EPIDERMOID CARCINOMA IN OSTEOMYELITIS: CASE REPORT

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The problem of chronic suppurating foci is met frequently in the practice of surgery. Chronic osteomyelitis is one of the most common examples of such a condition. Every surgeon is cognizant of the difficulties of successful treatment and of the necessity for persistent cooperation on the part of the patient. Inadequate observation and therapy may result in eventual permanent disability or even loss of life. As the disease progresses, extensive local changes take place in the tissues owing to the constant irritative effects of the discharging suppurative material. Chronic irritation, both physical and chemical in nature, has long been accepted as a factor in the production of malignant growth. Carcinoma as an end result of a chronic suppurative process has been reported by Benedict (1), Blanco (2), Collins (4), Devars (5), Wakeley (9) and others. But that this condition is rare is shown by the fact that of 365 cases of osteomyelitis cared for at this hospital in twenty-two years, only one has been accompanied by malignant growth. The tendency for such a growth to remain localized for a long time is shown in the case herein described and in the others reported in the literature. The growth may progress, however, to such an extent as to undermine the vitality of the patient in a marked degree.

CASE REPORT

A forty-seven-year-old woman, unmarried, was admitted to the Peter Bent Brigham Hospital complaining of weakness and inability to walk, owing to a sore leg. Eighteen years previously she had struck the left leg above the ankle against a table. Several weeks later she was taken to a hospital where incision and drainage were performed for what was apparently an acute osteomyelitis. During the ensuing year four additional operations were undertaken for drainage. Spontaneous drainage occurred intermittently after these procedures. Further professional aid was not sought because of the patient’s faith in Christian Science. She could walk with the help of a cane until one year prior to admission, when a fracture of the tibia occurred and she was compelled to use crutches. At that time the narrow opening of the sinus became larger, and ulceration slowly extended up the leg toward the knee. A sinus also developed in the upper third of the tibia. At the same time the patient became weaker and lost weight. Three weeks before admission to the hospital she fell and fractured the left tibia below the knee.

Physical examination showed extreme emaciation, pallor, bilateral inguinal lymph node enlargement, and the disease process in the left leg (Fig. 1). From the left knee to the ankle the entire anterior, medial, and lateral aspects of the leg were ulcerated, showing an exuberant overgrowth of coarse granular tissue which bled easily when touched. Anterior to the head of the fibula was the opening of a tract which extended deeply into the underlying muscles, and from which there was a purulent discharge. Above the ankle, anteriorly, was another sinus tract in which a fragment of tibia was exposed to view. A hard, tender cord was present in the medial aspect of the left thigh in the region of the internal saphenous vein. The leukocytes in the blood numbered 12,800 per c. mm.; the erythrocytes...
3,850,000 per c. mm.; the hemoglobin was 55 per cent (Tallqvist), and the blood smear showed the usual findings of secondary anemia. The urine was normal. The Wassermann and Hinton reactions were negative. Biopsies of several regions of the granulating surfaces and of the skin edge showed epidermoid carcinoma. Roentgenograms demonstrated irregular thickening of the soft tissues and a picture compatible with chronic osteomyelitis in the middle and lower thirds of the tibia.

Operation: A mid-thigh amputation was performed under spinal anesthesia and was followed by transfusion of 500 c.c. of blood. The patient withstood the procedure well and

made an uneventful recovery. The wound healed by primary intention in seven days. Roentgen examination of the surgical specimen showed irregular areas of destruction in the sclerosed tibia, with a gap at the upper end 11 cm. in length and one in the lower third 5 cm. long. This suggested the purely destructive invasion of carcinoma (Fig. 2).

Roentgen treatment, 750 r units, was given over both inguinal regions, and the patient was discharged from the hospital on the twenty-first postoperative day. Two months later no abnormal lymph node enlargement was present. Another roentgen-ray treatment of 750 r was given to the inguinal regions and further treatment was considered unnecessary. Two years after operation the patient’s general condition is excellent; there is no evidence of metastasis and she has gained sixty pounds in weight.
Pathological Description: The leg showed ulceration extending from the ankle to the knee well above the patella anteriorly, involving the anterior, medial, and posterior aspects, leaving only a narrow longitudinal strip of skin on the postero-lateral aspect of the calf and over the lower portion of the leg laterally. The denuded area had a granular and roughened surface which was moist and covered with a thin purulent material. The leg was covered with granulation tissue, which on examination was seen to be composed of irregular, firm nodules varying in size from 2 to 8 mm. in diameter. These nodules had coalesced to form the irregular, pinkish-gray surface previously described. The firmness of these structures suggested the possibility of diffuse carcinomatous involvement, and later microscopic examination showed that this was epidermoid carcinoma.

Upon the anterior aspect of the leg, at a point 7 to 8 cm. below the patella, was a gaping sinus 1.5 × 2 cm. leading down into the substance of the leg. This sinus directly entered the region of what was previously the upper part of the tibial shaft, and in this wound the upper end of the remaining shaft could be seen. From this sinus there exuded some thick, yellow, purulent material following pressure over the middle third of the leg. The margins of this wound and the walls of the sinus were also covered with a nodular, granular tissue similar in all respects to that previously described on the surface of the leg. A second
small sinus 6 or 7 mm. in diameter opened on the antero-medial aspect of the leg at the junction of its lower and middle thirds.

On incision there were seen a marked pallor and atrophy of all the muscles of the posterior tibial, anterior tibial, and peroneal groups. In those portions of muscle adjacent to the tibia there was chronic inflammation with pockets of purulent exudate. These collections were grouped especially along the middle third of the leg. The fibula showed a diffuse chronic osteomyelitis with very rough and irregular surface. In many places the bone was so soft that a knife blade could easily be pushed into the bony cortex. In some places the bone was definitely eburnated. The tibia showed a fracture at the junction of its upper and middle thirds, with the upper fragment completely separated from the lower one and projecting anteriorly into the ulcerated neoplastic tissues already described. This portion of bone was very irregular; while in some places it was soft and necrotic, elsewhere it was dense, smooth, and eburnated. Also it was greatly eroded and extended out into a sharp point at its lower tip.

![Figure 3](image)

**Fig. 3. Epidermoid Carcinoma Arising in Osteomyelitic Sinuses, with Many Well Formed Pearls of Keratin. × 37.5**

Extending up from the lower fragment of the tibia was a solid column of firm tissue approximately 9 cm. in length. This was rounded, about 3 cm. in diameter, and was continuous with the lower portion of the tibial shaft. This firm substance had a fibrous consistency and in it there were no bony spicules either of new bone formation or sequestrum. Cross-section of this material showed a light grayish substance through which were scattered many small whitish, rather firm areas about 1.0 to 1.5 mm. in diameter. In short, approximately the middle third of the shaft had been replaced by a column of carcinomatous tissue, continuous above and leading directly into the large upper sinus on the anterior aspect of the leg.

The lower third of the tibial shaft showed irregularity of its surface indicative of a chronic osteomyelitis. The surface of the bone was much eroded and ragged. There were numerous small cavities varying from 1 to 7 mm. in diameter in the cortical surface of the shaft. The most prominent of these was loosely filled in with firm, friable, grayish white tumor tissue. This material was directly continuous with a very small sinus, only 6 to 7 mm. in diameter, which led onto the lower, antero-medial aspect of the leg. Here again tumor had grown down the sinus tract and filled the osteomyelitic cavity in the tibia.
The carcinomatous mass on the anterior middle third of the leg surface was directly adherent to the underlying bone along the anterior surface of the tibia, forming a layer of neoplastic tissue varying from 5 to 15 mm. in thickness.

**Microscopic Examination:** Sections were taken from fourteen sites in different portions of the large ulcerated area on the leg, from the two sinuses, and from the tissue previously described as replacing the mid-portion of the tibial shaft. All of those taken from the external aspects of the leg showed the nodular tissue to be composed of epidermoid cancer (Figs. 3 and 4). This was of a fairly well differentiated type. Mitotic figures were abundant. An acute and chronic inflammatory reaction was present throughout this neoplastic tissue.

A section taken from an osteomyelitic cavity again showed epidermoid carcinoma, some islands of superficial granulation tissue, and a severe acute and chronic inflammatory reaction. Blocks taken from the substance which had replaced the mid-portion of the tibial shaft showed an epidermoid carcinoma with a somewhat more prominent connective-tissue stroma than that previously seen on the external aspect of the leg. Sections of bone removed from the upper fragment of the tibia, the lower end of the tibia, and from a portion of the fibula showed an acute and chronic osteomyelitis, destruction of bone, and with new bone formation, the development of a dense involucrum.

**Discussion**

The life history of carcinoma developing in osteomyelitic foci, as demonstrated in this and in various cases in the literature, is one of slow progression. In view of the tendency of the tumor to remain localized a good result may confidently be expected after amputation of the involved limb. Considering the very slow growth of the lesion and the failure to metastasize there may be some doubt as to whether it represents true epidermoid carcinoma. Yet the
extensive invasion with replacement of soft tissue and bone must place the neoplasm in that category. Devars (5), in 1894, reported 39 cases of carcinoma in the sinuses of chronic osteomyelitis. He concluded that the neoplasm followed prolonged irritation. He noted, also, that tuberculous lesions of bone may produce papillary vegetative growths that are difficult to distinguish clinically from epithelioma. The progress and histology of such lesions reveal their true identity. With the exception of one patient, a child of thirteen, the average age in Devar's series was fifty years and in each case the osteomyelitis had existed for more than thirty years. The location of the lesions was predominantly in the tibia (26 cases). Other regions affected were the femur (5 cases), foot (5 cases), arm (2 cases) and knee (1 case). Amputation was advised in all instances.

Benedict (1) published an historical review of this subject in 1931, reporting 12 instances of carcinoma occurring in a series of 2400 cases of osteomyelitis. Collins (4) and Blanco (2) have subsequently reported two cases of squamous-cell carcinoma in chronic osteomyelitis. Wakeley (9) has recorded one instance of carcinoma occurring in an actinomycotic sinus tract of the mandible.

We have not found in the literature any instance of carcinoma secondary to osteomyelitis in which there were distant metastases. Biopsy of nearby enlarged nodes has shown only chronic lymphadenitis. The process, however, is locally malignant and may make great inroads on the vitality of the patient. That the highest incidence of the disease is in the tibia may be attributed to the great tendency for persistence of sinuses there. The dependent position with less active circulation is certainly an important factor in slow healing.

Lubarsch (7) in 1906 noted the association of heterotopic proliferation of epithelium and carcinoma. He considered the former to be an antecedent of the latter. Wolbach (10) in 1909 emphasized the close association between epithelial changes produced by long-standing inflammatory processes and the occurrence of carcinoma. Milgram (8) and Brunschwig (3) have commented on the tendency of osteomyelitic cavities to become epithelialized. This process exposes the epithelial cell to prolonged irritation, and repeated attempts at repair with associated degeneration on an abnormal supporting tissue. In relation to roentgen-ray production of epidermoid carcinoma Wolbach (11) has stated that the acquisition of malignant properties follows sustained proliferative activities in contact with an abnormal supporting tissue.

Graves (6) has pointed out that inflammation does not produce cancer unless it is frequently repeated for so long a time that it finally overtaxes the reparative processes of the injured tissues. Also, he noted that it is rather the mild, recurring, invasive infections which, by continually irritating the regenerating cells, lead eventually to neoplastic growth. His description of the predisposing factors in development of carcinoma of the cervix seems to apply to cancer forming in osteomyelitic sinuses. It is generally agreed that chemicals and roentgen-ray will produce carcinoma more rapidly than pyogenic inflammation. The duration of sinuses has varied from ten to fifty years before malignant changes were manifest and discovered. There are two exceptions to this: namely, a patient of Devars (5) and one of Collins (4). The latter
showed malignancy one year after the occurrence of osteomyelitis. This is the shortest time within which malignancy is known to have developed as a complication of osteomyelitis.

SUMMARY

A case of chronic osteomyelitis of the tibia with epidermoid carcinoma in the sinuses extending up the anterior, medial, and lateral aspects of the leg, with invasion of the soft tissues and bone, is reported. Following mid-thigh amputation the patient made a striking recovery from an advanced state of general physical debility and cachexia. She is well and without evidence of metastasis twenty-four months after operation.

When epithelial cells during the process of regeneration are exposed to the products of chronic inflammatory exudate for many years their normal repair is altered to an extent which may eventually result in neoplastic growth.

BIBLIOGRAPHY