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Case report

Parachordoma: an ultrastructural and immunohistochemical study

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Abstract. A case of parachordoma of the left calf in a 19-year-old Chinese female is reported. The tumour showed multinodular growth pattern and consisted of round or oval tumour cells with abundant eosinophilic cytoplasm and myxoid matrix. Tumour cells formed small nests and sometimes showed concentric arrangement. Physaliferous-like cells and undifferentiated spindle cells were occasionally observed among the cell nests. The myxoid matrix was positive for high-iron diamine stain, indicating the presence of chondroitin 4- and 6-sulphates and keratan sulphate. Ultrastructurally, well-developed rough endoplasmic reticulum, abundant intermediate filaments, microvillous cytoplasmic processes, pinocytic vesicles, and desmosome-like junctional structures were found. Tumour cells were positive for S-100 protein and vimentin, but negative for cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, and desmin. These results are consistent with the definition of parachordoma as a soft tissue neoplasm consisting of cells with histology and ultrastructure similar to those of chordoma cells but with immunohistochemistry similar to that of chondroid tumour cells.

Key words: Parachordoma – Extraskeletal myxoid chondrosarcoma – Chordoma – Immunohistochemistry – Electron microscopy

Introduction

Parachordoma is a rare soft tissue neoplasm first reported by Laskowski and later extensively studied by Dabska (1977). According to Dabska's report, the lesion usually arises in the deep soft tissues of the extremities adjacent to the tendons, synovium, and osseous structures. This neoplasm can be distinguished from extraskeletal myxoid chondrosarcoma, which is also called chordoid sarcoma (Enzinger and Shiraki 1972; Mehio and Ferenczy 1978; Dardick et al. 1983; Enzinger and Weiss 1988a), because of its distinct histological appearance. Although parachordoma resembles the fetal chorda dorsalis or notochord histologically, the exact histogenesis of the tumour is uncertain. In the present study, we performed ultrastructural and immunohistochemical studies in a case of parachordoma to elucidate its histogenesis.

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Case report

The patient was a 19-year-old Chinese female with a history of a tumour of the left calf which had been resected under the diagnosis of myxomatous tumour at a hospital in Shanghai in 1987. However, no detailed clinicopathological information about the lesion could be obtained. She had subsequently noticed a painful mass in the same region of the lower leg in 1990, and was admitted to the National Medical Center Hospital on 30 November 1990. Computed tomography revealed a low-density tumour without calcification in the left lower leg. It appeared as a low-intensity mass on T1-weighted magnetic resonance imaging (MRI) and as a nodular high-intensity mass on T2-weighted MRI. Recurrence of the tumour was suspected, and wide resection was performed on 7 December 1990. There has been no evidence of local recurrence or metastasis for over 1 year after the operation.

Materials and methods

Histological sections stained with haematoxylin and eosin, periodic acid-Schiff (PAS) with and without diastase digestion, Azan Mallory, and silver impregnation were examined microscopically. For histochemical study of the tumour myxoid substance, sections were stained with alcian blue at pH 2.5, colloidal iron with and without testicular hyaluronidase (Sigma) digestion, and high-iron diamine (HID).

For electron microscopy, small fragments of tumour tissues were fixed in 2.5% glutaraldehyde in 0.1 M cacodylate buffer at 4° C. They were then post-fixed in 1% osmium tetroxide and embedded in Epon 812. Ultra-thin sections were stained with uranyl

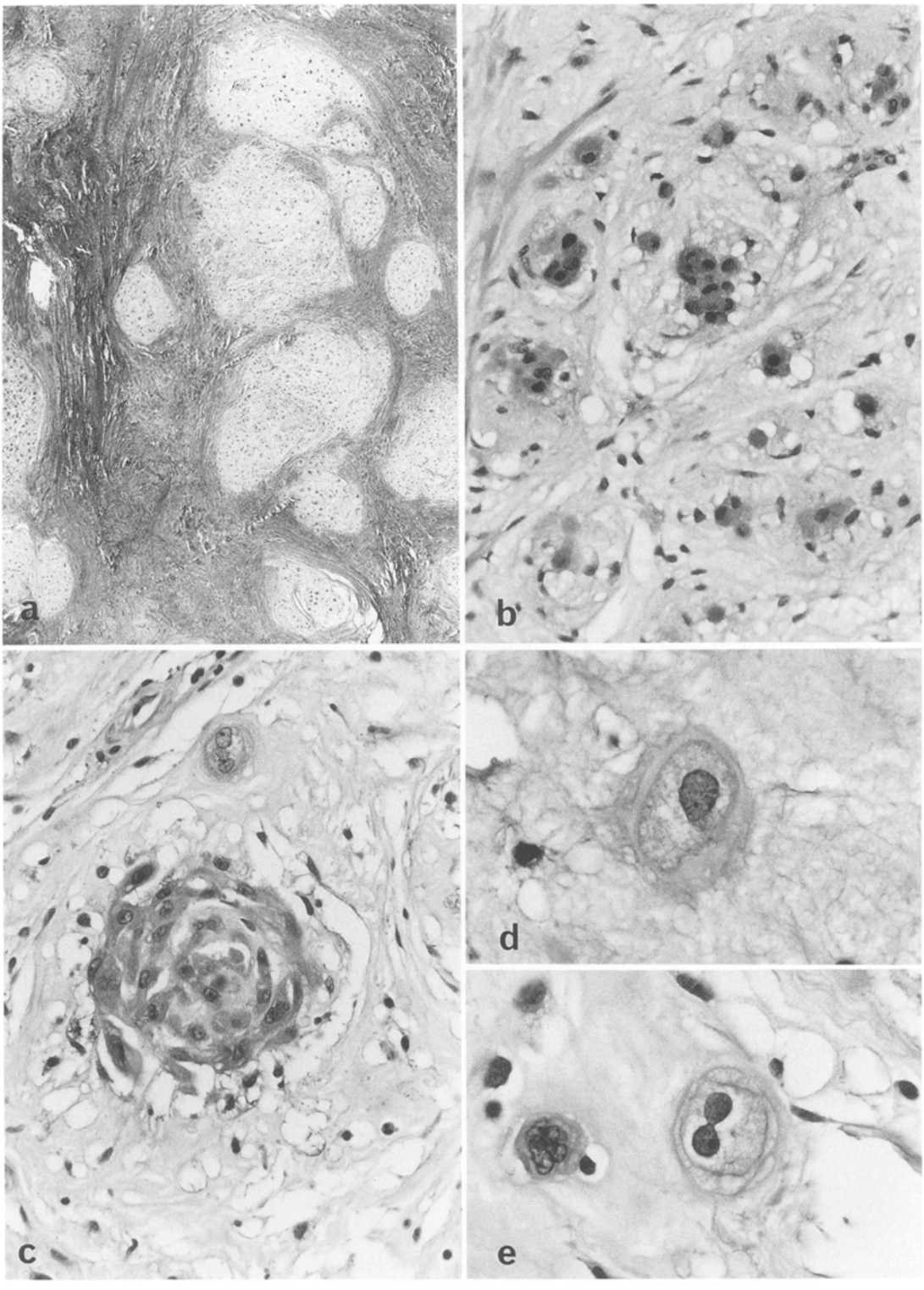

Fig. 1. a The tumour shows a multinodular pattern. Haematoxylin and eosin, ×17. **b** Tumour cells form small nests, and undifferentiated spindle cells are sparsely scattered in the myxoid matrix. Haematoxylin and eosin, ×340. **c** Concentric arrangement of crescent-shaped cells. Haematoxylin and eosin, ×340. **d**, **e** Physaliferous-like cells. Haematoxylin and eosin, ×680

acetate and lead citrate, and examined in a JEOL JEM-1200 EX electron microscope.

Immunohistochemical studies were performed on paraffin-embedded sections using the avidin-biotin-peroxidase complex (ABC) method (Hsu et al. 1981). Normal mouse or rabbit IgG was used for a negative control instead of the primary antibodies. For immunohistochemical studies, monoclonal antibodies for cytokeratin (KL-1, Immunotech), epithelial membrane antigen (EMA, DAKO), vimentin (DAKO), and desmin (ICN) and polyclonal antibodies for carcinoembryonic antigen (CEA, DAKO), S-100 protein (DAKO), and factor VIII-related antigen (FVIII-RA, DAKO) were used.

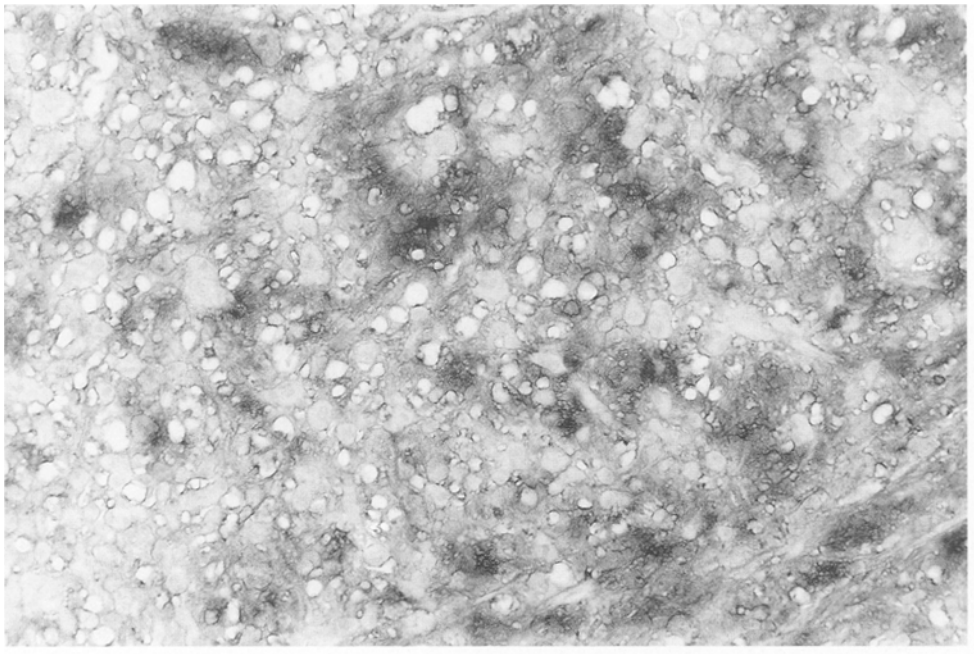

Fig. 2. The myxoid matrix is stained black by high-iron diamine stain, indicating the presence of chondroitin sulphates and keratan sulphate. ×170

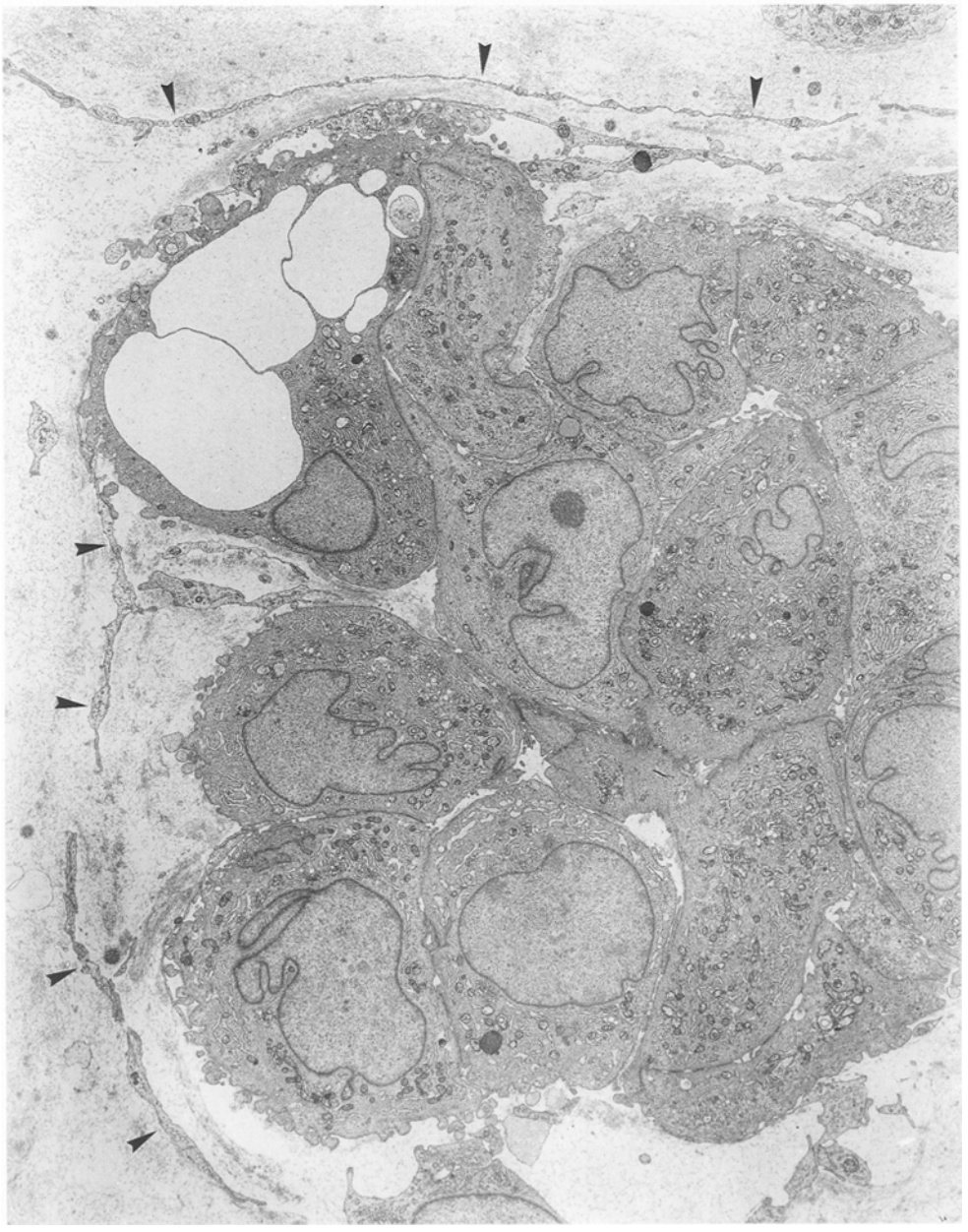

Fig. 3. Adjacent round or ovoid tumour cells form a tumour cell nest. A vacuolated physaliferous-like cell is found. Some very elongated undifferentiated spindle cells are seen surrounding a tumour cell nest (*arrowheads*). ×3860

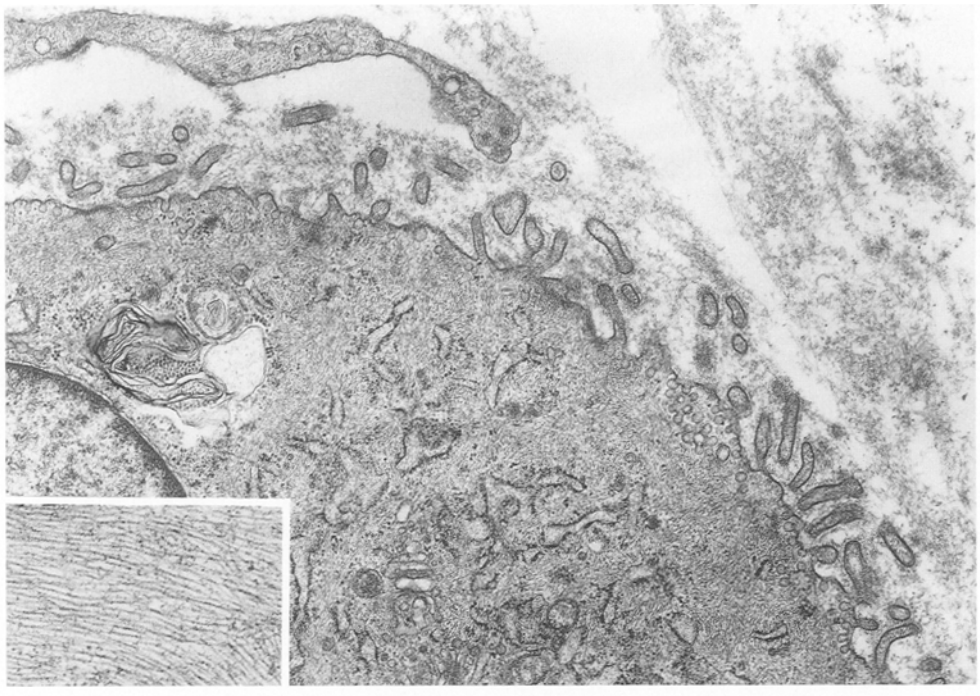

Fig. 4. Microvillous cell processes protrude from the cytoplasm and pinocytotic vesicles are also found. ×16000. *Inset*: Intermediate filaments are abundant and occasionally arranged in bundles. ×48250

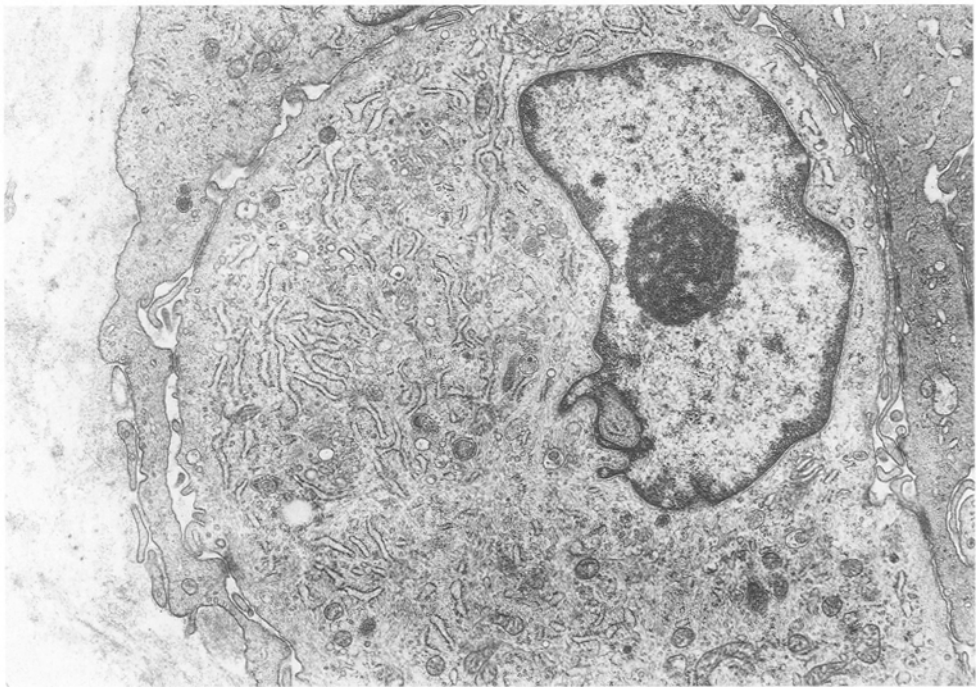

Fig. 5. Rough endoplasmic reticulum and Golgi complexes are well developed. Desmosome-like junctional structures are also found. ×9600

Results

Macroscopically, the tumour was situated in the left soleus muscle and attached to the Achilles tendon from which it was easily separated. It was white with ill-defined, multinodular and myxoid appearance, and measured 3 cm in diameter. Microscopically, it showed multinodular growth pattern with abundant myxoid matrix (Fig. 1a). Tumour cells formed small nests or cords similar to those in chordoma (Fig. 1b). Small nests of cells sometimes showed a concentric arrangement (Fig. 1c) and were enclosed by crescent-shaped tumour cells. The nuclei were round and the cytoplasm was abundant, usually eosinophilic and occasionally vacuolated as in physaliferous cells (Fig. 1d, e). Moderate amounts of glycogen granules were present in the cytoplasm demonstrated by PAS stain. In addition, small, undifferentiated spindle cells were found around the tumour cell nests in the myxoid matrix. The myxoid matrix contained a large amount of acid mucopolysaccharide which showed

Table 1. Summary of light and electron microscopic differences between parachordoma, extraskeletal myxoid chondrosarcoma and chordoma

Findings	Parachordoma	Extraskeletal myxoid chondrosarcoma	Chordoma
Undifferentiated spindle cells	+	−	±
Vacuolated cells (physaliferous cells)	+	−	++
Intermediate filaments	++	+	++
Pinocytic vesicles	+	±	+
Junctional structures	+	±	+
RER-mitochondrial complex	−	−	+
Microtubular aggregates in RER	−	+	±

−, Not found; ±, rarely found; +, commonly found; ++, abundantly found; RER, rough endoplasmic reticulum

Table 2. Summary of immunohistochemical characteristics of parachordoma, extraskeletal myxoid chondrosarcoma and chordoma

	Parachordoma	Extraskeletal myxoid chondrosarcoma	Chordoma
Vimentin	+	+	+
Cytokeratin	−	−	+
Desmin	−	−	−
S-100 protein	+	+	+
EMA	−	−	+
CEA	−	−	+
FVIII-RA	−	−	−

+, Positive; −, negative; EMA, epithelial membrane antigen; CEA, carcinoembryonic antigen; FVIII-RA, factor VIII-related antigen

positive reaction for alcian blue, colloidal iron and HID stains (Fig. 2). Colloidal iron staining of the myxoid matrix was decreased after testicular hyaluronidase digestion.

Ultrastructurally, the tumour cells forming the nests or cords presented a round, indented nucleus with evenly distributed heterochromatin and prominent nucleolus (Fig. 3). The cytoplasm of the cells was abundant and round or ovoid in shape, with microvillous cell processes and pinocytic vesicles (Fig. 4). Golgi complexes and rough endoplasmic reticulum (RER) were well developed, and prominent intermediate filaments were found (Fig. 5). RER-mitochondrial complexes, a characteristic ultrastructural finding in chordoma, were not seen. Tumour cells containing the large cytoplasmic vacuoles which characterize physaliferous cells were seen both light microscopically and electron microscopically. Desmosome-like junctional structures were relatively well developed. The undifferentiated spindle cells seen by light microscopy showed electron microscopic characteristics which were essentially the same as the other cells observed in the tumour. The myxoid matrix contained granulofibrillar material. Light and electron microscopic differences between parachordoma, extraskeletal myxoid chondrosarcoma, and chordoma are summarized in Table 1.

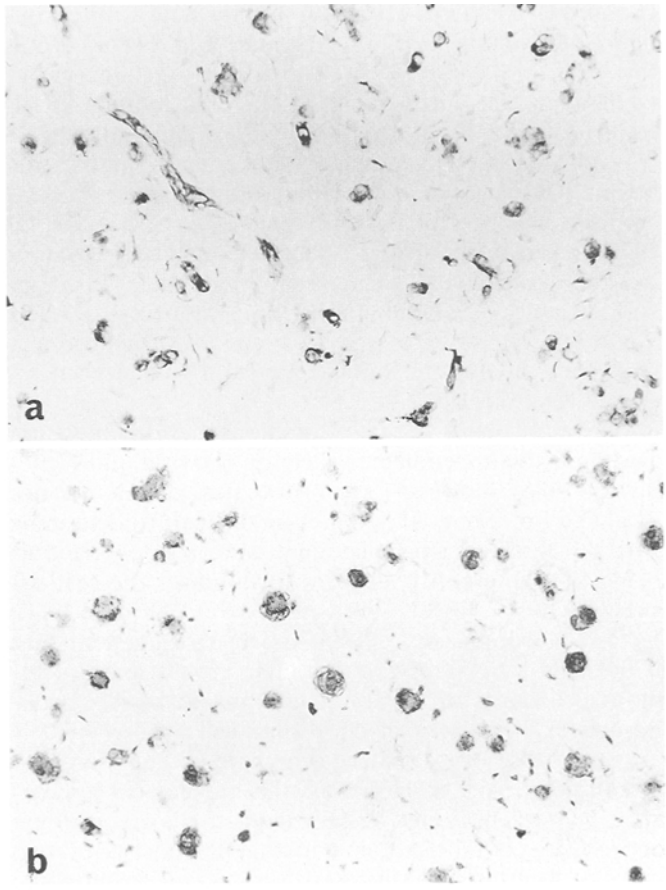

Fig. 6. a Tumour cells and capillary endothelial cells are positive for vimentin. Methyl green counterstain, ×225. **b** The cytoplasm and nucleus of tumour cells are positive for S-100 protein. Methyl green counterstain, ×225

The immunohistochemical results are summarized in Table 2. The cytoplasm of tumour cells was positive for vimentin (Fig. 6a). Positive immunoreaction for S-100 protein was observed in the cytoplasm as well as in the nucleus (Fig. 6b), whereas tumour cells were negative for KL-1, EMA, CEA, desmin, and FVIII-RA.

Discussion

Parachordoma was first described by Laskowski and has been recognized as a separate clinicopathological entity since Dabska's report of 10 cases in 1977 (Dabska 1977). Only 11 cases of parachordoma including that described by Enzinger and Weiss (1988c) have been reported in the English literature. The mean reported age is 35 years and the age distribution of the patients, 7 of whom are under 30, is bimodal. In contrast, extraskeletal myxoid

chondrosarcoma is a neoplasm which usually afflicts patients older than 35 years (Enzinger and Shiraki 1972; Enzinger and Weiss 1988a) and is rare in children and adolescents (Jessurun et al. 1982; Hachitanda et al. 1988; Klijanienko et al. 1990). Chordoma, other than spheno-occipital chordoma, is uncommon in patients less than 35 years of age (Dahlin and Unni 1986). Parachordoma affects males and females equally (Dabska 1977), whereas both extraskeletal myxoid chondrosarcoma and chordoma show male preponderance (Enzinger and Shiraki 1972; Dahlin and Unni 1986; Enzinger and Weiss 1988a). Four of the 12 cases of parachordoma have recurred locally, but no metastasis have been reported (Dabska 1977).

There are also a few cases of chordoma periphericum arising in the appendicular skeleton (Povysil and Matejovsky 1985); however, the histological details are not available for review. It is therefore difficult to determine whether chordoma periphericum can be categorized as being the same entity as parachordoma of the soft tissues.

Parachordoma is very similar to chordoma in that it presents lobular or multinodular growth pattern tumour cell cords in an abundant myxoid matrix background. This pattern of chordoma cell arrangement is similar to that of extraskeletal myxoid chondrosarcoma (chordoid sarcoma). However, the histological appearance of parachordoma differs from that of chordoma or myxoid chondrosarcoma in that it consists of two types of tumour cells, those with abundant eosinophilic cytoplasm which form cords or whorls and the small spindle-shaped cells.

The myxoid substance of chondroid and chordoid tumours contains chondroitin 4-sulphate, chondroitin 6-sulphate, and keratan sulphate (Kindblom and Angervall 1975). In other myxoid tumours of the soft tissues, such as intramuscular myxoma, myxoid liposarcoma, and myxoid malignant fibrous histiocytoma, mucosubstances sensitive to testicular hyaluronidase have been demonstrated (Martin et al. 1973; Kindblom and Angervall 1975; Enzinger and Weiss 1988b). Enzinger and Weiss (1988c) reported that parachordoma contains hyaluronidase-sensitive mucinous material and that it was thought unlikely to be of chondroblastic or chordoid origin. Testicular hyaluronidase digests not only hyaluronic acid but also chondroitin 4- and 6-sulphates. Although the matrix of normal hyaline cartilage is hardly digested with testicular hyaluronidase, colloidal iron staining of the matrix in poorly differentiated chondrosarcoma, extraskeletal myxoid chondrosarcoma, and chordoma is reduced after digestion with testicular hyaluronidase (Martin et al. 1973; Tsuneyoshi et al. 1981; Fletcher et al. 1986). The mucosubstances in our case showed reduced staining with colloidal iron after testicular hyaluronidase digestion but was positive for HID stain. This result indicates that the mucosubstances in parachordoma contain chondroitin 4- and 6-sulphates and keratan sulphate, as does chondroid or notochord.

Electron microscopically, the cells of both chordoma and extraskeletal myxoid chondrosarcoma show prominent RER, Golgi complexes, glycogen granules, and microvillous cell processes (Enzinger and Shiraki 1972; Weiss 1976; Mehio and Ferenczy 1978; Tsuneyoshi et al. 1981; Dardick et al. 1983; Valderrama et al. 1983; Povysil and Matejovsky 1985; Hachitanda et al. 1988). We have found that parachordoma cells contain all these structures. Although microtubular aggregates in the RER in some cases of extraskeletal myxoid chondrosarcoma and chondroid chordoma have been described (Vernick et al. 1977; Wetzel and Reuhl 1980; Dardick et al. 1983; Valderrama et al. 1983; Povysil and Matejovsky 1985; DeBlois et al. 1986), they were not detected in our case. Desmosome-like cell junctions are reported to be scarce in extraskeletal myxoid chondrosarcoma (Wetzel and Reuhl 1980; Tsuneyoshi et al. 1981; Povysil and Matejovsky 1985; DeBlois et al. 1986), while they were relatively well developed in this case, as they are in chordoma. RER-mitochondria complexes, which are characteristic of chordoma (Valderrama et al. 1983; Persson et al. 1991), were not seen in this parachordoma. The abundant intermediate filaments observed in the cytoplasm of parachordoma cells by electron microscopy correspond to the eosinophilic cytoplasm of tumour cells observed by light microscopy. All these ultrastructural findings as well as the microvillous cell processes suggest that the tumour exhibits chordoid rather than chondroid differentiation, in spite of the absence of RER-mitochondria complexes.

Not only normal chondrocytes but also benign and malignant cartilaginous tumour cells show positive immunoreactivity for vimentin and S-100 protein. The parachordoma cells in this case were positive for both vimentin and S-100 protein. Extraskeletal myxoid chondrosarcoma has also been reported to be positive for vimentin and S-100 protein (Fletcher et al. 1986; Fukuda et al. 1986; Hachitanda et al. 1988; Klijanienko et al. 1990), whereas chordomas, even in the chondroid areas of chondroid chordoma, are positive not only for immunoreactive vimentin and S-100 protein but also for cytokeratin, EMA, and CEA (Miettinen et al. 1983; Abenoza and Sibley 1986; Meis and Giraldo 1988; Persson et al. 1991). The tumour cells in the present case were negative for cytokeratin, EMA, and CEA, and thus showed distinctive immunohistochemical differences from those in chordoma. These immunohistochemical results suggest that parachordoma is chondroid in nature despite its chordoma-like histology and ultrastructure.

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