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Metastasizing chordoma of the lumbar spine

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Abstract Chordoma is a dysontogenetic bone tumour that appears in the region of the axial skeleton. Its malignant transformation has been underestimated in the past, since the incidence of metastasis is disputed. This paper describes a chordoma of the fifth lumbar vertebra, which at first was monolocular, but in the course of the disease led to a diffuse metastasis of the spine. Specific histological findings and the differential diagnosis of the chordoma are discussed, as well as previous descriptions in the literature relating to course, diagnosis, and therapy.

Keywords Chordoma · Metastasis · Histology · Therapy

Introduction

In the middle of the 19th century, Rudolf Virchow first described small tumours with large, round, so-called “physaliphoric” cells in the region of the clivus, whose origin he erroneously assumed to lie in the synchondrosis spheno-occipitalis. In 1858, Müller described the similarity of these tumours to the chorda tissue. Thus, he suggested the term “chordoma”.

Because of the aetiology, the chordoma belongs to the dysontogenetic bone tumours. This is the consequence of an incorrect differentiation of embryonic predisposition. Wright [25] has the opinion that the chordoma may only develop from aberrant residual chorda, since there are no reports of a chordoma ever having developed from normal

residues of the chorda – the nuclei pulposi. Corresponding to the course of the chorda dorsalis, chordomas primarily appear in the region of the axial skeleton. Their malignant power was underestimated for a long time, because the classic patho-histological marks of a malignant tumour often did not appear [1]. Similarly, the fact that these tumours can metastasize was not generally known, because histological study proved metastases were either missing [12] or were very rare [11]. With time, the fact that chordomas do metastasize has come to be generally accepted. The reported rates of incidence of such metastases, however, vary widely, ranging from 3 to 48%. For the purpose of treatment of patients, it is important to establish clinical or histological prognostic parameters.

Fig.1 Chordomas are characterized by a lobular structure of physaliphoric cells, which grow trabecularly. Besides that, a lot of mucoid material and stroma areas interspersed by inflammatory cells can be observed (staining technique: haematoxylin and eosin; original magnification $\times 150$)

Histology

Chordomas are tumours that grow infiltratingly, and are often lobulated by septums of the connective tissue. Histologically, they consist of so-called physaliphoric cells, which primarily grow trabecularly (Fig. 1).

In some cases, malignant areas with a clear cellular pleomorphism, hyperchromatism, and a raised mitotic activity may be observed [22]. Some chordomas degenerate malignantly. In such cases, various differentiations, such as undifferentiated spindle cell tumours [8, 14] or malignant fibrous histiocytomas [2, 15, 20], have been observed.

The histological differential diagnosis of chordomas, especially in small biopsy particles and in frozen sections, comprises metastases of carcinomas, pleomorphic adenomas (craniocervical), and chondrosarcomas. The chordoma shows a mixed mesenchymal-epithelial phenotype and immunoreactivity for vimentin as well as for cytokeratin and the epithelial membrane antigen (EMA) (Fig. 2A). Furthermore, a positive reaction with antibodies against the S100-protein is achieved, while chondrosarcomas S100 and sometimes EMA express but are negative for cytokeratin (Fig. 2B). Carcinomas show a positive reaction with antibodies against cytokeratin and EMA and they do not react with those against S100. Besides, carcinomas may be distinguished from chordomas by a different pattern of ceratin subtypes [16].

Fig.2 **A** The epithelial nature of this tumour becomes visible through a positive reaction with antibodies against the epithelial membrane antigen. **B** A comparable pattern may be achieved with antibodies against the S100-protein (PAP-technique; original magnification $\times 150$)

Fig. 3 **A** January 1999: a tumorous destruction of the fifth lumbar vertebra is shown on a T1-weighted magnetic resonance (MR) image. The other vertebral bodies are depicted less conspicuously. **B** October 1999: a diffuse tumorous affection of the entire spine is shown on a T2-weighted MR image. A metastatic formation of the known chordoma in the 11th thoracic vertebra was proved biotically

Case report

Early in September 1998, a dorsal decompression of L4-S1 was carried out on a 72-year-old adipose patient on the basis of the clinical and radiological features of lumbar stenosis of the spinal channel in a peripheral hospital. At that time, a reduction in height of the fifth lumbar vertebra had been detected radiologically, so that a test biopsy was taken from the fifth lumbar vertebra intraoperatively. It was found to be inconspicuous. After initial signs of

recovery, severe low back pain and sciatica of the right lower limb reappeared. The magnetic resonance imaging (MRI) examination for the lumbar and thoracic spine, which was done consequently, showed a complete tumorous destruction of the fifth lumbar vertebra (Fig. 3A). Apart from that, no other vertebral bodies were found to be affected. The patient was transferred to the orthopaedics department at Mainz University Hospital, and was investigated for tumour metastases for the purpose of tumour staging. This involved computed tomography (CT) of the abdomen and thorax as well as scintigraphy for the bone. All revealed no other tumour site, establishing the primary tumour as situated in the region of the spine. In spite of repeated histological examination of the stanza biopsy, which was done at another hospital, no evidence of tumour was found. Because of progressive destruction of L5, a new open biopsy was done. The results of microscopic examination of the frozen section determine whether only a dorsal intralesional tumour reduction or an extensive extralesional extirpation from ventro-dorsal should take place. The material obtained intraoperatively was judged, from an immediate section taken for microscopic examination, to be a metastasis of an adenocarcinoma. As far as it is possible from a dorsal access, the tumour was resected from the entire vertebra. After the interposition of a palacospacer, L4-S1 transpedicular spondylodesis was done (Fig. 4A). The final histopathological evaluation of the obtained tumour tissue, made after an immunohistochemical examination, resulted in the finding of a chordoma (Fig. 4B). Since indications for metastases were missing at that time, a ventral retroperitoneal evacuation of the remaining local destructively growing tumour was carried out. Postoperative radiotherapy was planned, but the patient refused the medical advice.

Three months after the operation an MRI examination revealed multiple foci of suspected metastases in nearly all the vertebral bodies of the lower thoracic and lumbar part of the spinal column (Fig. 3B). In addition to this, evidence a local tumour recurrence was found on the MR images. CT of the thorax and abdomen was done again as part of follow-up looking for metastases. No further metastases were seen. By means of scintigraphy, on the other hand, the multiple foci of suspected metastases in nearly all vertebral bodies of the lower thoracic and lumbar part of the spinal column, which had already been revealed by MRI, were seen. Consequently a CT-controlled test biopsy of one of the foci (the 11th thoracic vertebra) was done, which resulted in the finding of a metastatic formation of the known chordoma. Because of this situation, no further therapy was applied. At the end of the year 2000, the patient is still alive, and without neurological complications. By request of the patient no additional diagnostic measures were performed.

Fig. 4 **A** Pathological compression fracture of the fifth lumbar vertebra after a chordoma was histologically proven. **B** Spondylodesis of L4-S1 after the dorsal extirpation of the tumour and interposition of the palacospacer

Discussion

With an incidence of 3.5–4%, chordomas belong to the rare bone tumours in the region of the spine. They mainly appear in mid-life, between the ages of 40 and 60, and primarily affect the male sex, with a proportion of between 2:1 and 3:1 [11]. Aetiologically, the tumours originate in rudiments of the embryonary notochorda tissue, and thus belong to the dysontogenetic bone tumours. The notochorda corresponds to the primitive tissue of the axial organ. Consequently, the primary localization of the chordoma may be found exclusively in the course of the spine as well as in the region of the clivus, intracranially. Sacrococcygeal localization has been observed most frequently (50–60% of all cases), followed by an intracranial location (in 25–40% of all cases). Primary vertebral tumours were described in 9–15% of all cases. According to Jenny and Sulser [11], chordomas that are clearly benign are described as symptomless incidental findings on the clivus blumenbachii in 1.5–2% of all autopsies.

However, the chordoma usually is a slowly locally destructively growing tumour, which is surrounded by a connective tissue-like pseudocapsule. An infiltration of the capsule by chordoma cells may often be found histologically. The latter also grow into the adjacent tissue. Only a dorsal, ventral, and lateral expansion of the tumour is observed. A vertical expansion is obviously prevented by the cartilaginous endplate of the vertebral bodies and the intervertebral discs. Because of the spinal localization and the destructive growth, a radical surgical resection is often impossible from an oncological point of view, so that local relapses may be observed frequently.

The clinical symptomatology is determined by the location and expansion of the tumour and the relation to adjacent anatomic structures connected with it. The place of origin of the tumour – which is centrally based in the vertebral body – may be explained by the embryological development. It is responsible for the fact that there often is a long latency between the development of the tumour and the diagnosis (1.5 years on an average) [18].

In most cases, only a tumorous destructive space occupation can be depicted with the help of radiological examination. Specific diagnostic MRI features or radiological signs of the chordoma are not known. The diagnosis may only be secured by a biopsy of the tumour. In the literature, several cases are described in which disc prolapse was diagnosed, but only the critical histological evaluation of the extracted material made obvious the real cause of the intraspinal space occupation [17].

The incidence of chordoma metastases is estimated differently in the literature, and lies between 3 and 48%. Within the framework of a literature review, Chambers and Schwinn [5] found out that pulmonary metastases and lymph node metastases appear most frequently, followed by liver and bone metastases. Skin metastases are described to appear with a frequency of 6.3–10% [21]. According to Hingnbotham et al. [7] and Chambers and

Schwinn [5], metastases have more frequently been observed with primary localized vertebral chordomas than with sacrococcygeal chordomas. For primary tumours of the skull base region, however, metastases have only been described in a small number of cases [11]. The appearance of metastases depends mainly on the histological differentiation of the tumour, and should not be correlated to the duration of the clinical course. However, a histological judgement is difficult, since significant prognostic influences of the cellular structure have not been proved yet [23, 24]. The histological differential diagnosis comprises mucinous adenocarcinoma, chondrosarcoma, chondroma, pleomorphic adenoma, and the myxopapillary ependymoma. Because of the difference in prognosis, the differentiation between chordoma and chondrosarcoma is important. In spite of intensive therapy, chordoma has been found to have a worse prognosis than chondrosarcoma. While a 99% survival rate of 5–10 years has been achieved with chondrosarcomas, it is only 40–70% with chordomas [19]. Larger tumour size, inadequate surgical margins, microscopic tumour necrosis, Ki-67 > 5% (Ki-67 is a nucleolar protein, which is tightly associated with somatic cell proliferation) and local recurrence were found to be adverse prognostic factors [3]. The prognosis of vertebral chordoma has been valued in different ways. In 1973, Jenny and Sulser [11] described an average survival rate of 17.5 months. Cheng et al. [6] published in 1999 the results of 23 patients with a lumbosacral chordoma after surgical resection and radiotherapy. The overall survival rate after 5 years was 86% and the local recurrence-free survival was 60%. More pessimistic results were reported by York et al. [26], with a disease-free interval of 2.27 years after radical resection of sacral chordoma. Jeanrot et al. [10] also described a disease-free rate after 5 years of only 10–20% in cases of sacral chordoma after surgical resection, but the overall survival rate was 64%. Because of the small number of cases, a reliable judgement of the prognosis seems to be impossible.

The current case represents the histological diagnosis problems of the chordoma. The frozen section resulted in the findings of an adenocarcinoma, which is one of the typical histological differential diagnoses for the chordoma. Later on, several reference pathological findings revealed the chordoma. Due to this misinterpretation, initially a palliative intralesional tumour reduction was done. With the knowledge of the final diagnosis of a chordoma, however, a combined ventro-dorsal procedure with a wide extralesional tumour extirpation was necessary on the basis of oncological criteria.

In 1992, Magrini [13] noted that the natural history of the disease seemed to be only marginally affected by any treatment, and demanded new therapeutic options. The current therapy primarily involves a more or less complete resection of the tumour, depending on the anatomic-topographical conditions. In many cases, an en bloc extirpation is only successful with inclusion of the adjacent soft tissues, the coccyx, and parts of the sacrum. Chor-

doma inevitably recurs after intralesional removal or tumour resection without a safety margin. Therefore, radical surgery should be attempted whenever technically possible. In the literature, evaluations of the benefit of postoperative radiation vary widely. It has even been stated that number of metastases increases after radiation [5]. More recent studies, however, show that, at least after an incomplete extirpation of the tumour (without safety margins), postoperative radiation leads to prolongation of the disease-free interval. Hug et al. [9] reported on 33 patients with a chordoma of the skull base, in whom fractionated proton radiation therapy was administered following various surgical procedures. Target dosages were, on average, 70.7 Co Gy equivalent. They described local control rates of 76%. All tumours with volumes of 25 ml or less remained locally controlled, but this was so for only 50% of

tumours larger than 25 ml. Berson et al. [4] also described a significantly better local tumour control rate in cases of tumour volume less than 20 cc after subtotal surgical resection of chordoma.

In conclusion, every surgical effort should be made to reduce tumour bulk, because smaller tumour size is correlated with improved outcome. Our case shows the need for an exact preoperative histological diagnosis. With radiological suspicion of a spinal tumour, a representative biopsy according to tumour-surgical criteria should be done similar to a peripheral primary bone tumour.

Because radiation therapy may prove to be more successful in controlling microscopic disease [4, 5, 9, 23], it should be considered as a pre- or postoperative adjuvant to a macroscopically total and subtotal resection.

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