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A FOLLOW UP STUDY OF OSTEOGENIC SARCOMA

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The progressive increase in the knowledge of the pathology and biology of bone tumors during recent years has given rise not only to certain changes in the anatomical and pathological classification, but also to new conceptions regarding their treatment and prognosis. This concerns even the osteogenic sarcomas. The five-year survival figures in the literature vary between 5 and 30 % (*Jaffe* 1958). Figures from the orthopaedic clinics here in Sweden are not so far available.

In the orthopaedic clinic of the Karolinska Institutet, due in part to collaboration with Radiumhemmet, a relatively large and uniformly assessed material of bone tumors is gathered, which we have followed and analysed with great interest. This article will throw light on the prognosis in our material of osteogenic sarcoma and in this connection the proposed treatment method of Sir Stanford Cade will be discussed.

DEFINITIONS

We mean by the term "osteogenic sarcoma" or osteosarcoma, those primary malignant tumors of bone which apparently have their origin from osteoblasts, and abnormal and malignant bone and osteoid are formed as tumor components. Since the precusor cell it totipotential, osteosarcomata may contain fibroblastic components and malignant cartilage in addition to bone and osteoid. Depending on the predominant differentiation observed microscopically in sections taken from various parts of the tumors, they may be classified as osteoblastic, chondroblastic or fibroblastic. With few exceptions, it is possible to make a clear-cut differentiation between chondro- or fibroblastic osteogenic sarcoma on the one hand, and chondro- or fibrosarcoma on the other hand; the latter two are not included in this investigation.

MATERIAL

The material consists of 41 proven cases of osteogenic sarcoma from the orthopaedic clinic during the twenty year period 1940–April 1959, and treated surgically either by amputation or disarticulation. In a little more than one half of the cases the operation was performed in the clinic, with or without preoperative radiation therapy, and in the remaining cases the operation was performed elsewhere and the patients were referred to us for prosthesis training and rehabilitation.

We would like to express our gratitude to Professor L. Santesson and his associates for their assistance in this study and we are particularly indebted to Dr. H. Spjut from Barnes Hospital, St. Louis, U.S.A. for critically reviewing the microscopic sections from our patients, during his time at the Radiopathological institute in Stockholm in 1960.

Age and sex distribution.

The average age for osteogenic sarcoma is lower than for such related tumors as chondrosarcoma and fibrosarcoma, as shown in table I.

TABLE 1

	Number	Males/ females	Agedistribution	Average age
Osteogenic sarcoma	41	24/17	7¼–76 years	20
Chondrosarcoma	10	5/5	23–70 years	43
Fibrosarcoma	7	3/4	30–62 years	48

The ages are taken from the time when symptoms of the tumor first developed. With regard to the ages the material is homogeneous. Only one patient is remarkably older than the others (see fig. 1). 32 patients (78 %) are aged 20 or younger. The number of males is 60 %.

Location.

The distribution of the osteosarcomata according to site of involvement is indicated in fig. 2.

34 (83 %) of the osteosarcomata were in the vicinity of the knee, and 3 of the remaining 7 were in the proximal end of the humerus.

As shown in fig. 2 there are only 2 cases in this series in which the osteosarcoma is situated outside the long bones, namely one in the scapula and one in the big toe, and these two patients were the only ones that exceeded 40 years of age (41 and 76 years respectively).

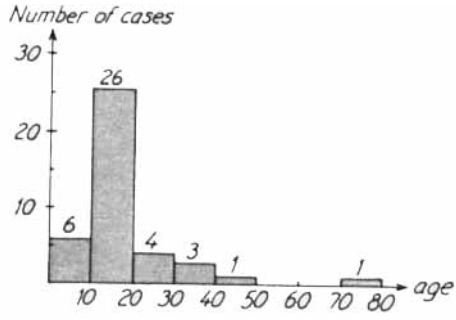

Fig. 1.

Age distribution of patients with osteogenic sarcoma.

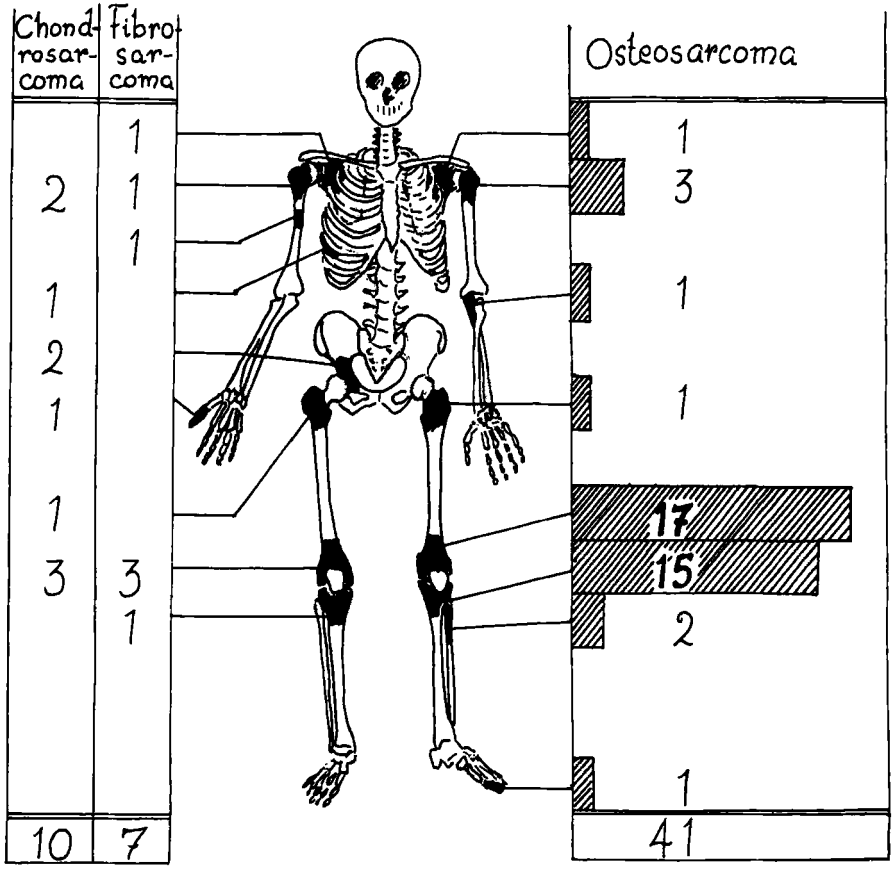

Fig. 2.

Anatomical distribution of bone sarcomata.

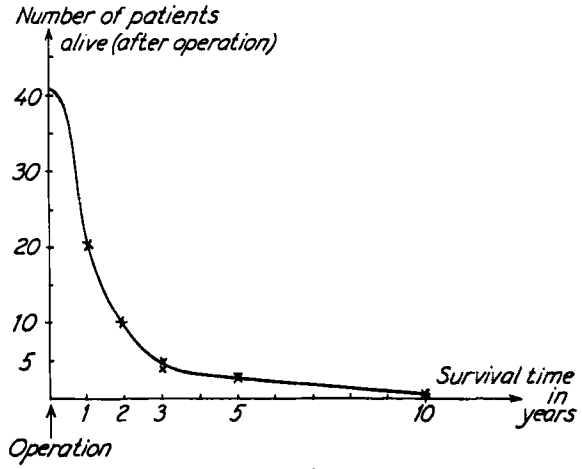

Fig. 3.
Survival time after operation for osteogenic sarcoma.

Survival rates.

The length of survival is computed from the date of the operation. The five year survival rate is based on 27 patients treated before April 1955, and the ten year group consists of ten cases treated before April 1950.

There were *only 3 patients* who *survived 5 years* (11 %). (One of these succumbed with pulmonary metastases 6 years and 9 months after an above-knee amputation for osteosarcoma in the end of the tibia).

Only *1 patient out of 10 is still alive 10 years* after operation.

In the whole series of 41 cases of osteosarcoma 20 died in less than 12 months after operation. Another 11 patients succumbed between 12 and 24 months after surgery, while the remaining 10 cases (24 %) survived more than 2 years. The diagram in fig. 3 shows the survival at different periods of time.

The relation of the survival rate to the position of the tumor and the promptness of operation.

One might think that immediate ablation of the affected limb would be the best and most uncontroversial course of action. In the present material, however, the patients with a longer interval between the onset of symptoms and operation apparently have a somewhat longer survival

time than those with less delay before operation (table 2), but the significance is not certain.

TABLE 2

Postoperative survival time	Number of cases	Average interval between onset of symptoms and operation
<12 months	20	3.8 months
>12—<24 months	11	4.7 months
>24 months	10	6.8 months

It is a prevalent opinion that the prognosis is more favourable when the tumor is in the tibia than in the femur. Out of the 4 patients who survived more than three years, the site was in the tibia in 3 and in the distal end of the femur in 1.

The significance of preoperative radiotherapy can not be assessed in this material. It is possibly worth mentioning that the only patient who lived more than 10 years was the only one who received a preoperative radiation dose which could be called large (more than 9000 r during three months).

The relation of the survival rate to the microscopic appearance.

The microscopic differentiation of tumors has a certain significance in the prognosis. Without doubt the most common type of osteosarcoma is the osteoblastic. Only three cases of this type were found among the ten patients who survived more than two years while six belonged to the chondroblastic and one to the fibroblastic variety.

Three out of the six cases of chondroblastic osteosarcoma were in the tibia and the others were in a big toe, humerus, and femur respectively. The fibroblastic osteosarcoma was in the distal end of the femur. That is, independent of their position, the chondroblastic and fibroblastic osteogenic sarcomata apparently have a somewhat better prognosis than the osteoblastic type and this is the opinion held by most authors on the subject.

DISCUSSION

Our material is highly selected. The tumor site in all cases, except one in the scapula, was in the extremities, and thus there are no tumors in the more "inoperable" central positions. Some of the patients had

their operations in other hospitals, and not until some months later were they admitted to this clinic for rehabilitation, and in this way some of the most urgent cases never lived to come here. Despite these favourable factors the five-year survival is discouragingly low (11 %).

This series of 41 cases is small but it is more homogeneous than others published on the subject. 85 % of the patients are under 25 years of age. All but one have pure osteosarcoma in the extremities (see fig. 2). Operation was performed early. The interval from onset of symptoms to surgery was less than 12 months in 39 cases. The other two were amputated 14 and 18 months respectively after the onset of symptoms.

The value of early mutilating surgery must be considered as small in view of the fact that 50 % of the patients will die from metastases in less than one year after operation. It seems tempting therefore to advocate the treatment, as proposed by *Cade,* of deferring amputation or disarticulation until sometime after the lesion has been treated by heavy irradiation. In this way the most fulminating cases will be spared unnecessary, ablative surgery. The definitive results of this therapeutic regime have not yet been published by *Cade*; but it appears from his preliminary report that the prognosis is better than after amputation at an early stage. It is not yet clear whether the reason for this improved prognosis depends on the intensive radiation therapy or on surgical treatment being reserved for the biologically least malignant tumors.

Considering the depressing survival figures resulting from the scheme of treatment we have employed up to now—one half dead within a year after operation, only 3 of 27 living after 5 years, and only 1 living out of 10 after 10 years—it is natural that we, together with colleagues from Radiumhemmet, have begun to study and to apply the new therapeutic approach.

The principles of the new treatment are carried out in the following way: Confirmation of the diagnosis by open biopsy, radiation by the supervoltage X-ray machine (6000–8000 r) during a period of 30–40 days, expectancy for 6 months thereafter, and if metastases have not appeared, high amputation of disarticulation.

To assure that the patients with bone tumors get the benefit of expert opinions from as many quarters as necessary (tumor biology, tumor pathology, radiotherapy, roentgenography and orthopaedics) we have for several years carefully aired these cases at clinical-pathological conferences. The difficulty of the problem and the relative rarity of malignant tumors of bone, make desirable a certain centralization

of bone tumor cases to clinics possessing the necessary facilities. This centralization also benefits pre- and post-graduate teaching. The Swedish bone tumor registry (*Lindbom & Santesson*, 1957) is greeted with satisfaction.

SUMMARY

A total of 41 cases of osteogenic sarcoma, considered from the anatomical and pathological viewpoints, and operated by amputation or disarticulation (with or without pre-operative radiation) from 1940–April 1959 inclusive, have been studied. Twenty died within one year and a further 11 died during the second year. 10 cases (24 %) survived more than 2 years. The five-year survival rate based on 27 cases operated prior to April 1955, amounted to 3 (11 %). Only one patient operated before April 1950 is living now!

The value of early amputation is questionable. The plan of therapy proposed by Sir *Stanford Cade*, with intensive pre-operative radiotherapy and delay of amputation for 6 months, is discussed. A certain centralization of bone tumor cases is desirable.

RESUME

41 cas de sarcome ostéogénétique, opérés par amputation ou disarticulation (avec ou sans radiation pré-opératoire) entre 1940 et avril 1959 inclus, ont été étudiés en partant de considérations anatomiques et pathologiques. Vingt des malades sont morts dans l'espace de la première année et 11 dans l'espace de la deuxième année. 10 cas (24 %) ont survécu plus de 2 ans. Le taux de survivance de plus de cinq ans a été calculé sur la base de 27 cas opérés avant avril 1955. Il s'élève à 11 % (3 malades). Un seul des malades opérés avant avril 1955 vit encore aujourd'hui.

La valeur de l'amputation précoce est douteuse. Discussion du plan de thérapie proposé par Sir *Stanford Cade*, avec radiothérapie pré-opératoire intense et un délai de 6 mois avant d'effectuer l'amputation.

Il serait souhaitable d'effectuer une certaine centralisation des cas de tumeur osseuse.

ZUSAMMENFASSUNG

Eine Gesamtzahl von 41 Fällen von osteogenetischen Sarkom, vom anatomischen und pathologischen Gesichtswinkel betrachtet, die mittels Amputation oder Exartikulation (mit oder ohne präoperative Be-

strahlung) von 1940–April 1959 behandelt wurden, sind untersucht worden. Zwanzig starben im Verlaufe eines Jahres und weitere 11 während des zweiten Jahres. 10 Fälle (24 %) überlebten mehr als zwei Jahre. Die Zahl der Überlebenden nach 5 Jahren war, unter Zugrundelegung von 27 Fällen, die vor April 1955 operiert worden waren, drei (11 %). Nur ein einziger Patient von denen, die vor April 1955 operiert worden waren, lebt noch.

Der Wert der frühzeitigen Amputation ist zweifelhaft. Der von Sir *Stanford Cade* vorgeschlagene Behandlungsplan, der in einer intensiven präoperativen Röntgenbestrahlung und späterer Amputation nach 6 Monaten besteht, wird besprochen.

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