Set 60

# SEMINAR
# on
# DISEASES OF COLLAGEN

Presented by
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Sponsored by
The Indiana Association of Pathologists
and
The Veterans Administration Hospital,
Indianapolis, Indiana

Conducted at
The Veterans Administration Hospital
1481 W. 10th. St.,
Indianapolis 7, Indiana

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9:30 A. M.

NOTE: Due to unforseen difficulties, it has not been possible to include in the slide sets typical examples of all the lesions in the following cases.

However, it is expected that Dr. Klemperer will offer a complete discussion of this group of diseases and will illustrate all phases of the pathologic anatomy with lantern slides.

RHEUMATIC FEVER: HEART and other organs.

CASE I: Presented by I.U.M.C.
R-1963

This ten year old white boy was first diagnosed as having rheumatic heart disease in March, 1948. This was thought to be his first episode of rheumatic fever. About Thanksgiving, 1948 the patient developed a cold in his chest and had since been in bed with weakness, loss of appetite and orthopnea. A swelling of the ankles and dyspnea developed five days prior to admission. There had been an intermittent fever but no joint pains nor epistaxis. Examination at the time of admission revealed a pale patient who appeared cyanotic, markedly orthopneic and weak. Jugular veins were distended. Coarse rales were heard in the left chest. Precordium was moderately active, revealed the presence of a systolic and diastolic murmur at the apex. The systolic thrill was palpable. BP was not obtainable. The liver was four inches below the costal margin. The spleen was palpable. There was a 4 plus pitting edema of the ankles. Death occurred shortly after the patient reached the ward.

Autopsy findings referable to the heart revealed an acute pancarditis plus shortening of the chorda tendineae of the left ventricle and a moderate insufficiency of the mitral valve. There was an acute valvulitis involving the mitral, aortic and tricuspid valves. In addition an articular fibrinoid degeneration was found in the peri-adrenal tissue, myocardium, endocardium and pericardium.

Pathology: Bowel & Kidney -

CASE II: L27-92 Autopsy case of Dr. Edw. Smith.

A 33 year old white man was admitted with the chief complaints of nausea, vomiting and painful swelling of the joints of the hands, elbows, knees and ankles of one week's duration. During this time the patient had also noted a fine petechial rash over the trunk and extremities and had noticed the onset of watery stools containing black material and bright red blood. Past history revealed that the patient had had a streptococcus sore throat four weeks prior to admission but with complete recovery. No other pertinent history was obtainable. Physical examination revealed a well developed, well nourished, white man thrashing about and moaning as in evident acute distress. The abdomen was tender with some splinting on the right. The temperature was elevated. There were petechiae over the legs and ankles and a few over the back and forearms. During the hospital course the abdomen remained tender and the temperature remained elevated averaging between 101 and 102 degrees. A diagnosis of acute regional ileitis with mechanical obstruction was entertained and exploratory laparotomy was performed. At that time a considerable amount of peritoneal fluid was found. The small bowel was distended and the bowel wall throughout the entire small intestine was thick and edematous. There was one area in the duodenum and another in the jejunum which were extremely discolored and there was a question as to viability. The condition of the remaining bowel was such as to preclude any definite surgical therapy. The mesentery contained many moderately enlarged lymph nodes. The operative impression was that of an acute regional ileitis with involvement of the ileum and jejunum. No definite obstructive lesion could be found. Following surgery the patient was placed on ACTH and demonstrated at first a temporary improvement. However, he continued on a downhill course and expired on May 26, 1951, approximately one month after admission.

Laboratory data: The hemoglobin averaged 9.5 grams, the WBC 15,000 and the differential demonstrated a marked shift to the left. The NPN the day before death was 175. The urine culture was positive for gram negative bacilli. Urinalysis demonstrated a specific gravity of 1.014, a heavy trace of albumin, 50-60 pus cells, and was loaded with red cells. Serology was negative. Repeated blood cultures were negative with the exception of one taken on April 27, 1951 which demonstrated a paracolon bacillus. The pertinent gross autopsy findings revealed petechial hemorrhages over the abdomen and legs. There were 3,000 cc of straw colored ascites in the abdomen. The large bowel seemed normal. The duodenum was pale lavender in color and was covered by many petechiae. The mucosa in this area was grossly hemorrhagic and appeared necrotic. Numerous 1-2 cm. nodules projected above the mucosal surface in the same segment. The mucosa in this area was grossly hemorrhagic and appeared necrotic. Numerous 1-2 cm. friable elevations projected above the mucosal surface in the same segment. The jejunum and ileum showed the same changes but they were apparently of lesser severity. The kidneys were twice normal in size and contained numerous petechiae over their surfaces. Both adrenal glands showed foci of coagulation necrosis. The pericardium and great vessels were essentially normal. The right heart was dilated. There were petechial hemorrhages covering the entire myocardial and endocardial surfaces. There were several noted on the valve leaflets.

LUPUS NEPHRITIS.

CASE III: Presented by South Bend Medical Foundation.

A50-311 N,B., salesgirl age 27. First admission to the hospital 9-26-50, with the complaint of swelling of feet and ankles of a few weeks duration. Blood pressure 152/102. Marked paller of the skin and edema of the extremities was noted. The temperature varied from 98 to 101 degrees. RBC 2,900,000, WBC 4,500, hemoglobin 8.2 grams %, polys 75%, lymphocytes 23%, monocytes 2%. A diagnosis of subacute nephritis was made. Three blood transfusions were given, and the patient was discharged slightly improved after three weeks. On 11-14-50, she was again admitted with the history of having become gradually worse during the interim. Edema had become more severe. A macular erythematous rash appeared on the legs, arms and trunk; the lesions were round, discrete and barely palpable, although some had slightly elevated borders; the face was not involved. Petechial lesions were noted on the legs. Joint pains had developed but were not severe. Fundoscopic examination showed slight edema of the optic discs. RBC 2,260,000, WBC 2,800, hemoglobin 6 grams %, BUN 127 mg. %, total protein 3.3 grams, albumin .9, globulin 2.4, AG ratio .38 to 1. Generalized anasarca developed. The spleen was palpable. Cortisone therapy was started on the day before death which occurred 11-21-50.

SCLERODERMA (several organs)

CASE IV: Presented by South Bend Medical Foundation.

A-50-84 P,A. W. F. age 70 years, first seen by admitting physician three weeks previously when the following history was obtained: Semi-invalidism for 15 years, said to be due to hypertrophic arthritis; progressive inanition and anorexia which became marked in the previous two weeks. Recent purulent drainage from the right ear responded to antibiotic therapy. On admission to the hospital, examination revealed a lethargic, deaf, emaciated woman with a blank fixed expression. All muscular movements were slow and limited. Pain was denied. The skin appeared atrophic with almost complete loss of elasticity. There was induration of the skin and subcutaneous tissues of the upper lip and chin. Inelasticity was more marked in the regions of the genitalia and rectum. The external ear canals were edematous and almost completely closed; a purulent discharge was coming from both canals. The tongue was not enlarged, but it was red and dry. Blood pressure was unobtainable in either arm. The pulse was regular, the rate 120. The heart sounds were of good quality. The joints were stiff but were not enlarged. The fingers were fixed in a position of flexion. The radial pulse was felt in both wrists, but the posterior tibial arterial pulsations were absent. On the day of admission, she began to have considerable abdominal pain. An x-ray of the chest revealed air under the diaphragm. Laboratory findings: Urine specific gravity 1.010, albumin 2 plus, blood urea 148, red blood count 5,400,000, hemoglobin 14.8 grams, white blood count 30,900, polys 89%, nonsegs 30%, monocytes 10%, lymphocytes 1%. Death occurred 24 hours after admission.

Autopsy: No evidence of arthritic disease was observed. Skin changes were as described previously. Two small perforations were observed in the ascending colon which were sealed with fibrinous exudate. All of the peritoneal surfaces, but particularly those of the small intestine and its mesentery, were the site of a mottling with tiny white spots which appeared to follow the blood vessels or lymphatics. On separation of the small intestine from its mesentery, the blood vessels stood out as thick-walled rigid structures. The kidneys were extremely contracted and granular. The same thickening and rigidity of the vascular structures were present in nearly all the viscera including the heart. The central nervous system, however, showed no significant vascular changes.

RHEUMATOID NODULE, SUBCUTANEOUS

S-51-1340

CASE V: M. R. 55 year old white farmer.

This 55 year old white farmer was seen in the hospital four times between August, 1949 and November, 1951. Each time he came in with severe congestive heart failure which was apparently controlled with some difficulty by digitalization and mercurial diuretics and other auxiliary therapy. When he was first admitted in 1949 a large cardiac border outline could be made out but with response to therapy the cardiac outline became normal once more. Physical examination of the chest revealed no murmurs, no thrills and no other clinical evidence of intrinsic cardiac disease. Electrocardiograms, aside from showing the presence of fibrillation, did not indicate myocardial disease. Physical examination during these admissions revealed hepatomegaly and bilateral enlargement of the breasts and evidences of congestive heart failure of severe degree. The findings associated with congestive heart failure all receded with response to the therapy. During the last admission 11/8/51 the only additional physical finding was the presence of numerous subcutaneous nodules along the flexor surfaces of the forearm and behind the elbow. Some of these nodules were in close approximation with one another so as to form small groups. The subcutaneous nodules ranged in size from 1 to 3 cm. in diameter.

PAST HISTORY: The patient denied rheumatic fever, scarlet fever, chorea, growing pains or epistaxis as a young man. However, the only pertinent history related to the onset in 1940 at the age of 45, of pain in the shoulders not associated with chest pain or dyspnea. In 1942 he had a painful swollen right hand and foot for which he was hospitalized for four to five weeks. Since then he has had recurrent pains of wrists and knees; these have not been associated with the swelling.

LABORATORY DATA: The hemoglobin stayed during all these admissions about the level of 14 grams. The WBC was within normal limits as was the differential. Urinalysis reveals specific gravities as high as 1.025. Albumin was present on only one occasion and at that time was 1 plus. There was no sugar and there were no red cells noted in the urine. White blood cells were noted on each admission and ranged from 6 to 8 per high power field to loaded. Total proteins were 6.5 grams with 4.7 grams of albumin and 1.8 grams of globulin. Serum cholesterol was 67 mgms. % and the esters 107 mgms. %. The thymol turbidity was 7 units in December, 1949 and the thymol flocculation was 2 plus. One year later the thymol turbidity was 5.5 units and the thymol flocculation was again 2 plus. The bilirubin was normal. A glucose tolerance test was normal.

X-RAYS: X-rays of the spine, knees and ankles revealed marked hypertrophic arthritic changes. Cardiac fluoroscopy revealed a normal cardiac silhouette in March, 1951 and there were good pulsations and no valvular calcifications were seen. A biopsy of one of the subcutaneous nodules was performed in November, 1951.

SCLERODERMA (several organs)

CASE VI: 13358 - submitted by Dr. Paul Klemperer,
Mt. Sinai Hospital, N. Y.

This was the second admission of a 49 year old white female whose chief complaint was stiffness of the skin and joints and burning sensations for two and one-half years. About four and one-half years before the patient had noticed onset of paresthesia and cyanosis of the hands and toes when exposed to cold temperature. The skin was otherwise unchanged at that time. Two and one-half years before admission edema of the hands appeared and they became stiff. The process subsequently affected the feet and was accompanied by hyperpigmentation of the involved areas. Substernal burning sensation after meals, edema of the ankles and twenty pounds of weight loss had been noted in the past year. Five months before admission the skin of her face was found to be hard and tight and there was difficulty in mastication and talking. At that time the BP was 190/70; the stool was guaiac positive on many occasions. X-rays showed disturbed esophageal peristalsis both pulmonary basis where a finely infiltrated and slight osteoporosis was noted in the hands. The sedimentation rate was 68 and the BMR normal. Mecholyl iontophoresis for two months gave no favorable results and progesterone (10 mgms. daily) given during one month apparently caused some softening of the skin. The drug was discontinued because of severe nausea. This was all on the previous admission to Mt. Sinai Hospital and the patient at that time was discharged essentially unimproved. In the three months between admissions, the symptoms progressed rapidly; there was marked limitation of motion of the joints, low grade fever up to 101.6 degrees was noted and the previous complaints persisted. On admission the last time her condition was grave. The soft tissues were markedly stiffened, the skin was bronzed and there were numerous achromic striae over the abdomen and legs which were thickened, hardened and leather like. The BP was 190/100. The lungs showed exaggerated breath sounds; the liver edge was palpable two fingers below the right costal margin; the deep reflexes were hyperactive. The joints showed limitation of motion. The temperature was 100. The hemoglobin was 39 per cent. The red count 2.7 million, the BUN 14 mgms. per cent, calcium 9.7 phosphorus 2.9. EKG was negative. X-rays revealed no peristaltic activity in the esophagus without dilatation and a tendency for segmental distribution and delay in the small intestine. Chest x-ray revealed cardiac enlargement and suggestive congestion in both lungs with a faint infiltration in the right lower lobe. In the hospital the temperature ranged between 101 and 105. The patient developed rales in both basis and received penicillin without favorable results. On the 35th. hospital day the patient was dyspneic, cyanotic and unresponsive. She was placed in an oxygen tent and developed Cheyne-Stokes respiration and gallop rhythm. On the following day the patient was in frank pulmonary edema and died.

16 d

LUPUS ERYTHEMATOSUS (several reports)

CASE VII: 14417 - submitted by Dr. Paul Klemperer,
Mt. Sinai Hospital, N. Y.

This is a 43 year old white seamstress with negative past history except for pneumonia at the age of 9. Four years before admission she had developed weakness and diffuse arthralgias and one year before admission was hospitalized elsewhere for fever, severe anemia and leukopenia with normal platelet count. At that time there were transient bilateral pleural effusions and she received several transfusions and was somewhat improved. Fever, weakness and anemia recurred five months before admission and a typical butterfly rash appeared. Two months later the patient became bedridden because of severe muscle and joint pains with limitation of motion and there continued to be fever, weight loss and severe debilitation. On admission the temperature was 104.4, the pulse 135, the respirations 32 and BP 120/50. She was somewhat disoriented, emaciated and appeared acutely and chronically ill. There were moist, bilateral, basal rales. The heart was hyperactive and a grade III systolic murmur was heard at the apex and at Erb's point. The skin showed an erythematous, macular, supra-orbital eruption, diffuse malar flush, a maculopapular and pustular eruption over the neck and the V of the chest and red and brown macules over the abdomen and chest. Marked muscular wasting of the extremities with marked tenderness was noted. There was fusiform deformity of the knees and elbows with limitation of motion in all joints because of severe pain. The extremities showed 2 plus edema, hyperreflexia was present and there was an equivocal Babinski reflex. The laboratory findings were: hemoglobin 4.6 grams, red blood count 2.4 million, platelets 50,000 to 275,000, WBC 5,700 to 17,800 with 71 segs and 20 non segs. The PSP test showed 15% retention and the concentration test 1.016. The sedimentation rate was 147 mm. There were lupus cells in the sternal marrow. The urine contained some albumin. The formol gel test was positive. The blood contained staphlococcus aureus. A/G was 2.4 over 4.9. Chest x-ray showed basal bilateral pleural exudate. There was questionable slight narrowing of the left elbow joint. EKG showed left axis deviation and low T-1. Skin biopsy showed no significant change and muscle biopsy showed atrophy. The temperature varied from 101 to 103 and a number of transfusions were given. At first the condition remained stationary but later deteriorated rapidly. Signs of pneumonia and friction rub were present at the left base and bilateral purulent kerato-conjunctivitis appeared. The edema increased and gallop rhythm was present. Treatment with penicillin, aureomycin, antihistaminics and digitalis was unavailing and the patient died two months after admission.

Lupus vs TTP (several organs)

CASE VIII: 14423 - Submitted by Dr. Paul K emperer,
Mt. Sinai Hospital, N. Y.

This was the first admission of a 31 year old white female with complaints of fever, painful swelling of joints, rash and weakness of three months duration. Seven years previously she had been hospitalized elsewhere for subcutaneous hemorrhages, bleeding from the gums and menorrhagia. Thrombocytopenic purpura was diagnosed and a splenectomy performed. Six weeks after surgery her platelet count was 55,000 and the hemoglobin 64%. She was well until three months before admission when she developed daily evening fever to 102 degrees. The knees, elbows, ankles, wrists and small joints of the hands became painful and there were swelling and effusion of the left knee and elbow. A butterfly rash appeared, aggravated by exposure to the sun and the hands became blotchy red. There was gradual loss of strength. On physical examination the BP was 104/58 and the temperature 102, the pulse 88 and respirations 24. Butterfly rash, edema of the eyelids and chapped sore lips were noted. Bilateral cervical lymphadenopathy was present. A soft systolic murmur was heard at the apex and along the left sternal border, P-2 greater than A-2. The hemoglobin was 9.1 grams, the red blood count 3.6 million, white blood count 3,900 with 65% neutrophils. The platelets were 245,000. Sedimentation rate 38, bleeding time 4 minutes, clotting time 20 minutes, tourniquet test positive. Stool guaiac was slightly positive. Urine concentrated to 1.014 and contained 1 to 3 plus albumin and occasional red blood cells. BUN was 19 to 38 and thymol turbidity 2 plus. The albumin was 2.9 and the globulin 4.6. L. E. cells were seen in the marrow. EKG showed low voltage and terminally the PSP totalled 46%. The temperature spiked daily to 103-105. Skin lesions progressed and nausea, pleural effusion and abdominal tenderness appeared. Treatment was with aspirin, testosterone, penicillin and sulfa drugs. Delirium and hallucinations appeared late and the patient died one month after admission.

PERIARTERITIS NODOSA (several organs)

CASE IX: 14988 - Submitted by Dr. Paul Klemperer,
Mt. Sinai Hospital, N. Y.

This 64 year old white man was well until seven years before admission when he had a one month episode of urticaria of the hands and face. Six months later pain and swelling of the joints of the hands appeared with subsequent involvement of the knees, ankles, shoulders and elbows. The arthritis progressed and he was treated later with gold, ACTH, cortisone, and liver injections. Two months before admission numbness, paresthesia and weakness of his feet and legs appeared and the gait became unsteady. The legs became edematous and occasional bloody and frequent tarry stools were noted. Two weeks before admission hypertension appeared and cortisone was discontinued. The patient was very pale, thin and cachectic. The fundi were normal. The neck veins were distended and filled from below. The lungs were clear and the heart not enlarged. Pulse 120. Heart sounds were distant and a short, blowing, systolic murmur was heard at the apex. BP 130/60. Liver 2 cm. below right costal margin. Small hemorrhagic crusted lesions were seen over the right foot and arm, evidence of deforming arthritis of numerous joints. Legs showed marked pitting edema and the calf muscles were tender. There was definite evidence of peripheral neuropathy of the lower extremities. Urine was essentially negative. The STS was negative. The hemoglobin was 10.2 grams and RBC 3.76 million. WBC was 12,500 with normal differential. Blood chemistry normal, serum albumin 2.5, globulin 3.9 and formol gel test negative. Sedimentation rate varied from normal to 128 mm. No L-E phenomenon in peripheral blood. Stools contained occult blood. Prothrombin time was prolonged but bleeding workup was otherwise negative.

X-ray suggested old tuberculosis in right upper lobe. GI x-rays were negative. X-rays of bones and joints showed narrowing of joint spaces and pseudocystic degeneration with osteoporosis of bones of arms.

Repeated bone marrows showed cellular marrow and 9-11 mature plasma cells. Bone biopsy essentially negative. No Bence Jones protein. EKG - evidence of old myocardial infarction. Spinal fluid was normal. Biopsy of skin and muscle of right calf showed acute myositis with prominent degenerative muscle changes and a vasculitis which is also seen in the deep corium and subcutaneous tissues. Biopsy from arm showed similar changes in muscle but none in the skin. Course characterized by intermittent episodes of fever, and involvement of various organ systems. Edema subsided with salt restriction. One week after admission there were purpuric lesions on the skin of the right leg. These became confluent, necrotic and sloughing to involve the skin, subcutaneous tissue and muscle. During the next week there was an acute abdominal episode with leukocytosis of 20,000 which subsided on supportive management. The next week neuropathy had involved the hands also. After four weeks in the hospital, there was an attack of paroxysmal auricular fibrillation. ACTH was started (100 mgms. daily) with rapid subjective improvement. Fingers and toes were cyanotic but cryoglobulins could not be demonstrated in blood. These changes progressed, became mummified and finally reverted to normal. Subsequent course during five and one-half months of hospitalization was of intermittent exacerbation of one or another of his symptoms. Terminally he developed evidence of acute abdominal involvement with tenderness, distention, bloody stools and evidence of peritonitis.