HIGH-GRADE METACHRONOUS OSTEOSARCOMA A CASE REPORT OVER A 23-YEAR PERIOD

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This is a case report on the remarkable 23-year course of a metachronous osteogenic sarcoma in a 31-year-old man. Histology invariably showed the features of a high-grade osteogenic sarcoma with predominantly chondroblastic cells. During the observed period the patient developed nine osseous metastases. The quiescent clinical course of some metastases was in sharp contrast to the histological pattern. The patient finally died from symptoms of increasing cervical spinal cord compression without ever developing lung metastases.

Keywords : osteosarcoma ; high-grade ; long term.
Mots-clés : ostéosarcome ; haute malignité ; long terme.

INTRODUCTION

Multifocal bone lesions of osteogenic sarcoma with absent or late appearing lung metastases are rare (1, 3, 4, 6, 8, 9, 10). They have been reported in only 0.5 to 1.5% of cases with osteogenic sarcoma (6, 8, 9). Although in earlier years elaborate classifications have been proposed to distinguish different patterns of multifocal osteogenic sarcoma (1, 10, 11), it seems more practical simply to distinguish two types (13) : multifocal lesions, which are either detected simultaneously representing synchronous lesions, and two or more lesions which are diagnosed after a time interval of several months, representing metachronous lesions. The synchronous or multicentric osteogenic sarcoma typically occurs in adolescents, more often in females. This type usually shows classic osteosclerotic lesions with rapid progression, early lung metastases and rapid demise (6). The metachronous osteogenic sarcoma is seen more frequently in adults. Subsequent lesions typically occur at an average time interval of 35 months after treatment of the first lesion. Lung metastases do not develop at all or only late in the course. Prognosis and survival rates seem to differ significantly from the former type (8, 9, 13, 15). Metachronous osteogenic sarcoma has been reported to be much more infrequent than synchronous osteogenic sarcoma (15).

This report presents the remarkable case of a 31-year-old man who developed a high-grade osteogenic sarcoma at nine different osseous sites over a treatment period of 23 years, and who ultimately died from the disease without ever developing detectable lung metastases.

CASE REPORT

In November 1972, a 31-year-old man presented after spontaneous onset of pain in the left shoulder with a radiographic pattern of an osteolytic lesion with stippled calcifications in the left proximal humerus. An incisional biopsy was done, and histology revealed a predominantly chondroblastic osteogenic sarcoma grade III according to the NCI

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Table I

Date	Tumor site	Histology	Surgical treatment	Chemotherapy	Radiation
Nov. 72	left proximal humerus	Osteosarcoma grade III (NCI) with chondro-blastic features	1.73 : wide resection, humeral head endoprosthesis		11.-12.72 : preoperative radiation (30 Gy)
Oct. 78	left ninth rib	same	wide resection	02.-07.79 : Adriamycin	
Feb. 83	right dorsal ilium	same	biopsy	03.-05.83 : Bleomycin, Actinomycin-D, Cyclophosphamide, Vincristine	03.-04.84 07.-08.83 : Twice 8 × 2.75 Gy
Jan. 87	left scapula	same	11.89 : scapulectomy		01.-02.87 : 30 Gy
Feb. 87	sternum				02. 87 : 60 Gy
July 89	vertebral body L2	same	04.91 : intralesional resection, Palacos implant, dorsal stabilization		06. 91 : 50 Gy
July 89	right costovertebral angle Th 1				
Feb. 92	left clavicle	same	08.92 : marginal resection		
Sept. 92	vertebral body Th 4	neoplastic cells	09.92 : intralesional resection, decompression, Palacos implant, dorsal stabilization;		03.93 : 40 Gy
		same (rare osteoid)	04.94 : intralesional resection recurrence Th 4 and decompression, intralesional resection, Palacos implant and dorsal stabilization Th 1;		
		same (rare osteoid)	10.94 : ventral intralesional resection and stabilization 2nd recurrence Th 4-5		
Jan. 95	vertebral body C 5	same	01.95 : decompression C 3-6		
Nov. 95	Death				

classification. We are unable to determine if treatment was standardized at our institution at that time ; treatment in this case included preoperative radiation therapy of the left shoulder with a total dose of 30 Gy . In January 1973 the patient underwent wide resection and reconstruction with a humeral head endoprosthesis (table I, figs. 1, 2).

Nearly 6 years later an osteolytic lesion of the left ninth rib was widely resected. Histology revealed a high-grade osteogenic sarcoma with a predominantly chondroblastic pattern. Postoperatively single drug chemotherapy with adriamycin over five months was given with a total dose of 1020 mg.

In February 1983, more than 11 years after tumor onset, an osteolytic lesion in the right dorsal ilium was biopsied, revealing the same histological diagnosis. Three cycles of multidrug chemotherapy including bleomycin 40 mg I.M., actinomycin-D 1.5 mg I.V., cyclophosphamide 2200 mg I.V., vincristine (table I) were given. Chemotherapy was stopped for tumor progression, and two cycles of local radiation therapy with 8 × 2.75 Gy were given. The lesion became sclerotic without progression (fig. 3).

In January 1987 a new lesion in the left scapula was radiated with a total dose of 30 Gy. The tumor remained unchanged in size until two years later,

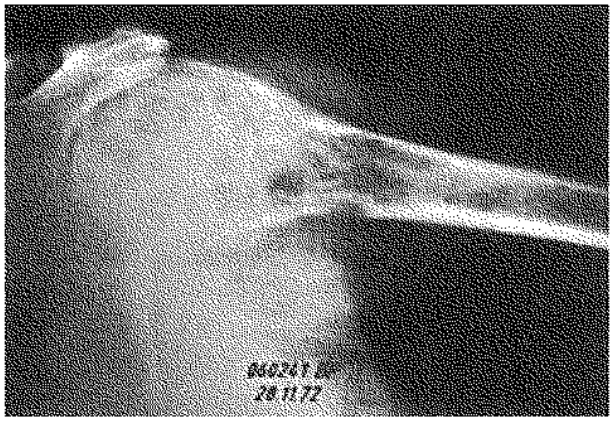

Fig. 1. — November 1972 ; Plain anteroposterior film shows radiographic pattern of an osteolytic lesion with stippled calcifications in the left proximal humerus of a 31-year-old man. Histology revealed a predominantly chondroblastic osteogenic sarcoma grade III.

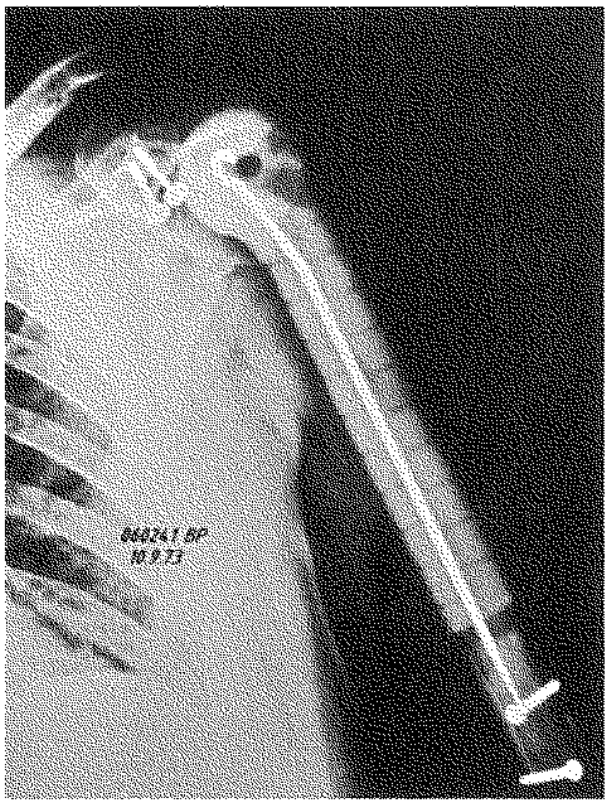

Fig. 2. — September 1973 ; Plain anteroposterior film after preoperative radiation therapy of the left shoulder followed by wide resection and reconstruction with a humeral head endoprosthesis.

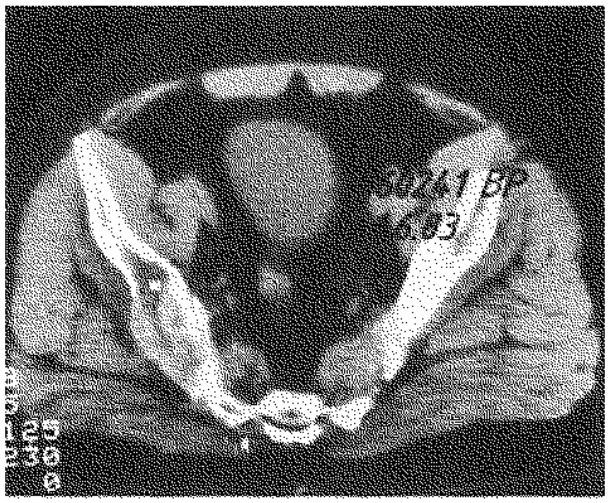

Fig. 3. — June 1983 ; Pelvic CT-scan more than 11 years after tumor onset shows an osteolytic lesion in the right dorsal ilium, revealing the same histological diagnosis. Three cycles of multidrug chemotherapy were given. Chemotherapy was stopped for tumor progression, and two cycles of local radiation therapy were added.

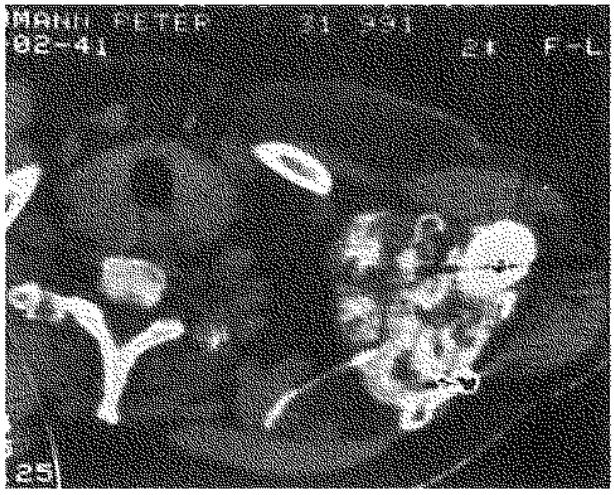

Fig. 4. — February 1988 ; CT-scan of the left scapula five years later shows a new lesion which was irradiated. The tumor remained unchanged in size until further progression occurred two years later. A scapulectomy was performed confirming the same histology as the initial tumor.

when further progression occurred. In November 1989, a scapulectomy was performed confirming the same histology as the previous lesions (fig. 4). Another lesion in the body of the sternum was radiated with a total dose of 60 Gy in February 1987.

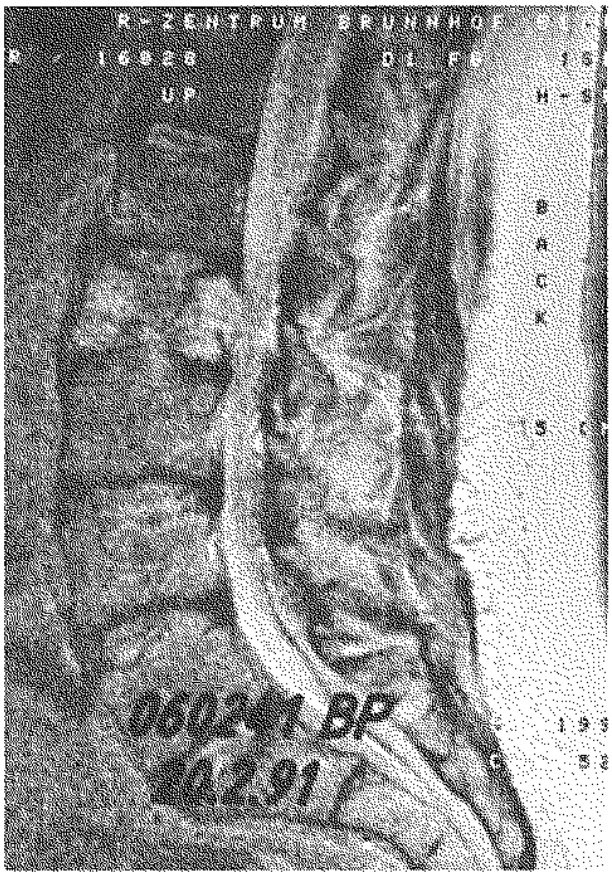

Fig. 5. — February 1991 ; MRI revealed tumor progression in the second lumbar body. Intralesional resection and Palacos implantation including dorsal stabilization of the second lumbar body was performed followed by radiation.

In July 1989 two other osseous lesions were detected. The first lesion was in the second lumbar vertebral body, and the second lesion was in the right costovertebral angle at the level of the first thoracic vertebra. In 1991 tumor progression in the second lumbar body occurred. Intralesional resection and Palacos implantation including posterior stabilization of the second lumbar body was performed. In addition the lesion was radiated with a dose of 50 Gy (fig. 5). A lesion in the left clavicle occurred in February 1992 leading to marginal resection.

In September 1992, seven months later, involvement of the fourth thoracic vertebral body was diagnosed. Intralesional resection, decompression and Palacos implantation including dorsal stabilization from thoracic level one to five was done repeatedly. Postoperatively the tumor site was treated with external beam radiation with a total dose of 40 Gy (figs. 6, 7).

In January 1995 the fifth cervical body revealed tumor with the same histological pattern. Decompression and dorsal stabilization were performed from cervical level three to six. The tumor however progressed with infiltration of the spinal canal leading to partial tetraplegia, respiratory insufficiency, pneumonia and ultimately to death in November 1995.

DISCUSSION

Although it can be speculated whether the lesions in the left scapula and left clavicle represent local recurrences of the primary tumor in the left proximal humerus, this case remains exceptional, representing one of the largest reported numbers of metachronous lesions without developing detectable lung metastases. The time interval between the first and second lesion was 60 months, which is considerably longer than the reported

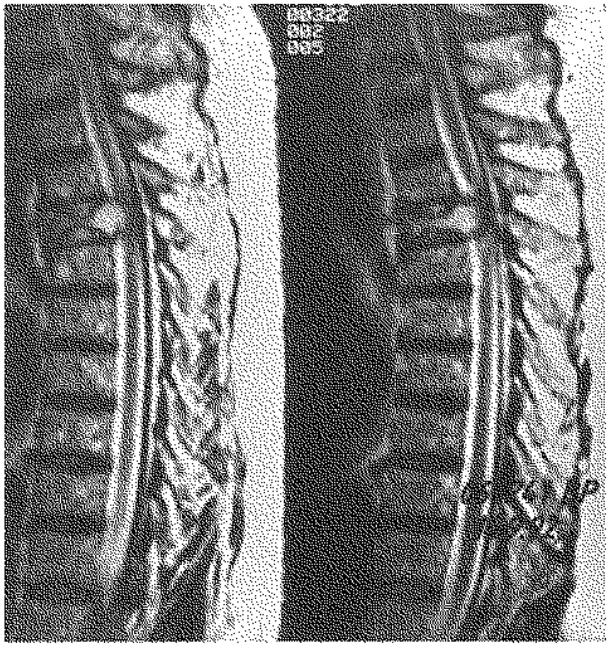

Fig. 6. — September 1992 ; MRI diagnosed involvement of the fourth thoracic vertebral body.

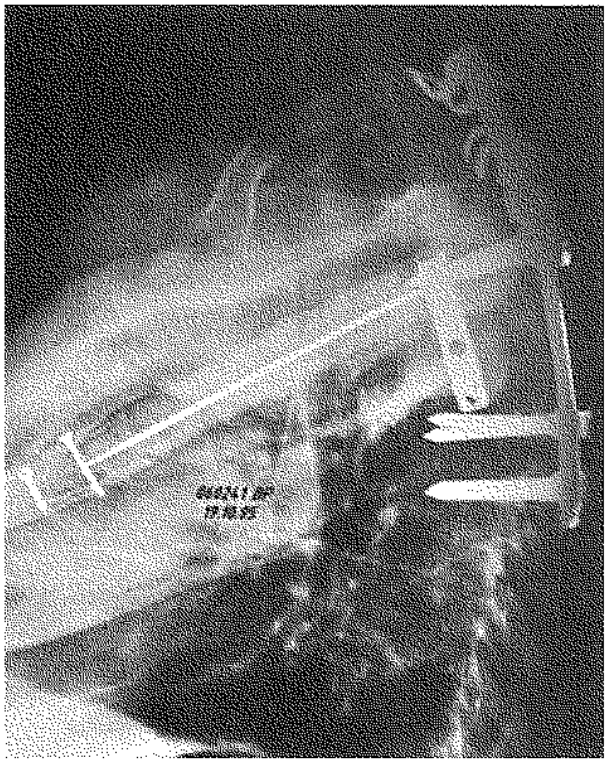

Fig. 7. — October 1995 ; Intralesional tumor resection including vertebral resection and spinal cord decompression with subsequent dorsal stabilization from thoracic vertebrae one to five was performed. Postoperatively the tumor site was radiated with 40 Gy.

mean time interval in the literature of 35 months. However the longest reported time interval so far was 163 months (8, 9).

There has been debate whether multifocal bone lesions represent a multicentric origin or rapid metastases of osteogenic sarcoma (6, 13). However, the answer remains speculative, and a clear distinction cannot be made by current histological means. In the present case there are several points which support metastatic disease. The large number of 10 subsequent lesions at different osseous sites, which do not represent typical sites of primary osteogenic sarcoma, render primary origin at each of these sites unlikely. The consistent histologic pattern of a high-grade osteogenic sarcoma with predominantly chondroblastic features throughout all the lesions also makes metastatic disease more probable. Histologic material was obtained from eight sites. Outside consultation confirmed the consistent diagnosis in two specimens. In addition the consistent biological behavior with unusually slow and relatively unaggressive growth are in favor of a common origin and biology. It should also be remembered that bone represents the second most frequent site for metastatic lesions of an osteogenic sarcoma (13).

A change of the metastatic pattern to more frequent bone metastases in osteogenic sarcoma subsequent to adjuvant chemotherapy has been discussed in earlier years (3, 4, 5). In the present case chemotherapy is unlikely to be the cause of an atypical metastasis pattern, since chemotherapy was used only later in the course after resection of the first recurrence. It consisted of a single drug therapy of adriamycin over 5 months. The second course of chemotherapy, which was a multidrug regimen, was abandoned after 3 cycles. It was administered 11 years after tumor onset after detection of the second relapse, but tumor progression in the right ilium proved chemotherapy to be ineffective.

It seems very likely that tumor biology and/or host immune response differed from the usual course of osteogenic sarcoma. Although histologically the tumor always represented a high-grade lesion, tumor growth and progression was unexpectedly slow and differed significantly from the typical course of a high-grade osteosarcoma. This is represented best by the slow progression of the lesions in the left scapula and right costovertebral angle, which were not treated over a period of two and four years respectively after detection. Radiation treatment alone of two lesions in the ilium and sternum proved to be unusually successful without further progression after seven and ten years respectively. An unusually slow progression of metachronous lesions of osteogenic sarcoma without any treatment also has been reported by other authors (13, 15). In addition it was noted that lesions formerly active on bone scans became quiescent without any treatment (15). Long-time survivors of more than 10 years have been described in metachronous osteogenic sarcoma despite histological high-grade lesions (9, 13, 15). The survival of 23 years in this case represents one of the

longest reported survivals of a metachronous osteogenic sarcoma. Further methods to understand tumor biology are needed. Attempts at discrimination of variant subtypes of osteogenic sarcoma have been made with immunohistochemical methods (7) and cytogenetic studies (2, 14). Alterations of distinct oncogenes and tumor suppressor genes appear to be correlated with the degree of tumor growth and aggressiveness and a variant risk for recurrent or metastatic disease (2, 14).

Metachronous osteogenic sarcoma seems to represent a separate entity with a better prognosis than classic osteogenic sarcoma metastasizing to the lungs. It seems reasonable to treat each subsequent osseous lesion as a primary tumor. Probably a less aggressive tumor treatment for metachronous lesions may be chosen in individual cases, especially when standard surgical treatment, aiming at a wide or radical resection margin, would lead to considerable disability. Slow tumor progression in older patients with a late onset of a metachronous lesion might even justify restricting treatment to less invasive radiation therapy or initially to follow closely the spontaneous course.

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SAMENVATTING

D. F. KALBERMATTEN, W. WINDISCH, K. A. SIEBENROCK. Hyperkwaadaardig osteosarcoom van het diachronische type (met golvend verloop). Een geval met verloop over 23 jaar.

De diagnose werd vanaf het begin gesteld bij een 31-jarige man. De evolutie spreidde zich uit over 23 jaar. Histologisch noteerde men doorheen het hele verloop dezelfde elementen, typisch voor een zeer kwaadaardig osteosarcoom met hoofdzakelijk chondroblasten. Tijdens de bestudeerde periode vertoonde de patiënt 9 metastasen. Sommige metastasen bleven zeer rustig, wat in scherpe tegenstelling stond met de histologische bevindingen. Uiteindelijk stierf de patiënt tengevolge van een cervicale mergcompressie, maar zonder ooit longmetastasen te hebben ontwikkeld.

RÉSUMÉ

D. F. KALBERMATTEN, W. WINDISCH, K. A. SIEBENROCK. Ostéosarcome diachronique de haute malignité : présentation d'un cas dont l'évolution s'est étalée sur 23 ans.

Les auteurs rapportent l'histoire d'un ostéosarcome diachronique diagnostiqué au départ chez un homme de 31 ans et dont l'évolution clinique s'est étalée sur une période de 23 ans. L'étude histologique a montré constamment d'un bout à l'autre les mêmes éléments caractérisant un ostéosarcome de haute malignité avec une prédominance de cellules chondroblastiques. Au cours de la période d'observation, le patient a présenté 9 métastases osseuses. L'évolution clinique quiescente de certaines métastases contrastait nettement avec les caractères histologiques. Le patient est finalement décédé après avoir présenté une compression évolutive de la moelle cervicale mais sans jamais présenter de métastase pulmonaire.