

GIANT CELL SARCOMA OF THE FEMUR (EPULIS TYPE) WITH METASTASIS IN THE FEMORAL VEIN

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THE so-called giant-celled sarcomata of the epulis type in bones form an anatomically and clinically well-defined group. Characterized histologically largely by spindle-shaped connective-tissue cells with a variable, but generally quite abundant, number of characteristic multinucleated giant cells, these growths are easily recognized microscopically. Grossly also, their frequent occurrence in the epiphyses of the long bones, the circumscribed, hemorrhagic and occasionally soft, jelly-like and cystic appearances and the local replacement of the bone, are conspicuous features.

The opinion has been growing that these growths are purely local affections and consequently clinically benign. It is shared to-day by a number of competent pathologists and surgeons. Thus Ewing states that he has never known these tumors to yield metastases; Martland writes, "They recur after complete removal, in loco, but I have never seen one metastasize to distant parts," and in fact, he doubts the tumor character; Meyerding omits them from his studies of "Sarcoma of the Long Bones" carried on at the Mayo Clinic because they are considered non-malignant. Similar conclusions are reached by Bloodgood and some others.

Without questioning this general experience and opinion regarding the nature and biological behavior of these growths, the following case is presented as an exception, and more particularly to illustrate the difficulty which confronts the pathologist and the surgeon in the decision as to the nature of neoplastic growths from purely histological evidence. In other words, is it possible to ever state with definite assurance that any growth of so labile and embryonic structure is benign and is the biological position of a tumor always accurately reflected by the histological picture? One must bear in mind that the classification of growths is fundamentally only of didactic value and that precise "pigeon-holing" of these conditions is not supported by natural laws, but remains more or less artificial and academic.

Frank W., a farmer, age forty-one, American, was a strong healthy individual until five months ago. At that time he was working in a quarry and struck his left knee on a piece of stone. This merely made him limp temporarily and he continued work for three weeks. At the end of that time the knee became painful and swollen, movement was limited, and he was forced to give up his employment. He consulted a physician who gave various local treatments and

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finally a six weeks course of X-ray treatment. The knee became gradually more and more swollen and three weeks before admission (approximately seventeen weeks after the injury) the thigh became swollen to the groin and greatest difficulty was experienced in moving the limb both because of its great weight and because of weakness on the part of the patient.

Family History.—The patient has three brothers and one sister alive and well. His father died at the age of sixty-five and his mother died at the age of sixty-three. The cause of death in each case is unknown to him. There is no history of cancer or tumor.

Status Præsens.—Admitted to the Royal Victoria Hospital, orthopædic service of Dr. W. G. Turner, by ambulance May 31, 1922. Temperature, pulse

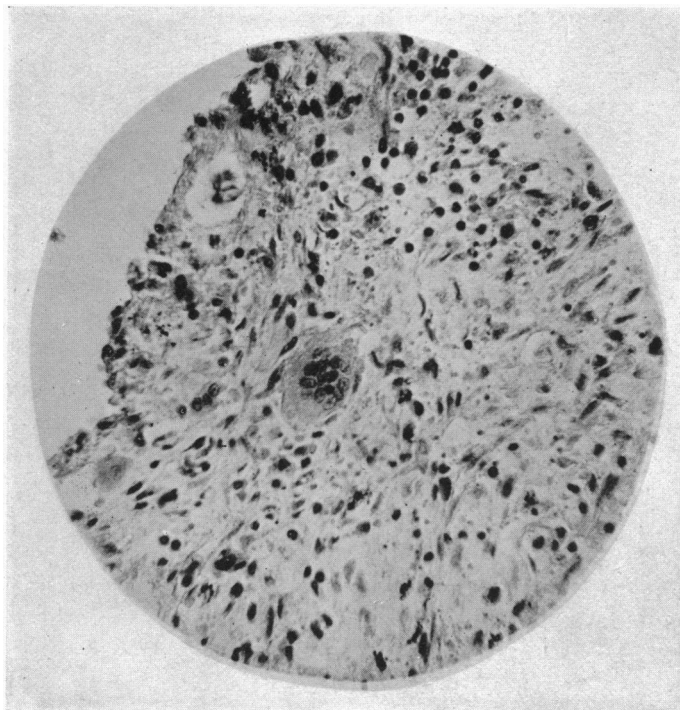


FIG. 1.—A microphotograph of the primary growth in the distal extremity of the femur.

and respirations normal. The patient is a large powerfully built man appearing stated age. Cheerful mood. Obese. Lies in bed with left leg in moderate flexion at the hip and knee and in slight external rotation. This leg is hard, œdematous, does not pit on pressure and measures $5\frac{1}{2}$ inches more in circumference at the thigh and 3 inches more in circumference at the calf than the right leg. It is so swollen and the œdema is so hard that palpation is extremely difficult but there is definitely greater enlargement on the inner side of the lower third of the femur and on the outer side of the popliteal space. The heart and lungs, digestive system, genito-urinary system, and nervous system are negative.

Laboratory Examination.—Blood: Red blood cells, 5,000,000. White blood cells, 8,000. Hæmoglobin, 85 per cent. No abnormal blood picture, Wassermann negative. Urine: Sp. Gr., 1022; acid, clear, no albumen, no sugar, no casts. Dr.

A. H. Pirie, radiologist, submitted the following report: "The X-ray of the knee-joint shows the presence of a malignant tumor arising at the lower end of the femur. It has eroded the femur both in front and behind just above the epiphysis. The tumor has a capsule which casts a shadow suggestive of a little bone or calcification in its periphery. There is also a second large nodule with radiating lines in it going downwards and backwards from the lower end posterior to the main mass of the tumor. The appearance is more suggestive of sarcoma than any other lesion. An X-ray made of the lungs does not show any definite secondary growth."

Clinical Diagnosis.—Sarcoma of the left femur. Thrombosis of the left femoral vein.

Operation.—On June 8th, the left leg was disarticulated at the hip. Notes: Ether well taken. Incision over femoral vessels. Hard œdema and great depth to

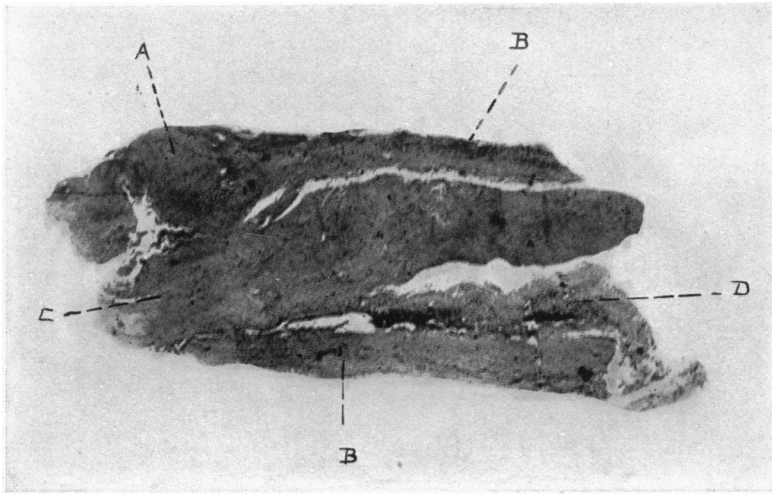


FIG. 2.—Longitudinal section of femoral vein in stump. The section is cut slightly obliquely. A. Tumor growth in vessel wall. B. Venous wall. C. Thrombus. D. Hemorrhagic organizing granulation tissue.

expose vessels. Femoral artery much diminished in volume. Vein completely thrombosed. Both ligated. Circular amputation of upper third and limb removed. Practically no hemorrhage. Disarticulation rapidly done and large flaps partially sutured. Dressing.

The following report (surgical 790/22) was submitted by the pathological department.

Macroscopical Examination.—1. A left leg which has been amputated about the junction of the upper and middle third; it is markedly swollen, œdematous and firm. Over the knee is a roughened area where the skin is thickened and desquamating. 2. Approximately the upper third of the femur including both trochanters, head and part of the shaft, with some tags of muscle and tendon adherent thereto.

After fixation and freezing the leg was split with a band saw and the section shows a tumor growth in the lower end of the femur. This growth is dark red in color, of a gelatinous homogeneous appearance and towards the centre shows cystic softening. It has completely destroyed the bony tissue and projects beyond the bony outline, but as far as can be seen in this gross specimen it is still surrounded by the periosteum and synovial membrane covering the end of the bone.

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The capsule thus formed has been expanded by the increasing tumor mass so as to encroach on the joint cavity, but the cavity itself has not been invaded by the growth. In its longitudinal and transverse diameter it measures 9 by 7 cm.

Microscopical Examination.—Where the tumor is best preserved it is seen to consist of cells which are apparently of connective tissue derivation. For the most part they are elongated or spindle-shaped. Others are more embryonic and are oval or round. Fibril formation is not a marked feature, but rather a tendency to fuse. Many large typical giant cells with centrally placed nuclei are scattered throughout. Towards the periphery of the tumor spicules of bone in various stages of destruction complete the picture.

Diagnosis: Giant-cell Sarcoma (Epulis Type).

Course.—General condition following operation excellent. Dressings every two days and condition improved steadily. Patient could move in bed easily and had only moderate pain referred to toes. Œdema of the stump however persisted. No pitting. July 8th (one month post-operative): Patient feeling quite well until 11:25 A.M. when, on raising up in bed, he suddenly

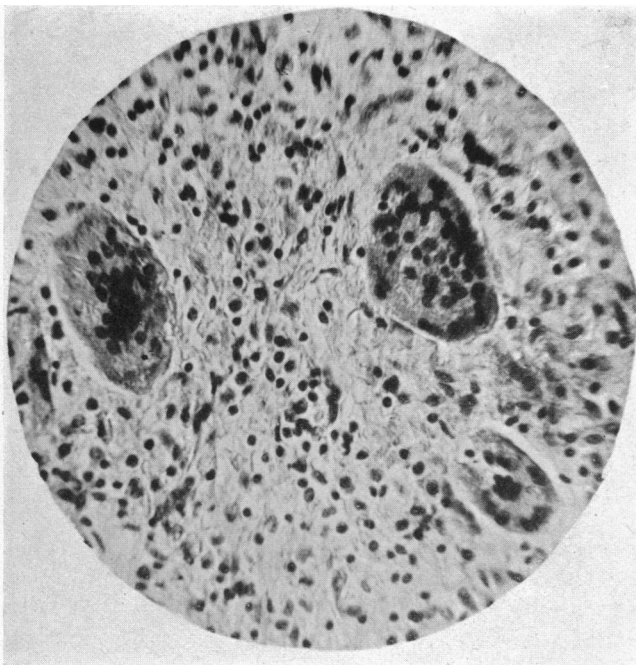


FIG. 3.—A microphotograph of the metastatic growth in the wall of the femoral vein at the groin.

complained of abdominal pain and rapidly lost consciousness. He died in a few minutes with cyanosis of the face and lips.

Summary protocol of autopsy findings. Section performed eight hours post-mortem by Doctor Grant. The body is that of a very fleshy male, and appears of stated age. Chest and abdomen are well developed. Has had a recent operation of disarticulation of the left leg at the hip-joint. The stump of the leg is much swollen; about five inches more in circumference than the right. At the end of the stump is an open wound 10 cm. long, infiltrated around by a bluish-red granulation tissue, ending in a closed scar 12 cm. long. The stump is closed by an anteriorposterior flap. Above the main incision scar are two longitudinal incisions into the œdematous tissue, each about 5 cm. long. The stump is firm and does not pit on pressure. Cyanosis is marked in the face and neck.

On opening the thorax the lungs lie free, collapsed superiorly, but retain their shape inferiorly where they are subcrepitant. The præcordial space is wide and there is a large amount of mediastinal fat. Pleuras free except for slight apical

scarring. Pericardium is free. Section of the lungs shows no evidence of neoplastic involvement.

The right side of the heart is considerably dilated; the left side is contracted and firm. The right auricle contains fluid blood and post-mortem clot. The tricuspid orifice admits three fingers. There is a recent, red, soft thrombus attached to the tricuspid valve. The right ventricle contains post-mortem clot. On opening the pulmonary artery there is found a large yellowish-gray, firm, but friable embolus extending upwards from the pulmonary valves to the bifurcation. The left side of the heart is free. Musculature yellowish but firm. The coronary arteries are free.

On opening the abdomen the parenchymatous organs are found relatively normal. There is general evidence of passive congestion; the spleen is hyper-

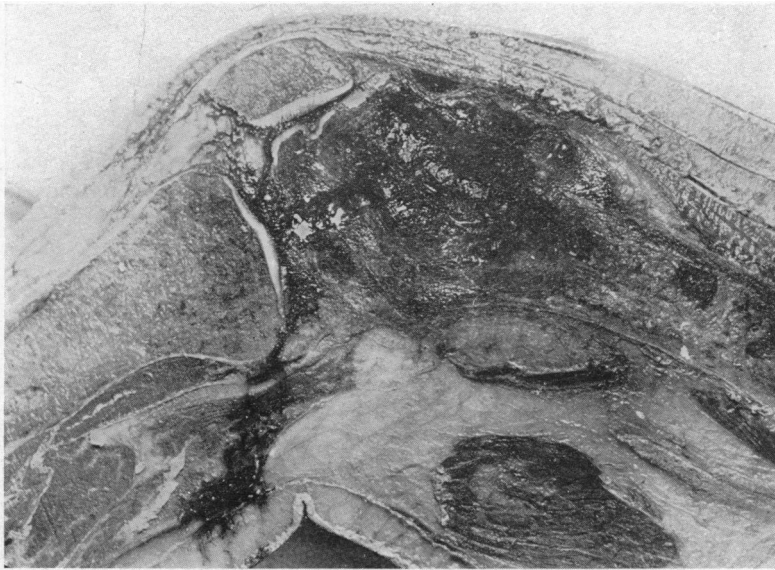


FIG. 4.—Longitudinal section of the left leg at the knee, showing the primary growth in the femur.

plastic and the kidneys tend to bulge. On opening the inferior vena cava there is found a large but only very slightly adherent thrombus which extends upward from the bifurcation for a distance of 5 cm. The right common iliac vein below this point is free. The left common iliac vein is free for a short distance (probably separation), but at its bifurcation and extending down the left external iliac there is an old yellowish, pinkish to grayish, firm and adherent, rather fibrinous thrombus. This condition extends down into the amputated femoral region. The aorta shows very slight fatty intimal changes.

Microscopic Examination.—Sections from the embolus in the pulmonary artery present the typical picture of coagulated fibrin, red blood cells, leucocytes, etc. All rather necrotic looking. There is no evidence of neoplastic cells in the embolus. Sections from the thrombus in the inferior vena cava present a similar structure, with no evidence of neoplastic involvement. Sections from the femoral vein in the stump, present, however, a different picture. Within the lumen of the vessel lies a thrombus which at the centre is made up purely of necrotic, poorly staining more or less homogeneous fused fibrin, leucocytes, etc., while peripherally it is in part invaded by granulation tissue with many proliferating fibroblasts,

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endothelial buds and some small round cells. One portion of the wall of the vein however has been definitely replaced in this situation by a nodular neoplastic growth, which simulates the original growth in the lower end of the femur except that it is slightly more embryonic (sarcomatous) in character. This growth is thus inserted into and coextensive with the vessel wall. It is composed microscopically of large immature connective tissue cells which show only slight tendency to fibril formation and rather remain in an embryonic spindle-cell stage. Scattered throughout are large giant cells containing many irregularly arranged nuclei (typical epulis giant cells). The growth is vascular and furthermore infiltrated by a large variety of small round cells, lymphocytes, polymorphonuclears, large round cells often with lobated nuclei and transitions into plasma cells and eosinophiles. This infiltration is for the most part diffuse, but in places appears more intense or focal in character. It simulates in some areas myeloid tissue, but special stains do not substantiate this impression.

Sections of the heart show parenchymatous and slight fatty degeneration. The lungs give evidence of a moderate, but rather long standing passive congestion at the base. This condition is also present in the abdominal viscera. There is hyperplasia and pigmentation of the spleen and the prostate is the seat of a glandular hyperplasia.

Anatomical Diagnosis.—Pulmonary embolus; giant cell sarcoma (epulis type) in wall of left femoral vein with secondary thrombosis of femoral and external iliac veins and inferior vena cava; recent amputation of the left leg at the hip for giant cell sarcoma of distal extremity of femur. Passive congestion of lungs and abdominal viscera; parenchymatous degeneration of heart, liver and kidneys; slight fatty degeneration of heart; hypostasis of the lungs; hyperplasia and pigmentation in spleen; glandular hyperplasia of the prostate; fatty infiltration of the liver; obesity.

In retrospect we find an apparently clear-cut course extending over a period of approximately six months. Starting with a very definite history of moderately severe trauma of the lower end of the left femur in a healthy man, aged forty-one years, we have evidence of almost immediate development of a quite rapidly growing neoplastic process at the site of injury. The growth quickly erodes the bone, leaving only the periosteum. Within seventeen weeks a metastasis has occurred in the wall of the femoral vein leading to thrombosis. Unfortunately the location is high up near Poupart's ligament, so that amputation does not reach it. In the course of six weeks from the first evidence of thrombosis this condition has spread progressively up the iliac vessels and into the inferior vena cava. Slight exertion dislodges a large portion of the thrombus and pulmonary embolization brings about immediate death.

Two questions naturally arise for discussion. First, is the primary tumor a true giant-cell sarcoma of the epulis type? Secondly, is the growth in the femoral vein a metastasis? In answer to the first question, one may say that the tumor certainly presents both macroscopically and microscopically the characteristics of this type of growth and what variations from the usual picture occur may be attributed merely to its more active character, rather than to any real alteration in fundamental nature. Grossly it presents the usual reddish jelly-like replacement of the cancellous portion of the bone, with more rapid than usual absorption of the shaft, so the periosteum alone

remains. Histologically it is likewise typical, as shown by the accompanying microphotograph, and in no way to be confused with a malignant periosteal sarcoma containing fused tumor cells. The clusters of more embryonic, highly undifferentiated cells are but foci of active rapidly proliferating nature. The giant cells are typically abundant, large, diffusely scattered, with relatively clear pink-staining cytoplasm and contain many round or oval, discrete nuclei clumped for the most part centrally.

The growth in the vein, besides carrying an even macroscopically visible, nodular tumor character, and being thus easily distinguished and separated from the thrombus in the lumen of the vessel, presents a strikingly similar histological picture except that it shows even less tendency to fibril formation and a considerable infiltration of small round cells. The distance of this area from the original growth is approximately thirty centimetres and it seems quite improbable that its presence in the groin could be explained by direct extension; moreover the vein below the point of amputation is free from thrombosis and there is no evidence of growth in the tissue in this vicinity. That an embolic fragment from the original tumor entered the blood stream, lodged and took root at this point subsequent to the formation of the thrombus seems likewise untenable from the position of the tumor nodule well within the vessel wall. We must, therefore, come to the conclusion that we are dealing with a genuine metastasis in the wall of the femoral vein, and this is based on the position and tumor-like replacing character of the growth with its quite characteristic histological picture.

CONCLUSIONS

A case is presented of primary giant-cell sarcoma of the epulis type in the distal extremity of the femur with metastasis in the wall of the femoral vein. It shows that this tumor, generally held as local and benign, may metastasize and thus become malignant.

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