dockerty, M. B.: Lipomatous Retroperitoneal Tumors. American Journal of Surgery, Vol. 84:397-407, 1952.

CASE NO. 5 APRIL 14, 1962

ACCESSION NO. 11530

CONTRIBUTOR: Dominic A. DeSanto
Mercy Hospital
San Diego, California

(Low grade leiomyosarcoma of the stomach)

PATHOLOGY

As shown in my first slide, most of the tumor tissue in this case is so altered by old and recent hemorrhage that it is difficult to make out the cell type. It does appear to be a spindle cell neoplasm. Slide 2 is from one of the less disturbed portions of the tumor. Here the basic spindle cell character is confirmed, as is also the fact that there is some organization into fascicles or bundles. In slide 3 the nuclei are seen to have rounded rather than pointed ends, mitotic figures are illustrated and the cytoplasm of the cells is finely granular and somewhat fibrillar.

My diagnosis is well differentiated leiomyosarcoma of the stomach.

DISCUSSION

Leiomyomas and leiomyosarcomas of the stomach exhibit a range-spectrum of histopathology rarely shown by other tumors of the gastro-intestinal tract. So much is this so that almost any spindle cell neoplasm of the stomach may be included in this category. Some vascular ones in our files were called hemangio-endotheliomas. Some fibrotic ones we rescued from a small group called fibrosarcoma of the stomach. Others featuring prominent nuclear palisading had been called neurofibromas in the days when it was popular to classify as neurogenic anything that made the pathologist nervous. One of our cases we considered - and still consider to be - a glomus tumor of the stomach. (Slide).

Fortunately for the patient it matters little what we label these globular tumors with their characteristic feature of single or multiple and sometimes deep ulcerations. The small ones are usually benign, the large ones usually malignant. Malingnancy is determined for the most part by mitotic activity. Nodal involvement is very rarely found, and a rather short-sleeved resection will cure most of the well differentiated growths which are in the malignant category. Liver metastasis, rarely the mode of dissemination in low grade leiomyosarcomas, is frequent in patients with anaplastic lesions. Latent peritoneal dissemination is our biggest concern in the case under discussion at this time.

REFERENCE

Golden T., and Stout, A. P.: Smooth Muscle Tumors of the Gastro-intestinal Tract and Retroperitoneal Tissues. Surgery, Gynecology & Obstetrics, Vol. 73:784-810, 1941.

Giberson, R. G., et al: Leiomyosarcoma of the Stomach. Surgery, Gynecology & Obstetrics, Vol. 98:186-196, Feb. 1954.

CASE NO. 6 APRIL 14, 1962

ACCESSION NO. 11631

CONTRIBUTOR: Yosef L. Tiber
Los Angeles, California

(Schistosoma japonicum, colon; adenocarcinoma, rectosigmoid)

PATHOLOGY

My first slide shows what appears to be a fairly well differentiated adenocarcinoma of the sigmoid. There is good evidence of glandular formation - as indeed there is in 90% of colonic carcinomas. Later on we shall see some that are much more anaplastic. A special feature of this particular cancer is the occurrence of much fibrosis and hyalinization in the stroma. We shall have more to say about this scirrhous reaction in connection with some other cases. The second and following two slides exhibit the features which led to inclusion of this case in the conference box. The shiny structures which you see have the characteristic of parasitic ova and their subterminal spikes or spines mark them as being schistosome ova of the Japonicum type.

My diagnosis, therefore, is schistosomiasis in carcinoma of the sigmoid.

DISCUSSION

Japanese schistosomiasis is supposed to be confined to the orient. However, Schistosoma Mansoni was brought to the western hemisphere by African slaves. It is supposed to represent the only trematode parasite that has become endemic over here, but in such countries as Brazil, Venezuela, and in Puerto Rico it has posed serious health problems. Several million persons living in Brazil, particularly in the northeastern regions, are said to be affected. With the current tide wave of migration from Puerto Rico, with the general increase in world travel, with the world-wide deployment of U. S. military personnel, occurrence of Schistosomiasis can be expected to be encountered masquerading under different disguises and complicating established illness. In other words, there is a definite danger of Schistosomiasis becoming a problem in the continental United States.

For those of you Californians who bathe in crystal clear water stolen from neighbouring states, perhaps there is no need to sound a warning against paddling in polluted puddles. Should you engage in this pastime, here's how you catch Schistosomiasis - not cancer of the rectum.

Eggs from contaminated feces are ingested by snails. Miracidia invade the intestinal wall of the snail and metamorphose into cercaria. From this stage emerge free swimming larvae which penetrate the unbroken skin of wading Homo sapiens. They migrate through the heart and lungs to the intestines. Male and female like to copulate around the hemorrhoidal veins and the females lay their eggs in the mucosa and submucosa of the rectum and sigmoid. In picturesque, if not in scientific language, the eggs use their spines to penetrate the vessel walls, appearing in the feces in from 4 to 6 weeks and starting the cycle all over again. Symptoms and signs of egg migation vary

from none in 41% through congestion and edema, ulceration and pseudopolyp formation in the remainder.

Among 575 cases recently reported by Jose Pontes of Sao Paulo, four colonic polyps and one cancer were found to be infested with the ova in a picture similar to the one under discussion today.

A form of avian Schistomiasis has recently been found to produce swimmer's itch in Iowa, Wisconsin and Michigan. The Schistosomes are reported to have a special affinity for Methodists and at one Methodist camp in Iowa it has produced an epidemic. It is most interesting that the parasite, unlike its African and Asiatic cousins, has not developed, as yet, the ability to invade the blood stream and cause visceral lesions.

REFERENCE

Jose Theago Porks, Sao Paulo, Brazil: Diseases of the Colon and Rectum, Vol. 7, No. 5, Sept. - Oct. 1961.

CASE NO. 7 APRIL 14, 1962

ACCESSION NO. 11454

CONTRIBUTOR: Donald L. Alcott
Santa Cruz County Hospital
Santa Cruz, California

(Malignant lymphoma of the stomach)

PATHOLOGY

In the gastric mucosa shown in the first slide, we see an advancing "front" of small dark staining cells. The line of separation of neoplastic from non-neoplastic tissue is so sharp that it could be illustrated within the confines of a single high-power microscopic field. In the next section, we observe invasion and disintegration of the muscularis propria by patternless strands of small dark staining cells. Under higher magnification we observe that the tumor cells are somewhat larger than the lymphocytes which are shown in the same section. We also observe that the cells possess fair amounts of cytoplasm which is "misty" to the point of being almost granular. Some of the nuclei are indented. In my last section, we note a cell with a multilobed nucleus.

My diagnosis on this tumor is malignant lymphoma of the stomach, either reticulum cell or Hodgkin's in type.

DISCUSSION

When Kundrat in 1888 decided that lymphatic leukemia and generalized lymphosarcoma could be separated from a group of solitary lymphomas which behaved like carcinoma and were oftentimes curable surgically, his key case was a malignant lymphoma of the stomach like the lesion under discussion. But in the case of the stomach the problem goes deeper than merely deciding whether a given tumor is inflammatory or a primary or a secondary lymphomatous process. For certain gastric cancers composed of small dark cells may fail to organize into a cancerous architectural pattern; and no mucous cells may be present to indicate an epithelial origin. Fortunately, however, these cancerous masqueraders carry a prognosis which is about the same as the rather favourable outlook projected for patients in whose lesions the finding of things like Reed cells removes all doubt regarding their sarcomatous nature. I have personally observed over 100 of these lesions, mostly in males, mostly in the younger age group, and mostly represented by large and frequently palpable lesions. As compared with gastric cancers the lesions produced symptoms which were pretty nonspecific but massive bleeding was rare. At surgery growths as large as footballs were free from fixation and very frequently removable. Single and multiple ulcerative and polypoid growths were represented. None exhibited esophageal spread and in only 3 specimens were the lesions seen to involve the duodenum. Although nodes were positive in 40%, peritoneal involvement was uncommon because of the tendency for these growths to dissect underneath rather than to penetrate this layer. Lymph nodal involvement incidentally did not materially reduce the 50+% five year overall survival

provided that roentgen therapy was given postoperatively. I have observed three 5-year cures of irremovable gastric lymphoma treated by biopsy and x-ray therapy.

For what it is worth then - here is my philosophy with respect to these lesions.

1. Barring verified evidence of distant metastasis, every patient shown to have a cancer-like lesion of the stomach, regardless of size, should be surgically explored.

2. Generous biopsies should always be taken and examined in fresh frozen sections.

3. If the lesion is a "lympho," or suspected of being one, it should be treated aggressively. If the diagnosis is on firm grounds, the surgeon should not worry too much about leaving positive nodes behind.

4. If there is doubt regarding the sarcomatous versus the carcinomatous nature of the lesion on fixed sections, the pathologist should favor the former in his report because:

5. X-ray treatment, of itself, can eradicate residual tumor tissue and it may work equally effectively in cancers that have a lymphomatous appearance microscopically.

REFERENCE

Bernatz, P. E.: Small Cell Neoplasms of the Stomach. The Clinico-pathologic Study. University of Minnesota - Mayo Foundation Thesis, 1950.

CASE NO. 8 APRIL 14, 1962

ACCESSION NO. 12077

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Giant rugal hypertrophy - Menetrier's disease)

PATHOLOGY

My first section shows, under low magnification, a gastric fold that is tremendously thickened. This thickening can perhaps be better appreciated in slide 2 which represents a mounted microscopic of what I like to call convolutional hypertrophy of the gastric mucosa. In slide 3, we note that the constituent cells appear to be increased in number but that they are otherwise normal. Slide 4 depicts chief and parietal cells in normal relations, one with another. The picture fits the description of what is commonly called Menetrier's disease or polyadenoma en nappe of the stomach.

DISCUSSION

When Francis Kenny and I wrote up our series of 20 cases back in 1953, we had cornered approximately one-third of the world's supply of Menetrier's disease. It is indeed a weird and strange condition with many faces. First let me show you some typical gross appearances, because the condition is likely to be confused with multiple polyps and with gastric lymphosarcoma. Slides 3 to 7.

Apparently Menetrier's is not an atypical gastritis because it involves primarily the fundus of the stomach, free HCl is usually present and acid values are often very high; inflammatory cells are the exception rather than the rule in the sections studied and there is good preservation of chief and parietal cells.

The process may be circumscribed or diffuse. The lesser curvature is usually spared. Almost never associated with cancer over half of the reported cases have ulcer symptoms for an average period of 5 years. The correct diagnosis is made preoperatively in only 25%.

Rather than drone on with dull gross and microscopic descriptions of the pathologic manifestations, let me tell you of important associated conditions that should be looked for whenever the presence of Menetrier's disease is suspected.

The first of these is hypoproteinemia. It was present in 5 of our 20 cases and in one young man the condition presented in the form of severe edema and ascites. It appears that these stomachs weap protein much as do the surfaces of burns. Part of this protein is re-absorbed but much of it is lost in the stool. Loss is more rapid than formation by the liver and protein depletion with edema results. The protein loss is corrected promptly by partial gastrectomy.

Another strange association noted in our series consisted of multiple adenomas of ductless glands, particularly adenomas of pituitary, pancreas, and parathyroid. The patient with Menetrier's disease may present with the problem of a kidney stone secondary to hyperparathyroidism.

Thirdly, it has been recognized that a number of patients with Zollinger Ellison syndrome also have Menetrier's disease as the apparent sole cause for the hyperacidity and voluminous night secretion of very acid gastric contents. Some of these patients also show up with adenomas of several ductless glands. Our last such patient with this set-up had an extra pancreatic islet cell tumor in the wall of the duodenum.

Finally, I should like to present a series of "one cases" of Zollinger Ellison syndrome in which the gastric fundus, removed at the time of the third partial resection for intractable jejunal ulceration, presented the picture of Menetrier's disease with an odd, carcinoid-like neoplasm infiltrating the bases of the large folds. Possibly that was the situation we were dealing with in Case 11. (Accession No. 11490). (Polypoid adenomas with carcinoid pattern).

REFERENCE

Kenney, F. D., Dockerty, M. B., and Waugh, J. M.: Giant Hypertrophy of Gastric Mucosa. Cancer, Vol. 7, No. 4, July 1954.

CASE NO. 9 APRIL 14, 1962

ACCESSION NO. 11533

CONTRIBUTOR: D. Gordon Johnston
St. John's Hospital
Oxnard, California

(Malignant tumor of the stomach)

PATHOLOGY

My technique of analyzing these small cell neoplasms of the gastrointestinal tract must be familiar to all of you by now. As per established pattern, my first slide shows the growing edge of the lesion with the sharp line of demarcation between the "good guys" and the "bad guys." This is further emphasized in the second slide in which the individual tumor cells are seen to be somewhat larger than those in the adjacent focus of lymphocytes. Slide 3 is a blow-up of an area showing the somewhat polymorphous nature of infiltrate, and what I like to call mononuclear Reed cells with their large amphophilic nuclei. One would hesitate to venture a diagnosis of Hodgkin's on the basis of finding these cells alone. However, in slide 4, one observes the characteristic nuclear lobulation to clinch such a diagnosis.

DISCUSSION

Having shot my lymphomatous wad - so to speak - in my analysis of Cases 3 and 7, there remains nothing but to do some smoke blowing in connection with this case. It appears to represent a type of lymphoma which is multicentric and which expands the gastric folds rather than going about the business of forming a large ulcer crater. In our experience this picture is produced by about 20 per cent of gastric lymphomas. The gross picture does not correlate well with any specific type of lymphoma microscopically.

In our series of over 200 gastric lymphomas, Hodgkin's made up only about 8 per cent. The vast majority of the lesions were either of the lymphoblastic or of the reticulum cell variety. The former had the best, the latter the worst prognosis with cases of Hodgkin's falling in an intermediate position.

REFERENCE

Madding, G. F.: Lymphosarcoma of the Stomach with Special Reference to Reticulum Cell Variety. Mayo Foundation Thesis, 1938.

CASE NO. 10 APRIL 14, 1962

ACCESSION NO. 11795

CONTRIBUTOR: Harold A. Fanselau
USAF Hospital
Barksdale AFB, Louisiana

(Malignant mesenchymoma)

PATHOLOGY

Viewing the first slide 'through the glass darkly" and at low magnification, one gets the impression that we are dealing with a connective tissue tumor of some sort rather than an epithelial neoplasm. In the next slide, we encounter a cellular myxomatous zone with giant cells and begin thinking in terms of a liposarcoma. In this next section, rounded cells in a chondroid type of matrix recalled the picture of chondrosarcoma to some of us. And in slide 4 this material which stains so brilliantly with eosin could well pass for the osteoid matrix of a soft tissue osteogenic sarcoma. Myogenic cytoplasm features the extra nuclear constituent of the cells shown in the next two slides and consideration of leiomyo or rhabdomyosarcoma comes to mind. Accordingly, we call together all the blind men of Hindustan and conjure up the diagnosis of malignant mixed mesenchymoma.

DISCUSSION

Stout has observed the largest personal series of these cases and his 1959 count of them was 243. Originally he insisted on maturation of the constituent tissues to the point where bone, osteoid and cross striations were readily identifiable as such. Later, he stretched the definition to include growths like the one which we have just seen.

By some the growths are believed to be malignant hamartomas. By others it is felt that they represent various lines of differentiation from primitive cells of the mother mesenchyme. Perhaps indeed adult mature cells are capable of participation since it has been observed in the dog that the musculature of the urinary bladder is capable of transformation into striated muscle in response to chronic overstretching.

The range spectrum of histopathology reaches from reticulum cell sarcoma on the one hand to liposarcoma on the other. Frequently encountered are rhabdomyosarcomatous and osteosarcomatous elements. The lesions may feature benign components only in such growths as angiolipoleiomyomas of the kidney.

Metastasis of malignant mixed mesenchymomas is frequent with spread occurring via lymph and blood routes as well as by sedimentation. Metastatic deposits may exhibit pure growths of one, several, or all of the original tumor constituents.

REFERENCE

Stout, A. P.: Malignant Mixed Mesenchymomas. Annals of Surgery 1948, Vol. 127:278-290.

CASE NO. 11 APRIL 14, 1962

ACCESSION NO. 11490

CONTRIBUTOR: S. K. Abul-Haj
Walter Reed General Hospital
Washington, D. C.

(Gastric polypoid adenomas, carcinoid pattern)

PATHOLOGY

We are told that this patient had multiple polypoid tumors of the stomach and my first section is from the base of one of them. It shows on the surface a bifurcated gastric pit with goblet cells and Paneth cells indicative of an associated gastritis. In and beneath the muscularis mucosae we get a glimpse of the tumor that we are attempting to diagnose. In one area it appears to be growing in a lymphatic space. In the second slide we observe a group of gastric glands completely surrounded by alveolar clusters of small prismatic tumor cells which are uniform with respect to size and staining properties. In slide 3 - also taken from the mucosa, the tumor is seen to be differentiating into tubular structures. These likewise are lined by cells which are a good deal more mature than we expect to find in a gastric cancer. Slide 4, taken from the submucosa, brings to light another tumor pattern. This looks typical of carcinoid tumor except perhaps for a lack of the fibrosis that we ordinarily expect to find in carcinoids. Slide 5 is a blow-up of one of these carcinoid foci. Finally in slide 5 we note the presence of larger cells with prominent nuclei and nucleoli. Acidophilic granules are scattered about. Some of the cells resembled Paneth cells. Slide 6 is from another case in which there was a mixture of a well differentiated adenocarcinoma in which a carcinoid pattern predominated.

You will be interested to know that in this case, the only one in which I was interested in making special stains, the latter were all negative as for furnishing good clues on the nature of the growth.

DISCUSSION

As an introduction to this discussion, let me first admit frankly that I am quite uncertain as to the origin of this strange tumor. I believe that it is a cancer rather than an adenoma even though I may have to lean heavily on the carcinoid features to back up this interpretation. It is not like any gastric tumor that I have ever encountered. It does resemble the picture displayed in slide 6. This latter was thrown at Bill Meesner in a tumor seminar held in Colorado Springs last fall. It gave me some consolation to know that Bill, likewise, had trouble naming the lesion.

Is it a carcinoid? Gastric carcinoids are all small and never multiple to this degree. They invade the muscularis characteristically and do not present as polypoid mucosal nodules. They exhibit fibrosis and hyalinization to a pronounced extent. With such a bulk of carcinoid tumor, one would have expected the carcinoid syndrome clinically.

ACCESSION NO. 11490

Is the tumor by any chance of pancreatic vintage? Islet cell adenomas and carcinomas can mimic carcinoids and, in addition, reproduce the ductular structures which we observed in this particular case. The following two slides are from the proximal portion of the stomach in a patient of ours who over a period of 8 years required a total of three gastric resections for intractable duodenal and later gastrojejunal ulcers. In other words, he was suffering from the effects of the Zollinger Ellison syndrome and incidentally had a parathyroid adenoma removed along the way. His gastric fundus showed the picture of Menetrier's disease and in the bases of the thickened gastric folds I discovered myriads of cancerous foci of the type being illustrated. Special aldehyde stains were positive for granules, suggesting a pancreatic islet origin. The patient is living and well without recurrence of his ulcers or of his cancer some 5 years after this last resection.

Is it possible that our patient today has a multicentric non-functioning pancreatic islet cell type of gastric cancer?

REFERENCE

None found.

CASE NO. 12 APRIL 14, 1962

ACCESSION NO. 11972

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Ileal carcinoid)

PATHOLOGY

Slide 1 on this case shows mucosal origin of a tumor with small dark staining cells. There is some slight tendency towards glandular formation, but most of the cellular aggregates are in the form of solid cords. Slide 2 exhibits clusters of the same dark staining prismatic cells extending into the muscle and inducing in it a very marked fibrosis. This is a characteristic of the tumor under discussion and it results in intestinal obstruction from acute buckling or angulation of the bowel. Cytoplasmic granularity of the individual tumor cells is well displayed in slide 3 which is silver impregnated.

The diagnosis is, pretty obviously, carcinoid tumor.

DISCUSSION

I included this case as an example of the average carcinoid and as an excuse to tell you something about my experience with these tumors. We studied a total of 660 primary tumors of the small intestine, 50% were benign and 50% malignant. Of about 300 primary malignant neoplasms 50% were carcinoid tumors. Of these 85 were necropsy findings and almost always incidental, 67 were surgical carcinoids and 85% of these were symptomatic. Symptoms featured intermittent chronic intestinal obstruction which was episodic and progressive in over 60% and which for more than two years on an average. Three patients eventually developed acute abdomens resulting from acute bowel infarction from metastatic carcinoid masses occluding the mesenteric vessels. Only 10% of our patients in the surgical group exhibited the carcinoid syndrome of episodic flushing, diarrhea, and right sided heart failure. The presence of the syndrome almost always indicated bulky metastasis. An exception to this rule was furnished by one patient who was not in this series. Her carcinoid was confined to the wall of a left ovarian dermoid cyst. One additional patient, likewise not in this series, had the syndrome as a result of a bronchial carcinoid which had metastasized to the liver.

The correct clinical diagnosis was rarely made in patients who did not exhibit the carcinoid syndrome; although we have available now a urine test for the end product of serotinin.

At surgery 90% of the tumors were ileal and 30% were multiple. No less than 80% of them were associated with metastasis in the root of the mesentery or in the liver. These metastatic deposits were always larger than the primary growths which were pretty uniformly diminutive. In some it was

utterly impossible to do a curative resection. However, subtotal resection was recommended along with removal of accessible hepatic secondaries to delay the onset of the crippling cardiac signs of the carcinoid syndrome. Ordinarily the growth rate of carcinoid tumors is extremely slow.

Other interesting observations made in our study concerned the fact that the rectum was the commonest seat of a primary carcinoid tumor. Here the incidence of metastasis was 5% - and only from rectal primaries that exceeded a diameter of 5 mm. Appendiceal carcinoids are now third on our list of incidence. Only two metastasizing appendiceal carcinoids have come to my attention.

REFERENCE

Moertel, C., Dockerty, M. B., et al: The Life History of the Carcinoid Tumor of the Small Intestine. Cancer, Vol. 14:901-912, Sept. - Oct. 1961.

CASE NO. 13 APRIL 14, 1962

ACCESSION NO. 11796

CONTRIBUTOR: F. V. Rhudy
St. Francis Hospital
Lynwood, California

(Peutz-Jeghers syndrome)

PATHOLOGY

My first slide on this case shows that the tumor consists of a mixture of glandular structures that seem to be infiltrating the smooth muscle coats of the small bowel. In section 2, taken from a zone of infiltration, we note that the epithelial cells include ordinary secretory elements, goblet cells, and basal cells containing large granules which stain brilliantly with eosin. My next slide brings these epithelial elements into larger focus to fortify our previous notion that the cells are benign. One observes a lack of any fibrous reaction in the surrounding muscle such as one almost always encounters in a cancerous growth.

To me this picture is that of a benign hamartomatous complex and consistent with the picture of a Peutz-Jeghers polyp.

DISCUSSION

You are, I am sure, all familiar with the combination of familial mucocutaneous pigmentation and gastrointestinal polyposis which goes under the term of Peutz-Jeghers syndrome. Some of you may be in doubt as to the malignant potential of these polyps and, as pathologists, might wonder whether you should advise wide resection or polypectomy when a number of these growths are found in the small intestine. Should gastric resection be done for gastric polyps when they occur in this condition and how dangerous are the colonic polyps of patients with Peutz-Jeghers disease? In an effort to arrive at the answers to some of these questions, Dr. Gannon, one of our better surgical fellows, went over a series of 60 clinic patients with small intestinal polyps or adenomas, seen at surgery or at necropsy in Rochester over a period of 50 years. Nine of the 60 patients had Peutz-Jeghers syndrome; all with polyps of the hamartomatous types; all multiple and all benign. Thirty-seven additional cases had hamartomatous polyps but no mucocutaneous pigmentation. Six patients had gastric heterotopias. Only eight of the entire 60 exhibited what we might call ordinary adenomas of the small intestine. Seven of the nine patients with mucocutaneous pigmentation had polyps of the stomach and colon as well as of the small intestine. These gastric and colonic polyps exhibited the same benign mixture of native glandular elements along with smooth muscle strands as we have described in the small intestine.

Eleven additional cases of small intestinal polyps of the Peutz-Jeghers type were available to us from other sources. None showed any sign of malignant change. We know of no examples of metastasis from polyps of this type and accordingly do not recommend resection for such.

However, unlike Morson we are not yet willing to pronounce as being entirely innocent the colonic polyps which occur as a very frequent by-product in patients with Peutz-Jeghers syndrome. We have not observed cancer in those examples which we have studied. However, two of our nine cases with the syndrome developed infiltrating carcinoma of the colon. Perhaps this was circumstance, perhaps it was not.

Finally, let me say that we visualize atypical forms of the syndrome in which either the polyps or the pigmentation are absent. Viewed in this light it appears that the vast majority of small intestinal polyps occur as an incomplete form of the syndrome under discussion.

REFERENCE

Gannon, Paul M.: Mayo Foundation Thesis. 1961.

CASE NO. 14 APRIL 14, 1962

ACCESSION NO. 11725

CONTRIBUTOR: Harold Y. Yanamura
San Antonio Community Hospital
Upland, California

(Malignant melanoma of anus)

PATHOLOGY

Slide 1 shows the epithelium of the anus undermined by a very cellular growth of tumor tissue. The cell population is quite uniform as to type. The arrangement is in the form of alveolar groupings separated by delicate strands of connective tissue. The appearance is that of an epithelial neoplasm, but there is no sign of gland formation or of differentiation along squamous lines. I was unable in my sections to develop evidence of junctional contact with the overlying epidermis. My second section is a 1600 time magnification of the individual tumor cells. They look epithelial and many of them contain huge amphophilic nucleoli. After prolonged search, I found a bit of pigment which here appears in a phagocytic cell. Elsewhere I located it in several tumor cells which however were so "steamy" that they were not reproducible on the photographic plate.

My diagnosis is malignant melanoma of the anus.

DISCUSSION

Anal melanomas, according to Allen and Spitz, are supposed to comprise 1.5% of all malignant melanomas and one-half of one per cent of all malignant tumors of the anorectal region. This was about the incidence that Braastad and I found when we reported our experience with ten cases in 1949. Since that time we have encountered about one case every two years. There are perhaps 150 of them in the literature. The tumors are difficult to diagnose for two reasons - namely, (1) almost a third of them are amelanotic and liable to be mistaken for leiomyosarcoma or lymphosarcoma resulting in undertreatment or the wrong treatment; (2) only in the earliest phases will one see the typical junctional changes which one expects to find in an ordinary melanoma. Like other melanomas of mucous membranes these anorectal examples are atrociously malignant clinically. Our experience parallels that of Pack and of Allen and Spitz that they spread by the blood stream as readily as they do by lymphatics. Moreover, from an anal primary blood and lymph drainages carry tumor cells to both portal and peripheral depots.

They are extremely radioresistant and very radical surgery should be carried out for all but the very tiniest lesions. Pack recommended combined abdominoperineal resection plus incontinuity dissection of inguinal and femoral nodes. Yet he had only one 32-month cure following such a "Brunschwigian" procedure. Our own two cures came from wide local removal of tiny melanomas which were incidentally discovered during the routine sectioning of hemorrhoids.

REFERENCE

Allen and Spitz: Melanoma: Diagnosis and Prognosis. Cancer, Vol. 6: 1-45, 1953.

Pack, George and Martins, F. G.: Treatment of Anorectal Malignant Melanoma.

Braastad, F., Dockerty, M. B., and Dixon, C. F.: Melanoepithelioma of the Anus and Rectum. Surgery, Vol. 25, No. 1:82-90, 1949.

CASE NO. 15 APRIL 14, 1962

ACCESSION NO. 11682

CONTRIBUTOR: Haw Chan
St. Luke's Hospital
San Francisco, California

(Grade III mucous carcinoma of the colon)

PATHOLOGY

Slide 1 on this case shows the mucosa of the colon with an intermingling of benign and malignant appearing cells. This suggests but does not necessarily prove that the lesion is primary in this location. Slide 2 illustrates pools of mucus. This is epithelial mucus because we see signet ring cells scattered about. Slide 3 is a blow-up of a small cluster of such signet ring cells with nuclei pushed into eccentric positions by large globules of mucus.

This lesion I would classify as a fairly anaplastic - grade III - mucous adenocarcinoma of the colon.

DISCUSSION

Cancer of the colon arises from mucous cells and it is perhaps surprising that all colonic cancers are not classifiable as mucous in type. If we accept under this definition only those lesions in which at least 25 per cent of the cells are in the business of mucus production, the incidence of this type would be around 20 per cent. The vast majority of them would be well-differentiated as shown in the next slide. Many of them would be villous in architecture. Mucus production might be present in positive nodes and not in the mother tumor or vice versa. In only 20 per cent would the growths exhibit mucous pools and signets and in only 5 per cent would there be a "pure culture" of signet rings. Most of the latter will be found in the right rather than in the left colon. A much higher proportion of these anaplastic mucous cancers will be found when the malignant process stems from colons that are the seats of chronic ulcerative colitis.

I do not believe that mucus production, per se, makes any difference in the aggressiveness of a given colonic lesion. Surgeons, on the other hand, regard these growths in a very serious light. A cancerous rectal shelf will always kill the patient, but the surgeon remembers only those cases in which the shelf was coated with jelly.

REFERENCE

Grant, Russel: Mucous Carcinoma of the Stomach. University of Minnesota - Mayo Foundation Thesis. 1941.

CASE NO. 16 APRIL 14, 1962

ACCESSION NO. 11973

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Fibrous inflammatory polyp of stomach)

PATHOLOGY

The first slide shows that the bulk of this polypoid lesion consists of a fibrovascular matrix. It is covered by a somewhat thickened layer of mucosa which contains numerous mucous cells. An area of ulceration was present in the tip of the polyp. My next section is through the broad stalk, and in it we observe a peculiar whorling of elongated spindle cells about the numerous thin-walled vascular clefts which traverse the section. The appearance is somewhat reminiscent of hemangiopericytoma, but in this instance the pericytes are clearly fibroblasts. Numerous eosinophiles are scattered about. My next slide emphasizes the fibrovascular character of the tumor and pretty well settles the issue that we are not here dealing with a neoplasm. Slide 4 is a gross picture of the lesion.

Diagnosis: Fibrous inflammatory polyp of the stomach.

DISCUSSION

This case I wish to dedicate to our good and faithful servant, Dr. Weldon Bullock, who has done so much work in getting this seminar together and who is, in my opinion, the father of the tumor that we are discussing. His series of five cases illustrating this lesion was among the earliest to be reported and his 1953 article in Cancer is one that I recommend that you should all read. I should like to name the tumor after him, but the designation "Bullock's Bosselations" might lose out against that of "Moran's mounds" or "Helwig's Hillocks." In any case, it appears that these lesions represent an unusual response to some gastric irritants to the extent that a tumor of granulation tissue results. Like others, Dr. Bullock compares the lesions histologically to certain granulomatous nodules found in the prostate.

There are perhaps twenty-five examples of this particular species of gastric polyp in the literature.

REFERENCE

Bullock, Weldon and Moran, Terrance: Inflammatory Fibroid Polyps of the Stomach. Cancer, Vol. 6:448-493, 1953.

CASE NO. 17 APRIL 14, 1962

ACCESSION NO. 11974

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Villous adenoma of the colon)

PATHOLOGY

The microscopic features of this growth (slide) show it to be a papillary neoplasm of the colon with delicate villous cores of connective tissue covered by one or more layers of cells. Under higher power (slide) these cells are seen to consist of a 50-50 mixture of mucous producing and mucus-free elements. Mitotic figures are present but not in any large numbers. The picture is that of hyperplasia rather than of malignancy. Slide 3 shows the mucous carcinoma that was neatly concealed in the center of the growth.

DISCUSSION

This growth is a villous tumor of the sigmoid and if any of your sections disclosed cancerous changes, their inclusion was my mistake. For it was my express purpose to confuse you on this issue and point up the necessity of thoroughly sampling these growths before pronouncing the benign verdict. This can rarely be done from a single section. On the very day last January when I was preparing this discussion, one of my slaves brought into the laboratory a 10 cm. villous tumor of the cecum. Considering myself somewhat of an expert on this tumor, on the basis of having studied two large series, I pronounced the lesion benign on the basis of four frozen sections. My fifth was on a node - and it was positive for metastasis. An embarrassed search was begun all over again. Originally regarded as being villous cancers by Rokitansky, Quain in 1855 emphasized their apparent benign behaviour and it was not until Bowman's report in the 1930's that emphasis was once again placed on their malignant potential. Not too much has been written concerning large series. Dukes' and Sunderland and Binkley have traced the growths in point of origin to proliferations involving the necks rather than the bases of colonic crypts.

The following are some of the highlights which I personally gained from a study of 84 villous cancers encountered over a 2 year period and of 63 benign villous adenomata over a 6 year period. The former represented 8% of all colorectal cancers and the latter 5% of all adenomatous polyps. There was ample evidence that the carcinomata commenced in adenomata. Even Ackerman's man "Friday" steered away from villous tumors in his nefarious pronouncements on the chastity of colonic polyps. Our incidence of cancer in villous tumors figures stands at about 75%.

The pathologist should be interested in several seemingly unimportant symptoms which relate to the pathology. One, seen in 18% of our patients, was severe and sometimes prostrating weakness. This is owing to loss of potassium in the rectal discharges. The second is the presence of excess mucus in the stools - a feature in 25% of the larger cancerous growths in this category.

Average duration of symptoms is a matter of 2½ years rather than the usual six month period of trouble from other types of colonic carcinoma. Blood may be noted in the stools - but the average hemoglobin reading will be 13/ grams per cent because the patients are chronically dehydrated. Grossly the distribution of lesions, the association of other polyps and cancers are about the same as for colorectal cancers and adenomas of the ordinary types.

The tumors are nearly always bulky and they may be recognized at a glance by their velvety surfaces, covered by bouquets of delicate villi, sometimes agglutinated by thick mucus. Fifty per cent of the malignant examples will lack the expected induration of cancer. When the latter is found grossly and microscopically, it is most likely to be encountered toward the center of the lesion where it may lie some concealed by the enveloping tendrils of surrounding villi. Peripherally, the lesions show convoluted velvety margins and the mucosa of the bowel about the lesions appears to exhibit gradual replacement by a similar process. This latter accounts for a high incidence of recurrence following local operative procedures and fulguration.

Nodes were positive in 40%. Proctoscopic biopsy correctly appraised the nature of the lesion in 60% only.

The study of our group of 63 villous adenomas added little except by way of establishing the villous adenoma to villous carcinoma sequence.

REFERENCE

Welch, J. S., and Dockerty, M. B.: Villous Carcinoma of the Colon. Diseases of the Colon and Rectum, Vol. 1, No. 4, July - August 1958.

Harp, R., Dockerty, M. B., and Waugh, J. M.: Villous Adenomas of the Colon. In press.

CASE NO. 18 APRIL 14, 1962

ACCESSION NO. 11975

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Invasive polyp of the colon)

PATHOLOGY

These sections were taken from a pedunculated polyp of the colon, 1½ cm. in diameter. The polyp possessed a stalk and a bulbous tip, neither of which disclosed any gross hint that malignancy might be present. The first slide shows the picture of adenoma with some cellular atypias. In the second section the glandular spaces are lined by cells of a much darker hue and these lack continuity with glands that are obviously benign. A scirrhous reaction is present in the stroma and this, to me, is practically diagnostic of invasive cancer since one does not observe it with in situ growths of the colon. My fourth slide - the "piece de resistance" is from a regional node which we received when the surgeon did our bidding and performed a resection following his preliminary transcolonic excision for what he considered a benign lesion.

DISCUSSION

We have just finished discussing the case of a villous adenoma or villous polyp of the colon and pointed out the malignant potential of this type of growth. Even Ackerman and his good man Friday gave the villous group of tumors a wide berth when they started their subversive innuendos regarding peaceful coexistence with polyps. Shortly after Ackerman's article appeared in 1958, I sent him material on three cases of metastasizing polyps. He accepted all three as being genuine and yet as late as 1960 in the journal "Diseases of the Colon and Rectum" he states "one of us (L.V.A.) has encountered no example of metastasis from cancers situated entirely within adenomatous polyps." Fortunately his 1960 article was followed by a better one written by San Francisco's Bob Scarborough, who as early as 1948 was able to report examples of five metastasizing polyps of the colon.

Helwig of the Armed Forces Institute and his illustrious namesake from Kansas City have had similar experiences. This is one of six personal examples that I have seen.

I do not believe that one must be old fashioned or dumb in order to follow the concept that very many colonic and rectal cancers have their origin in polyps that were at one time entirely benign. For what it is worth - here is my creed:

1. Adenomatous colonic and rectal polyps in a significant but unknown percentage of cases serve as the starting points for cancers of the colon.

2. Colons containing polyps show an increased tendency to develop cancers later. Whether the latter commence in the polyps or not is immaterial from the standpoint of the patient.

3. Polyps showing atypias up to and including in situ cancer can be treated by local removal.

4. Any polyp with invasion even confined to its tip is capable of metastasis and should be treated as a cancer.

5. The pathologist and the surgeon should understand each other's language when they discourse on polyps and the operative mortality of the latter should be lower than the incidence of metastasis in the early invasive category.

REFERENCE

Scarborough, B. A. and Klein, R. R.: Polypoid Lesions of the Colon and Rectum. American Journal of Surgery, Vol. 76:723-727, 1948.

Scarborough, R. A.: The Relationship Between Polyps and Carcinoma of the Colon and Rectum. Journal of Diseases of the Colon and Rectum, Vol. 3:336-342, July - August 1960.

CASE NO. 19 APRIL 14, 1962

ACCESSION NO. 12021

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Lymphosarcoma complicating chronic ulcerative colitis)

PATHOLOGY

My first slide is a gross photograph showing the removed colonic segment. The colon shows the gross changes of an old colitis. At the splenic flexure one notes not one but two huge ulcerative perforating growths. One is not surprised to find unusual appearing cancers in chronic ulcerative colitis nor growths which appear to be multiple. Microscopically, the next section is through the edge of the lesion. A sharp line of demarcation features the junction of benign and malignant tissue and the cells in the latter zone do not at this magnification appear to produce any architectural pattern. The next section is through the muscularis propria and it shows a veritable sea of small dark staining cells quietly replacing the smooth muscle fibers. In the next slide, at much higher magnification, the growth displays the monotonous mosaic of a malignant lymphoma. Several cells with multilobed nuclei are shown as examples of fairly typical Sternberg-Reed cells and my diagnosis, therefore, is Hodgkin's sarcoma complicating chronic ulcerative colitis.

DISCUSSION

Prior to the time of Yoeman's report in 1927, it was not believed that chronic ulcerative colitis was ever complicated by malignant change. Late in the 1930's Warren and Somers found no cases of carcinoma in a large series of patients with colitis. But scarcely had the ink dried on their report when Catell observed the first case at the Lahey Clinic. In 1949 Warren and Somers reversed their field and reported a 5% incidence of this complication. Others have had a similar change of experience. Why?

The answer appears to lie in better treatment of colitis with patients surviving into the cancer age. Also current emphasis is on surgical management and lesions that once were thought to represent strictures are now discovered at operation to be inoperable carcinomas.

In general, the colitis has been of long standing, the patients young on average, their cancers oftentimes multiple and viciously malignant. Salvage is poor.

But what of lymphoma as a complication? It appears to be rare. At the Clinic, we have seen only three examples including the one presented here. Cornes, Smith, and Southwood reviewing the literature in 1961 found a total of six cases including two from their own experience at St. Mark's Hospital in London. It is perhaps surprising that a condition like chronic ulcerative colitis which features so much lymphocytic infiltration does not more

frequently show the complication of malignant lymphoma.

Finally it is well to remember that primary lymphoma of the colon is rare as compared with the incidence of this lesion in the stomach and small intestine. Prognosis is best for lesions of the stomach and worst for lymphomas of the colon. You are all familiar, I am sure, with the confusing picture displayed by submucosal lymphoid nodules. One should diagnose these as malignant lymphoma only as a last resort.

REFERENCE

Cornes, J. S., Smith, J. C., and Southwood, F. T. W.: Lymphosarcoma in Chronic Ulcerative Colitis. British Journal of Surgery, XLIX:50-52, July 1961.

CASE NO. 20 APRIL 14, 1962

ACCESSION NO. 11864

CONTRIBUTOR: S. M. Rabson
Mission Hospital
Huntington Park, California

(Adenoacanthoma of colon)

PATHOLOGY

My first section on this case illustrates what appears to be an ordinary adenocarcinoma of the colon. It is a type B Dukes' in that the pericolonic fat is being invaded and it shows perhaps more fibrosis in the stroma that we like to see. It is, however, not nearly as scirrhous as the tumor we discussed in connection with Case 12.

The contributor in this case was quite discerning because, scattered here and there were tiny foci in which the cells exhibited "burned bridges." By this I mean that all but the most doubting of Thomases would accept them as being examples of squamous cells. They are shown in the next two slides, the first of which displays transitions between glandular and squamous elements.

My diagnosis is adenoacanthoma of the colon.

DISCUSSION

If I were going to write an article on colonic adenoacanthoma, I would consult the literature on uterine and ovarian cancer on the one hand and of gallbladder cancer on the other. This literature will provide series of cases describing how primitive regenerating cells can differentiate along glandular and squamous lines simultaneously. On the other hand, I know of no series describing this interesting mixture of malignant elements in colonic growths. In connection with various thesis studies, I have personally been over many thousands of slides on colorectal cancers and this is my sixth exposure to a tumor of this type. Interestingly enough, two of them were in the colons of patients with chronic ulcerative colitis. Bryan Brooks among others emphasizes the atypical epithelial changes that occur in the healing processes of this ulcerative disease and he illustrates squamous metaplasia - both benign and malignant.

In none of the cases which I have been privileged to study did the squamous component appear to arise from a benign counterpart. And, in the cervix at least, squamous metaplasia is not at all regarded as being a precancerous lesion. Moreover, an adenoacanthoma in any organ, may metastasize as a squamous cancer, a glandular cancer or it may maintain its peculiar cell mixture of squamous and glandular elements in its secondary nodules.

Finally, some literature to the contrary notwithstanding, I do not feel that the presence of squamous cells in a glandular cancer of the colon or of any other site, confers on its host a better prognosis.

REFERENCE

Brooks, Bryan: Malignant Change in Chronic Ulcerative Colitis. Journal of Diseases of the Colon, Rectum, and Anus, Vol. 4, No. 6:393-399, Dec. 1961.

Dockerty, M. B.: Primary and Secondary Ovarian Adenoacanthoma. Journal of Surgery, Gynecology, and Obstetrics, Vol. 99:392-400, Oct. 1954.

CASE NO. 21 APRIL 14, 1962

ACCESSION NO. 12019

CONTRIBUTOR: C. P. Schwinn
Los Angeles County Hospital
Los Angeles, California

(Adenoacanthoma of stomach)

PATHOLOGY

Slide 1 shows an obvious adenocarcinoma underrunning the esophagus. This finding is of extreme importance since glandular cancers in this area have about one sixth as good a prognosis as do squamous cell carcinomas in the same location. We are currently studying a series of cases in an effort to discover the whys and wherefores of this well established fact. Slide 2 - surprisingly enough shows a squamous cell carcinoma. In slide 3 there is an intimate admixture of both squamous and glandular elements. In slide 4 an elastic imagination coupled with my muddy photomicrograph might bring some of you to the conclusion that primitive basal cells were differentiating into both glandular and squamous elements.

DISCUSSION

Being, as you have already discovered, old fashioned, I chose to call this lesion an adenoacanthoma rather than pile on to the mucoepidermoid band wagon. For after all is said and done, what is a mucoepidermoid other than a mucous adenoacanthoma? The squamous component in our tumor today is epidermoid, all will admit, but the glandular component is not mucous cancer by the average stretching of the imagination.

I have seen six other cases of gastric adenoacanthoma and reviewed Wood's report in 1943 dealing with this interesting entity. He was able to collect some 19 cases of gastric cancer featuring squamous elements; 9 were pure squamous and 10 were adenosquamous. Seven of these were pyloric rather than gastroesophageal. Wood added 2 personal cases to bring the total to nine. The reports of Straussman and of Milanes concerned more recent individual case documentations of pyloric adenoacanthomas. Two of our own 6 cases were pyloric and 4 were cardio-esophageal. It would thus appear, and somewhat paradoxically so, that the lesions occur almost as frequently away from as at the squamo-columnar junctional zone at the lower end of the esophagus.

With respect to pathogenesis much remains to be learned. Benign squamous metaplasia is not found in coexistence with gastric adenoacanthomas.

Squamous cell rests are likewise very rare in the stomach. One might well conclude with Wood and with Broders that undifferentiated basal cells in the gastric mucosa proceed in both glandular and squamous directions in generating the neoplasms under discussion.

REFERENCE

Bellegie and Dahlin: Proceedings of the Mayo Clinic 1951, Vol. 26. Two cases.

Wood, D. A.: Archives of Pathology, Vol. 36:177-189, 1943.

Strassman: Archives of Pathology, Vol. 41:213-219, 1946.

Milares: Gastroenterology, Vol. 15:518-522, 1953.

CASE NO. 22 APRIL 14, 1962

ACCESSION NO. 11968

CONTRIBUTOR: Weldon K. Bullock
Los Angeles County Hospital
Los Angeles, California

(Grade IV scirrhous mucous adenocarcinoma of colon)

PATHOLOGY

My first section shows mucosal involvement by a malignant process which features large numbers of signet ring cells. There appears to be a very abrupt transition from benign to malignant in contradistruction to what we observed in Case 12. In section 2 we note invasion of the pericolonic fat with signet ring cells which are almost arranged in single file. A fibroblastic reaction in the stroma is obvious. In slide 3 we note invasion of the wall of what appears to be a vein. In my last section, signet ring cells are seen growing singly, in small clusters, and in single file among the nerves and ganglion cells of the myenteric plexus.

My diagnosis is grade IV scirrhous, mucous adenocarcinoma of the colon.

DISCUSSION

As mentioned in connection with Case 12, whenever we encounter an anaplastic mucous carcinoma of the colon or rectum, we should have the surgeon carefully explore the stomach and pancreas. For metastatic cancers originating in upper abdominal location, can mimic primary carcinoma of the bowel. I assume that such a situation did not obtain here and I should like to discuss briefly with you primary scirrhous carcinomas of the colon.

Cancers ordinarily destroy their hosts by impeding the functions of tissues or organs in which they originate or to which they metastasize. In addition, certain neoplastic cells excite a profound hyperplasia of the connective tissue matrix in which they lie. The cells in this desmoplastic reaction are not in themselves malignant but by contributing to the bulk of the neoplasm they share in major degree in the production of its lethal effects.

Fibrosing or scirrhous cancers of the breast and stomach are common place. Comparable degrees of scirrhosity are rarely reported in the colon.

Almost 1% of 12,000 surgically resected colons screened by Fahl and myself exhibited a scirrhous reaction comparable to that seen in linitis plastica. There were three gross types - 10% exhibited a sleeve-like lesion which involved long segments of the bowel. The lumen was narrowed like the spout of a funnel. There was little by way of mucosal ulceration. Thirty per cent displayed a napkin ring type of growth featuring stony hardness and a tendency towards annularity.

In the remainder, the growths were ulcerative and not unlike those ordinarily seen in the colon. However, they were indurated on cut section and the involved nodes were hard and shotty.

Seventy-five per cent of these scirrhous cancers involved regional lymph nodes and not a single growth was confined to the bowel wall proper. The grading of the growths was almost the reverse of that seen in a control series. There were five times as many grade IV as there were grade I neoplasms by the Broders rating. Five-year survivals were less than half as good as one would expect for colonic cancer and this in spite of an average small size.

In the experimental field, Simpson and Bensley have shown that certain embryonic cells produce mucolytic enzymes which induce two side effects - namely (1) a spreading factor which promotes metastasis in experimental cancers; (2) a rapid proliferation of fibroblasts which undergo early collagenization. It is postulated that our scirrhous cancers of the colon operate on this basis.

REFERENCE

Simpson, W. L.: Mucolytic Enzymes and Invasion by Carcinoma. Ann. New York Acad. Sc., Vol. 52:1125-1132, 1950.

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CASE NO. 23 APRIL 14, 1962

ACCESSION NO. 12023

CONTRIBUTOR: Francis S. Buck
Los Angeles County Hospital
Los Angeles, California

(Leiomyoma of the lesser omentum)

PATHOLOGY

Slide 1 in this case shows the tumor to be a spindling growth of only moderate cellularity. The cells in this area appear to be ranging up in a peculiar fashion around vascular clefts, and the diagnosis of hemangiopericytoma is at once suggested. In section 2 on the other hand, one is struck by the bipolarity of cells with cigar-shaped nuclei displaying rounded ends. There is a prominent tendency for these nuclei to line up in rows or palisades. In slide 3 the cytoplasm of the tumor cells is seen to be granular and somewhat basophilic. No mitotic figures are depicted because none were found.

My diagnosis is leiomyoma of the omentum.

DISCUSSION

Golden and Stout in 1944 brought order out of chaos when they wrote their now-famous article on smooth muscle tumors of the gastrointestinal tract and retroperitoneum. They pointed out, among other things, that retroperitoneal leiomyomatous tumors were rarely benign. In their series of nine tumors of this type, 8 were symptomatic and 6 of these were malignant. They felt that it was rather hazardous to certify as being benign any myomatous retroperitoneal tumor except the small incidental ones found at necropsy. Like Evans, who did his studies on uterine myomas, Stout felt that the presence of mitotic figures decided the issue of malignancy in these growths. Because the life history of the tumors was so long, they favoured the designation of malignant myoma over leiomyosarcoma.

In the matter of differential diagnosis, they observed that nuclear palisading was frequently displayed by myomatous tumors in these locations. Previous investigators had expressed the view that such palisading was indicative of a neurofibromatous nature.

Retroperitoneal and omental tumors of this type quite often assume large dimensions. The larger the tumor the greater the likelihood of its being malignant. Both benign and malignant myomas of the retroperitoneum are prone to undergo cystic degeneration and necrosis. Such degenerated tumors frequently contain bizarre giant cell forms which, in the absence of mitotic activity, do not denote malignancy.

ACCESSION NO. 12023

Both benign and malignant tumors in these areas are prone to invade vital structures by direct extension and thus create lethal hazards for the surgeon attempting removal. Operative mortality is said to be in the neighborhood of 40%.

REFERENCE

Golden, Theodore and Stout, Arthur Purdy: Smooth Muscle Tumors of the Gastrointestinal Tract and Retroperitoneal Tissues. Surgery, Gynecology, and Obstetrics, Vol. 73:784-810, 1941.

CASE NO. 24 APRIL 14, 1962

ACCESSION NO. 11988

CONTRIBUTOR: Dominic A. DeSanto
Mercy Hospital
San Diego, California

(Leiomyosarcoma of the stomach)

PATHOLOGY

The low power view of a typical zone in this tumor shows a neoplasm that looks malignant on the basis of cellularity. However, it lacks the glandular or alveolar pattern that we expect in a gastric cancer. On the "zoom-up" of the next slide, we observe that the cells are basically spindling elements. This at once rules out malignant lymphoma and makes us think of leio, fibro, or angiosarcoma. In the next slide, we note cytoplasmic granularity with a basophilic staining in a picture which is quite reminiscent of a myogenic tumor. In my fourth slide, two mitotic figures are depicted. Mitotic figures are most important discoveries in a smooth muscle tumor because one very seldom finds more than a very scattered one in benign myomas.

My diagnosis on this tumor is moderately anaplastic leiomyosarcoma.

DISCUSSION

Ninety-eight per cent of primary gastric malignancies are cancer of one type or another. The 2% sarcomatous residue includes lymphosarcoma, leiomyosarcoma, angiosarcoma and others. Myosarcomas make up 25% of this residue. These growths deserve a "minority report" because they are large tumors affecting young individuals. Fifty per cent of them induce alarming hematemesis and melena. In spite of a large size they can usually be removed and 5-year survivers are better than 50%.

I have had the privilege of personally studying material from 40 cases of gastric leiomyosarcoma and would like to give you an abstract of the findings. The work was done in collaboration with Dr. Ray Giberson, one of our fellows in surgery. The period of study was from 1907 - 1952.

The average age of these 40 patients was 45 years and 8 of them were under 30. Gross massive bleeding from the gastrointestinal tract was the major complaint in 50%. Twelve had noticed an abdominal mass. The remainder complained of indigestion. Laboratory-wise the average hemoglobin was 10 gm. One pale-faced patient, 10 years of age, came in with a hemoglobin of 5 gm. Two years previously he had had his spleen out for a refractory anemia.

The roentgenographic picture was often that of a smooth, bulging, endogastric mass frequently surmounted by one or more ulcers which led down into barium-filled pockets within the tumor substance.

At surgery, 37 of the tumors (which averaged 10 cm. in diameter) were resectable; 34 with hope of cure. In 6 there was evidence of spread to the liver or to the peritoneum.

Grossly, the tumors were large and globular or lobulated. Five were pedunculated and endogastric, the remainder were either dumb-bell growths or growths which were mostly exogastric.

Twenty-three of them showed the presence of one or more deep crateriform ulcers over the mucosal aspects of the tumors. This phenomenon of ulceration was related to the history of hematemesis and melena. In several specimens the only solid remains of tumor tissue consisted of a peripheral rind in a growth which had undergone liquifactive necrosis and evacuated itself through the area of superficial ulceration. Microscopically, the picture varied with most of the tumors being moderately well differentiated. Seventeen of 22 non-metastasizing tumors were of a low grade of malignancy. At least one mitotic figure per high power field was present in each of 18 metastasizing leiomyosarcomas of the stomach. Lymph nodes were rarely involved other than by direct extension, but in at least 12 patients the liver developed secondaries before the patient succumbed.

Five-year survivals were 54%.

REFERENCE

Golden, T., and Stout, A. P.: Smooth Muscle Tumors of the Gastrointestinal Tract and Retroperitoneal Tissues. Surgery, Gynecology, and Obstetrics, Vol. 73:784-810, 1941.

Giberson, R. G., et al: Leiomyosarcoma of the Stomach. Surgery, Gynecology, and Obstetrics, Vol. 98:186-196, Feb. 1954.

CASE NO. 25 APRIL 14, 1962

ACCESSION NO. 12078

CONTRIBUTOR: Malcolm B. Dockerty
Mayo Clinic
Rochester, Minnesota

(Superficial carcinoma of stomach)

PATHOLOGY

Slide 1 is a low power view of gastric mucosa in which the glandular architecture is extremely disturbed. Benign gastric glands are in evidence at the bases of the gastric pits but the typical mucous glands which should cover the surface are replaced by cells which are quite dark staining. The process appears to be limited to the mucosa. In slide 2 benign glands are observed lying side by side with others in which cell stratification and mitotic activity are evident. In slide 3 the cells comprising the gland-like structures are cytologically malignant. Slide 4 is for the doubting Thomases. It reveals metastatic cancer in a lesser curvature lymph node.

DISCUSSION

This is an example of an unusual form of gastric cancer variously termed superficial cancer, superficial spreading cancer, carcinoma en nappe, "le cancer gastrique a marche lente" the German designation requires more saliva to pronounce than I can possible muster at this time and so I shall not try to disgorge it.

I put the case in because I have just completed with Dr. Friesen a study on 65 preserved specimens of the entity which accounts for about 1% of all gastric malignant neoplasma.

Clinically 60% of the patients gave an ulcer type of history - sometimes of long standing. Anemia was rare - the mean hemoglobin value being 13.8 gm. Gastric acids were usually elevated and only seven of the 65 patients exhibited the achlorhydria which one expects to accompany carcinoma of the stomach. Eight gastroscopic examinations were negative for cancer and cytologic studies done on the last two patients were positive in one after we re-studied the slides using the retrospectoscope.

X-ray diagnoses read like Russian double talk. Some roentgen abnormality was noted in 55, but in less than half of these was a diagnosis of cancer strongly suspected.

The correct diagnosis was rarely obvious to the surgeon and was definitely made by fresh frozen sections in each of the 65 cases. On more than one occasion it was necessary to hurry back to the operating room and inform the surgeon that he was about to sew cancer-to-cancer in the proximal

rim of his partial gastrectomy.

The following 5 or 6 slides show graphically why this type is difficult to diagnose clinically, surgically - and even grossly. In 48 instances the malignancy presented as one or more, usually large, irregularly outlined, depressed areas, surrounded by elevated folds of normal mucosa. Superficial erosions often were found in zones of malignant involvement and these erosions were frequently covered by a rather thick tenacious mucopurulent exudate. In the remaining 17 specimens the same general picture prevailed, but what appeared to be typical peptic ulceration was present in a more or less central position with respect to the depressed expanse of malignant involvement. In two lesions, total gastrectomy was necessary in order to achieve cancer free margins. The average size of the remaining lesions was large with measurements of up to 30 square centimeters in 75% of the specimens. In spite of the superficial character of the lesions no less than five were associated with positive nodes.

Multicentricity was common and it indicated the probability of a "field development" of this type of lesion. The presence of positive nodes in two cases in which there was apparent confinement to the mucosa taught me the difficulty of deciding that any of these gastric cancers were examples of in situ growths.

The most interesting facet in the study concerned the five-year survivals. The operation mortality was 5% and one patient was lost to follow. The five-year survival in the remainder was a whopping 93%. However, four of our five-year survivors died from recurrent or metachronous gastric cancer before the ten-year mark had been reached.

REFERENCE

Friesen and Dockerty: Superficial Carcinoma of the Stomach. Surgery, Vol. 51, No. 3:300-313, March 1962.