EWING'S TUMOR SIMULATING SARCOMA OF
SOFT-TISSUE ORIGIN

A CLINICAL, PATHOLOGICAL AND RADIOTHERAPEUTIC
STUDY OF FOUR CASES

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The clinical, pathological and therapeutic aspects of Ewing's tumor, or endothelial myeloma of bone, have undergone progressive classification in the past decade. Its histogenesis and cytogenesis still remain somewhat controversial, although the majority of observers now reject an endothelial origin and tend to view it as arising from undifferentiated mesenchyme (1). From a clinical standpoint, the osteomyelitic syndrome which occasionally ushers in this neoplasm is well known. This onset is particularly common in children, dependent probably not on any intrinsic differences in the neoplasm in the different age groups but rather on varying capacities of the host. In adults the symptomatology is classically that of malignant bone tumors in general, with pain and disability as the outstanding complaints. Swelling or a palpable mass may also occur, but this again is more common in children (2).

Soft-tissue masses, as distinguished from osseous swelling, occur late in the course of the disease and are usually associated with advanced bone pathology and frank cortical destruction. The soft-tissue mass may become very large in some cases and temporarily dominate the clinical picture, but only rarely does the primary origin of the neoplasm remain undiscovered.

It is the purpose of this paper to record a group of cases of Ewing's tumor with a soft-tissue mass as the presenting sign, in which the primary intracortical origin could not be established by the initial radiological and clinical examinations.

Case I (Montefiore Hospital No. 25505): Z. D., a married woman aged twenty-four years (at onset of illness), was admitted in February 1935. In November 1930 she had had

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a tumor, about 6 cm. in diameter, removed from the left upper scapular region. The report described it as a soft-tissue tumor lying in the supraspinous fossa of the scapula, histologically a malignant neoplasm of undetermined nature. No slide was available for study. In 1933 a local recurrence was first noticed by the patient. No therapy was instituted.

In 1934 a diagnosis was made of left-sided pleurisy with effusion. This was believed to be of tuberculous origin and the patient entered a tuberculosis sanatorium, though the sputum was persistently negative.

In February 1935, on admission to Montefiore Hospital, a large infiltrating mass was present in the supraspinous fossa of the left scapula. This was apparently adherent both to bone and to the scar resulting from the previous surgical procedure. X-ray examination of the scapula revealed no intrinsic bone pathology (Fig. 1). Films of the chest showed a left pleural effusion with a few scattered infraclavicular infiltrations. The pulmonary picture was considered metastatic in view of the persistently negative sputum and the sanguineous character of the effusion. X-ray therapy was therefore given both to the scapular region and to the left chest. The scapula was irradiated through an antero-superior and a posterior field, the former receiving 2000 r, the latter 3000 r, fields $6 \times 12$ cm., daily dose 200 r.\(^2\) The factors were 200 kv., 30 ma., filter 0.5 mm. silver plus 1 mm. aluminum, focal skin distance 50 cm. The mass receded rapidly and completely. The lung was irradiated through anterior, posterior, and lateral fields, each receiving 1600 r. The effusion disappeared, the pleura thickened, and the lung underwent progressive fibrosis.

The patient remained asymptomatic for seven months, at the end of which time, two tender nodules, about 0.75 cm. in diameter, were observed at the site of the original scapular tumor. These nodules appeared to be subperiosteal. After a short period of observation, during which time they grew slowly, irradiation of the scapular region was again undertaken. The nodules proved to be extremely radioresistant and, despite intensive therapy, six months

\(^2\)All r measurements in air.
after their appearance evidences of dissemination of the tumor appeared in rapid succession. Involvement of the supraclavicular and cervical lymph nodes was first noted. These yielded to roentgen therapy but diffuse osseous and pulmonary metastases rapidly developed and death ensued. The total duration of the disease from the onset of symptoms was six years and six months.

Post-mortem Examination: The soft tissues of the left supraspinous fossa of the scapula were infiltrated by grayish, firm tumor tissue. The bone was invaded and greatly thinned. The axillary, cervical, mediastinal and tracheobronchial lymph nodes were involved and there were metastases also in the ribs, vertebrae, lungs, pleura, pericardium, and diaphragm.

Microscopic examination of the scapula demonstrated destructive changes in the cortex, with diffuse tumor infiltration of the marrow. The structure was typical of Ewing's tumor (Fig. 2).

Discussion: The initial manifestation of the disease in this case was such that the original investigation led to the diagnosis of a soft-tissue tumor. The tumor was excised and the microscopic diagnosis was sarcoma. A slowly growing local recurrence infiltrating the soft tissues, as well as a pleuropulmonary process accompanying it, proved radiosensitive. A subsequent intraosseous recurrence was radioresistant. X-ray examination of the scapula was negative at all times. Widespread bony and pulmonary metastases led to a fatal outcome.

The course of the disease (elective bony metastasis), the response to radiation, and the histology are in favor of the diagnosis of Ewing's tumor of the scapula, though the possibility of a soft-tissue origin remains. The soft tissues of the extremities and around the scapula are not infrequently the site of a round-cell tumor which is difficult to distinguish histologically from Ewing's tumor. The radiosensitivity of these tumors is marked, their response approaching that of Ewing's sarcoma. It is likely that histogenetically these two round-cell tumors are closely related, a common origin from undifferentiated mesenchyme being probable. In the bone marrow this cell is represented by the reticulum cell. This usually develops in a hematopoietic direction, but in the soft tissues the evolution is generally towards a fibroblast. The observations of Poujol and Barone, in a case of round-cell sarcoma of the heart, lend support to this hypothesis of the origin of the round-cell sarcomata. The tumor studies showed marked desmoplasia and in areas it appeared that the tumor cell was assuming a fibroblastic function and producing collagen. Phemister, in speaking of these soft-tissue tumors, has designated them as parosteal round-cell sarcoma. Geschickter and Copeland have described them as Ewing's tumor of the soft parts. Such a designation is unfortunate; the term Ewing's tumor should, we believe, be reserved for round-cell tumors arising in bone.

Case II (Montefiore Hospital Radium Clinic No. 4713): S. S., a married woman aged forty, gave a history of an acute sciatic syndrome in November 1933. One month after onset, rectal examination revealed a firm circular mass, roughly 4 cm. in diameter, attached to the sacrum in the left lower sacro-iliac region. Neurological examination confirmed the presence of a typical left sciatic syndrome. There was no evidence of disease elsewhere. Radiologic examination of the sacrum showed no pathological changes in the bone (Fig. 3). A soft-tissue mass was visible in the left sacro-iliac region.

The impression at this time was of a primary malignant sarcoma, probably a fibrosarcoma of periosteal or extraperiosteal origin. Because of its deep location, the lesion was considered inoperable and difficult to approach for biopsy.
Roentgen therapy was instituted, two courses being given at four-month intervals. The patient first received a total of 3900 r directed to the left anterior, lateral, and posterior pelvic fields in the course of six weeks. Subsequently, 4800 r were given to similar fields, the treatment being protracted over four months. Following irradiation the tumor and pain disappeared for six months. At the end of this time (September 1935) sciatic pain recurred and the patient presented herself at the Radiotherapy Clinic of Montefiore Hospital. Examination again revealed a hard mass in the sacral hollow, firmly adherent to the underlying bone. X-ray examination of the sacrum was negative.

At this time, a biopsy was considered essential for any future plan of therapy. Accordingly the mass was approached pararectally through the perineum with a Hoffman punch. The tissue removed showed no tumor.

A week after biopsy the patient developed an acute pulmonary syndrome consisting of dyspnea, cyanosis, and fever. Roentgenograms of the chest revealed diffuse nodular infiltration of both lungs, typical of metastatic malignancy. Death occurred shortly thereafter. Unfortunately no films of the chest were made prior to biopsy. The total duration of the disease was two years and two months.

Post-mortem Examination (Dr. L. R. Ferraro, Fordham Hospital): A firm lobulated mass was present in the left sacro-iliac region, extending from the brim of the pelvis down to the sciatic notch. It was situated retroperitoneally in its entirety, and was firmly adherent to the periosteum of the sacrum. On section of the bone, it was seen to be only superficially involved by tumor. The lungs were studded with numerous metastatic nodules. The mediastinal and tracheobronchial lymph nodes were diffusely invaded by tumor. The liver, stomach, and jejunum presented a few isolated tumor nodules. No bony metastasis was noted.

Microscopic examination revealed a small-round-cell sarcoma of the type seen in endothelial myeloma of bone (Fig. 4).

Discussion: The primary symptomatology in this case was referable to a soft-tissue mass encroaching on the sciatic nerve. The mass was adherent to bone but repeated radiological examination revealed no destructive or proliferative bony changes. The most likely clinical diagnosis was extraperiosteal fibrosarcoma; yet the tumor proved to be radiosensitive. The true nature of the neoplasm might have been suspected at this time. Recurrence after radiotherapy was rapid (six months) and death occurred soon thereafter, due to acute pulmonary dissemination.

It is interesting to speculate on the relationship of the biopsy to the pulmonary spread in this case. Unfortunately, no roentgenogram of the thorax was taken prior to the biopsy. Clinically, however, there appeared to be a rather clear-cut relationship between the biopsy and the pulmonary syndrome. Autopsy revealed a Ewing's tumor (confirmed by Ewing).

Case III (Montefiore Hospital No. 22588): I. H., a man aged fifty-two years, was admitted to Montefiore Radiotherapy Clinic in August 1933, complaining of pain and a mass over the right sternoclavicular region. He had many subcutaneous nodules scattered over the body and declared that a nodule had been present over the sternal end of the clavicle for ten years, with progressive growth during the past year.

On examination, a firm mass, 5 x 5 cm., was found, adherent to the mesial fourth of the right clavicle. Whether it arose from bone or invaded it secondarily from without could not be determined. X-ray studies of the clavicle were completely negative (Fig. 5). In view of this and the ten-year history of a soft-tissue nodule antedating the present mass, a soft-tissue origin of the tumor had to be seriously considered. Multiple dermic and subcutaneous nodules of soft consistency were also present, which appeared to be lipomata. A biopsy of the clavicle had been done at another institution, and the report had been hemangio-endothelioma (Fig. 6).

The patient was treated with a radium element pack at 6 cm. distance; field 10 x 10
FIGS. 3 AND 4. CASE II: ROENTGENOGRAM OF SACRUM SHOWING NO LESION.  
PHOTOMICROGRAPH OF TUMOR. × 480
Figs. 5 and 6. Case III: Initial Roentgenogram of Right Clavicle (1933) Showing No Lesion. Photomicrograph of Original Tumor. X 480
Fig. 7 shows the impacted fracture of the inner third of the clavicle (1936) and Fig. 8, taken a year later, shows its complete destruction. Fig. 9 shows the solitary pulmonary metastasis in the peripheral portion of the left lower lobe and Fig. 10 its complete regression following irradiation.

For a period of three years the patient was symptom-free and negative to examination. At the end of this time pain recurred and a roentgenogram of the clavicle revealed changes suggestive of an impacted fracture (Fig. 7). Clinical examination was negative. The patient now disappeared from the clinic for a year. He returned with a large mass, 7 × 6 cm., obviously arising from the sternal end of the right clavicle. X-ray revealed complete destruction of the mesial third of the bone (Fig. 8). In addition, a large circular metastatic nodule was noted in the left lower lobe (Fig. 9).

Roentgen therapy was instituted to the clavicle through two fields, each including half the mass. A total dose of 2000 r was administered to each field in the course of three weeks, and a 50 per cent regression of the mass was noted. The pulmonary tumor was treated through anterior, lateral and posterior fields, each receiving 2000 r, and complete regression was obtained (Fig. 10). The patient is still under observation and, except for the residual clavicular tumor, is clinically and radiographically free of disease.

Discussion: This patient had a large soft-tissue mass adherent to the clavicle. Clinically and radiographically there was no evidence of involvement of the bone. The original biopsy diagnosis was hemangio-endothelioma.
A subsequent review of the slide established the diagnosis of endothelial myeloma. Recurrence was frankly intra-osseous with massive bone destruction. The initial tumor was radiosensitive. Its recurrence was relatively radio-resistant and only partial regression followed intensive therapy. The survival period, since the onset of symptoms, is now five and a half years. A pulmonary metastasis disappeared with irradiation.

Case IV (Montefiore Hospital No. 29115): J. M., a thirty-four-year-old man, was admitted to Montefiore Hospital in March 1938, and died one week later. In 1930 a “ganglion” had been removed from the region of the left ankle. No histologic examination had been performed. Six months later a firm, immovable, slowly growing mass appeared at the

operative site. Biopsy was not done until 1933, at which time histologic examination revealed a round-cell sarcoma. The patient was then (March 1933) referred to Mt. Sinai Hospital, New York City. Radiography of the left ankle joint (Fig. 11) revealed a soft-tissue mass lateral to the external malleolus. The fibula showed minimal absorptive changes, which were possibly of no pathological significance but might have represented invasion from without.

Radiotherapy was administered to the left ankle region, at Mt. Sinai Hospital, as follows: from May 25 to June 5, 1933, 300 r to each of four fields—anterior 6 × 8 cm., lateral 6 × 12 cm., internal 6 × 12 cm., posterior 6 × 12 cm. (180-200 kv., 40 cm. focal skin distance, 0.5 mm. copper + 1 mm. aluminum filtration); on June 19, 1933, radium element pack to the lateral aspect of the ankle (field 12 × 15 cm., 2 cm. distance, 1 mm. platinum filtration) for 23,750 mg. hours (210 mg. radium for 113 hours); June 25, to the mesial aspect of the ankle (12 × 13 cm. field) 210 mg. radium for 120 hours, or 25,820 mg. hrs. (same factors as to lateral aspect). Following this treatment the mass receded completely. Pulmonary metastases, which were first noticed in 1933, were also treated at this time and disappeared.

In 1936, a necrotic ulceration appeared in the soft tissues of the treated areas, for which amputation was performed below the knee.

Early in 1937, a mass developed above the right knee. Biopsy (Mt. Sinai Hospital)
revealed Ewing's sarcoma and roentgen therapy was instituted, 1500 r being given to each of four fields—anterior, posterior, medial, and lateral—in the course of five weeks, total 6000 r (factors as previously stated). Partial regression occurred after the treatment.

Several months later, signs of a transverse myelopathy developed from pressure of a metastatic vertebral focus. Examination on admission to Montefiore Hospital at this time showed evidence of a destructive cord lesion at the fifth dorsal segment. There was a large sacral decubitus with an osteomyelitis of the sacrum. In the right lower thigh was a fusiform swelling with a large soft-tissue mass surrounding the femur. Radiography of the femur showed a sclerosing lesion, with periosteal new bone formation, involving the lower half of the bone (Fig. 12). The immediate cause of death was sepsis and meningitis secondary to a bedsore.

Post-mortem Examination: Autopsy revealed diffuse osseous metastases involving the ribs, vertebrae, and right femur. The lungs, liver, pancreas, and suprarenals were involved; also their regional lymph nodes. Surrounding the right femur was a large soft-tissue mass. On longitudinal section numerous grayish hemorrhagic nodules of tumor tissue were seen in the substance of the bone, with a marked osteoclastic reaction surrounding them. Longitudinal trabeculae of bone of periosteal origin were evident. There was no distinct cortical or periosteal destruction and thus no gross continuity between the soft-tissue tumor and the osseous growth. Microscopically the tumor was seen to lie in the haversian canals, extending subperiosteally. The structure was typical of Ewing's tumor (Fig. 13).

Discussion: This patient with a round-cell tumor probably arising in the fibula had, as the first evidence of his disease, a soft-tissue mass which was interpreted as a ganglion. The tumor recurred after excision and receded with radiotherapy. Radiologic studies at no time showed changes which could be interpreted as primary neoplastic osseous disease. The treated area in the leg
broke down six years after radiotherapy and necessitated amputation. Pulmonary metastases receded after roentgen therapy but subsequently recurred. Death occurred with generalized bony metastases and cord compression. The total duration was eight years.

**Summary**

In each of the four cases described the tumor occurred in an adult, arising in a flat bone in three and in a long bone in one. On its first manifestation, the tumor process appeared essentially to be extra-osseous, with secondary adherence to bone but no definite evidence of bone destruction. Radiography of the flat bones involved in these cases is not always satisfactory or decisive and cannot be used as an absolute criterion of bony involvement. This argument is less cogent in the fourth case, in which a long bone was involved. It is probable that in all four cases there were bony changes which were not demonstrable radiographically. The bony pathology could not have been very extensive, however. It is probable that the tumor growing in the haversian canals reached the soft parts at an early stage in the disease, either by perforation of the periosteum or by extension along perforating lymphatics or blood vessels. Once outside of the bone, the larger part of the tumor growth occurred in the soft tissues. Following radiotherapy, the soft-tissue component of the tumor regressed rapidly. In Case IV, regression was complete and permanent; in Case II, incomplete. In Cases I and III, although the soft-tissue tumor was probably completely destroyed, some of the cells of origin of the tumor persisted in the bone and from these recurrence took place.

The question of soft-tissue origin of the tumors in question has been touched upon in discussing Case I. In the final analysis, unquestionable proof that the tumors arose in bone cannot be adduced, the evidence being only presumptive. In Case IV in particular, we have no proof that the fibula was at any time involved. Unfortunately, the amputated specimen was not examined histologically and we do not know whether tumor persisted in the bone or whether there existed microscopic changes compatible with the view that tumor had existed and been destroyed by irradiation. The evidences of bone involvement in the other three cases, which were seen late in the course of the disease, either clinically or at autopsy, are not conclusive proof of an origin in bone. That bone may be secondarily involved is undeniable, but it must be stated that in general the capacity for bone invasion by fragile, undifferentiated cells is very slight. The clinical evolution of the disease has been regarded as in favor of the diagnosis of Ewing's sarcoma. We must, however, admit our ignorance of the potentialities of evolution of the uncontrolled round-cell tumor of the soft parts.

The original tumor was in each instance radiosensitive and it is possible that with more vigorous treatment a lasting sterilization of the tumor might have been obtained. Certainly in the evaluation of the total dose to be delivered, the response of the soft-tissue mass is a misleading criterion and the total dose administered should considerably exceed that necessary for the complete disappearance of that tumor.

In two cases the recurrent tumors were subjected to a further course of
irradiation. They both proved to be radioresistant. Metastatic deposits, however, probably derived from the recurrent growth, proved to be radiosensitive. This would suggest that radioresistance acquired after previous roentgen therapy is not dependent on intrinsic cytological changes but rather upon alteration of the stroma of the neoplasm.

**Conclusions**

Four cases of Ewing's tumor are described in which radiographic examination of the affected bone did not reveal any pathology. Three of the tumors, however, occurred in flat bones (scapula, clavicle, and sacrum) in which slight changes in structure are difficult to demonstrate roentgenographically. The greater part of the tumor growth appeared to occur outside the bone, and a soft-tissue origin was suspected in each case. The tumors regressed after radiation therapy but subsequently recurred and metastasized.

**Bibliography**