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CASE REPORT

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Phalangeal intraosseous well-differentiated osteosarcoma of the hand

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Abstract A case of intraosseous well-differentiated osteosarcoma in one phalanx of the hand is reported. A 78-year-old man noticed swelling in the little finger of his right hand approximately 7 years before referral. Imaging disclosed a tumour with a "ground glass appearance and irregular mottled calcification occupying almost all of the phalanx marrow and suggested slight invasion into the soft tissue. Open biopsy suggested a diagnosis of well-differentiated fibroblastic osteosarcoma. The finger and its metacarpal bone were amputated and a tumour measuring 3.5×2.2×2.0 cm and with an indistinct soft tissue margin was found in the bone marrow. Histologically, the tumour was composed of fibroblastic cells with few mitoses, and neoplastic bone formation was apparent. Although the tumour appeared to be a fibrous dysplasia, the presence of nuclear atypia, hypercellularity, and the absence of a typical woven bone pattern in addition to the soft tissue invasion indicated otherwise. Ultrastructural examination showed focal myofibroblastic differentiation, and immunohistochemistry revealed smooth muscle actin, vimentin, osteocalcin, osteonectin and MIB1 in the tumour cells. This ultrastructural and immunohistochemical study is believed to be the first detailed report of an intraosseous well-differentiated osteosarcoma of phalangeal bone.

Key words Intraosseous well-differentiated osteosarcoma · Immunohistochemistry · Ultrastructure · Phalanx

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Introduction

Intraosseous well-differentiated osteosarcoma (IWDO) is a relatively new and rare bone tumour entity, comprising only 1.9% of all osteosarcomas [6]. Fewer than 1% of all osteosarcomas arise in the finger [7]. Thus, IWDO in the finger is extremely rare. Kurt et al. reported only two such cases, with very little details, among the general IWDO cases they investigated [6]. The present paper reports the results of an ultrastructural and immunohistochemical study of a case of IWDO arising in one phalanx of the hand.

Case report

A 78-year-old man noticed swelling without pain in the proximal phalanx of his right little finger approximately 7 years before examination. When the swelling increased, the patient visited a local doctor and was referred to our hospital. He had no remarkable medical or family history except for a perforated duodenal ulcer 9 years earlier, nor did standard laboratory tests reveal any particular abnormalities. The proximal portion of his right fifth finger was swollen, but there was no skin discolouration. Antero-posterior and lateral radiographs showed an intramedullary osteolytic lesion with mottled calcification, a poorly defined margin and extensive proliferation to the soft tissue (Fig. 1). Computer tomography (CT) revealed intralesional and nodular sclerosis with focal interruptions of the cortex, suggesting slight soft tissue invasion. The proximal phalanx of the affected finger was approximately twice as thick as those of the other fingers. Magnetic resonance imaging (MRI) revealed a low-signal intramedullary lesion with higher signal intensity focal areas on the T1-weighted image and much higher intensity regions on the T2-weighted image (Fig. 2). Digital subtraction angiography revealed slight hypervascularity while a bone scan detected ^{99m}Tc accumulation at the lesion site. Radiographs also suggested an invasive intramedullary tumour with calcification and slight soft tissue invasion. The patient underwent an open biopsy, the results of which suggested a diagnosis of IWDO. On 5 April 1994 the finger and its metacarpal bone were amputated.

Materials and methods

The specimen was fixed in 10% buffered formalin, embedded in paraffin, and stained with haematoxylin and eosin. Immunohisto-

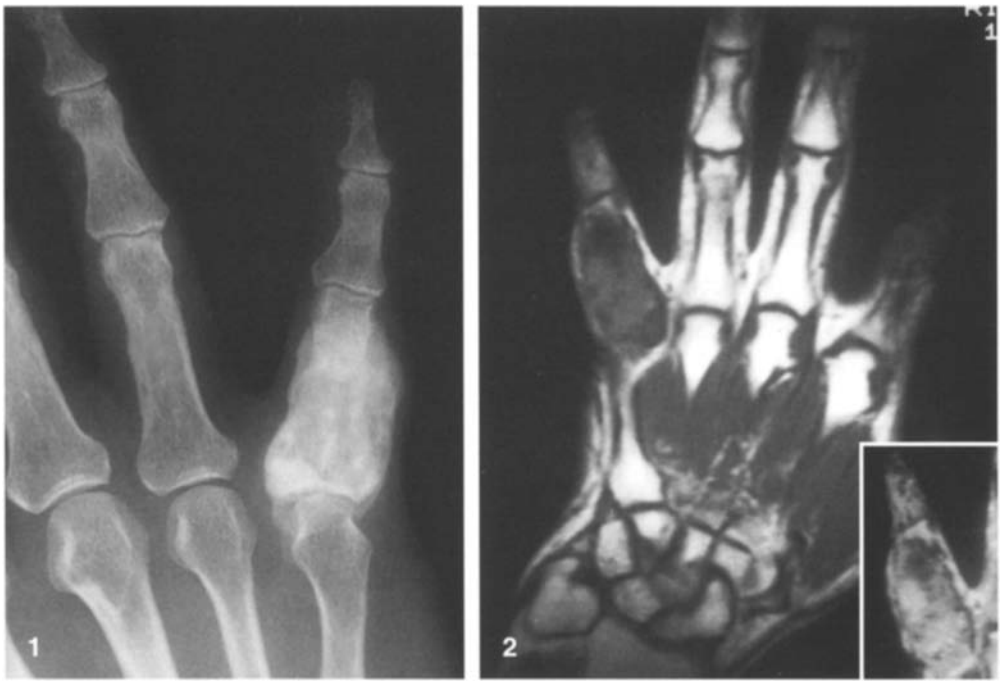


Fig. 1 Plain radiograph of right fifth finger showing an intramedullary tumour with a ground glass appearance and focal cloudy calcification in the proximal phalanx

Fig. 2 On MRI: the tumour exhibited a higher signal intensity than muscle, with foci of very high signal intensity. The bone cortex was irregular and interrupted. *Left* T1-weighted image, *inset* T2-weighted image

chemical studies were performed on the paraffin-embedded tissue sections using the avidin–biotin-peroxidase technique and antibodies against cytokeratin, epithelial membrane antigen (EMA), vimentin, smooth muscle actin, osteonectin, osteocalcin, and MIB1 (Ki-67).

Tissue from the biopsy specimen was preserved in 2.5% glutaraldehyde for subsequent electron microscopic analysis. After post-fixation in 1% osmium oxide and dehydration in alcohol and propylenoxide, the tissue was embedded in Epon. Thin sections were double-stained with lead nitrate and uranyl acetate for visualization using a JEOL 1200EX electron microscope.

Table 1 Immunohistochemical findings (*EMA* epithelial membrane antigen, *SMA* alpha smooth muscle actin, *LI* labelling index, percentage of positive nuclei per 500 tumor cell nuclei, – negative, ± less than 50% of tumour cells positive, *3+* more than 75% positive)

Antibody	Result	Dilution	Source
Cytokeratin	–	(1:50)	Nichirei, Japan
EMA	–	(1:100)	Dako, Denmark
Vimentin	3+	(1:20)	Dako, Denmark
SMA	+	Prediluted	Nichirei, Japan
Osteonectin	+	(1:200)	Takara, Japan
Osteocalcin	+	(1:200)	Takara, Japan
Ki-67 (MIB1)	0–2% LI	(1:100)	Immunotech, France)

Pathology

Macroscopically, the cut surface had a ground glass appearance with focal brown discolouration and an indistinct margin with the soft tissue. The tumour tissue had replaced most of the bone marrow, with only a sparse amount of marrow in the distal region (Fig. 3).

Histological examination showed that fibroblastic tumour cells had permeated the marrow, forming mature irregular trabecular bones with an appositional pattern and faint osteoid (Fig. 4). Slight but definite soft tissue invasion was detected on the palmar side (Fig. 5). Some tumour cells contained atypical nuclei and appeared to proliferate in a hypercellular pattern. The number of mitoses ranged between zero and two per 10 high power fields (Fig. 6). The typical woven bone pattern of fibrous dysplasia was not present. A small amount of cartilaginous differentiation was observed in the dorsal portion near the phalangeo-metacarpal joint, which was consistent with the previous MRI images (Fig. 7).

Positive immunohistochemical staining for tumour cell cytoplasm was detected in the smooth muscle actin. The staining pattern was diffuse but definite, although weaker than that in the vascular walls (Fig. 8). Diffuse vimentin immunoreactivity was also evident in all areas whereas the epithelial membrane antigen and cytokeratin was not. Osteocalcin and osteonectin were stained in some of the tumour cells. MIB 1-labelled nuclei were most likely to occur at the periphery of the tumour, close to the cortex. The number of nuclei labelled with MIB 1 was 0–10 per 500 nuclei, a labelling index of 0–2% (Table 1).

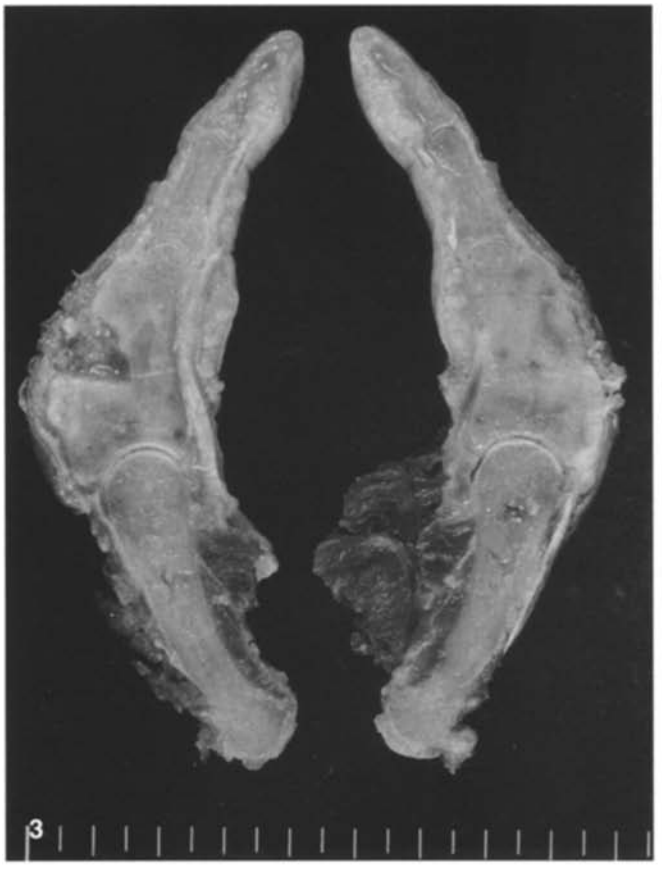
Ultrastructurally, the tumour cells were fibroblastic with irregularly indented nuclear membranes, a small amount of rough endoplasmic reticulum (Fig. 9) and des-

Fig. 3 Cut surface of little finger. Most of the medullary cavity was occupied by a tan-white hard tumour ▶

Fig. 4 Histologically, the central medullary cavity was replaced by a fibrous dysplastic lesion with soft tissue invasion (*arrow*)

Fig. 5 A narrow area of the soft tissue on the palmar side was invaded by tumour cells (high power view of arrowed lesion shown in Fig. 4)

Fig. 6 The tumour cells exhibited mild nuclear atypias and mitoses (*arrow*, high-power view)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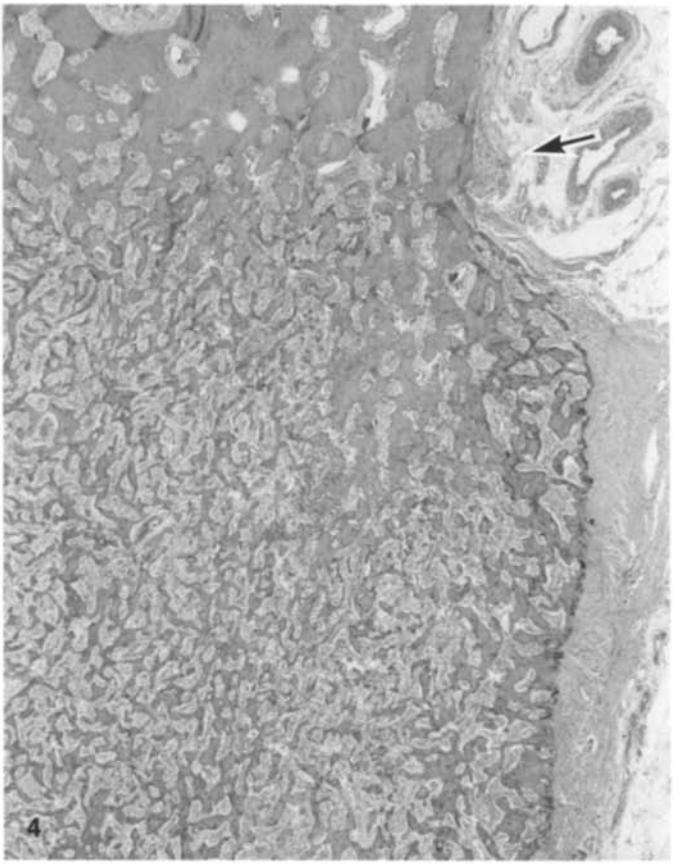
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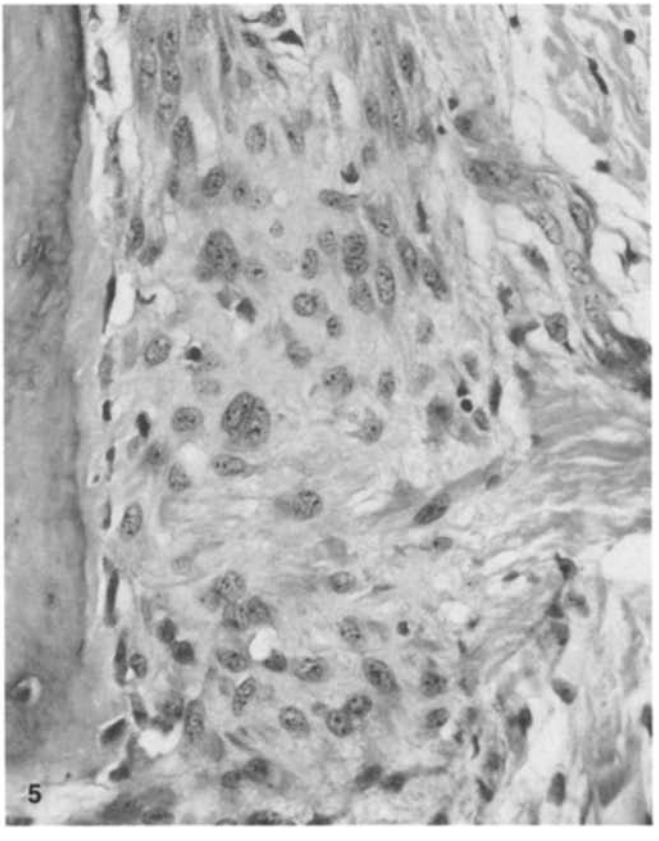
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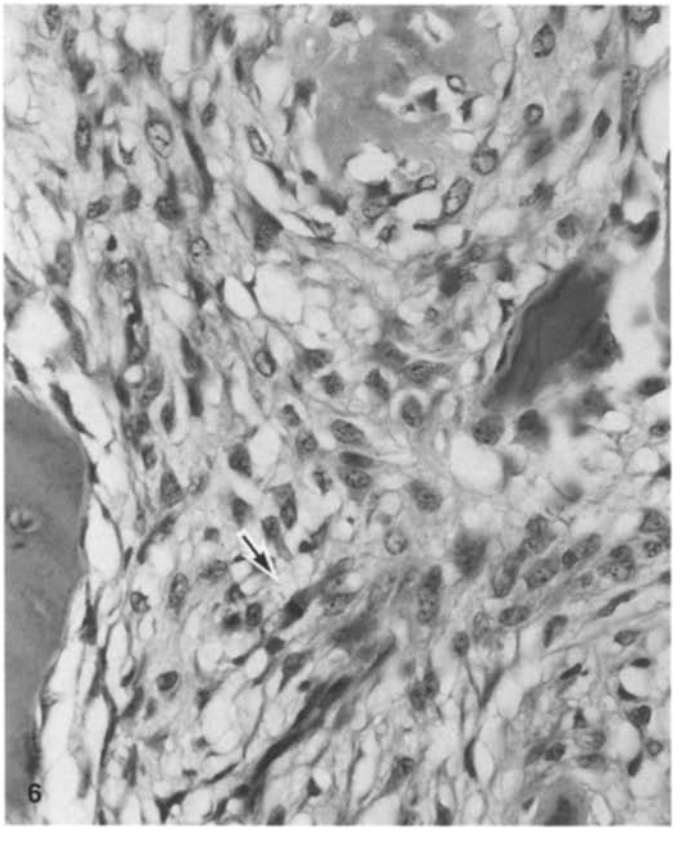
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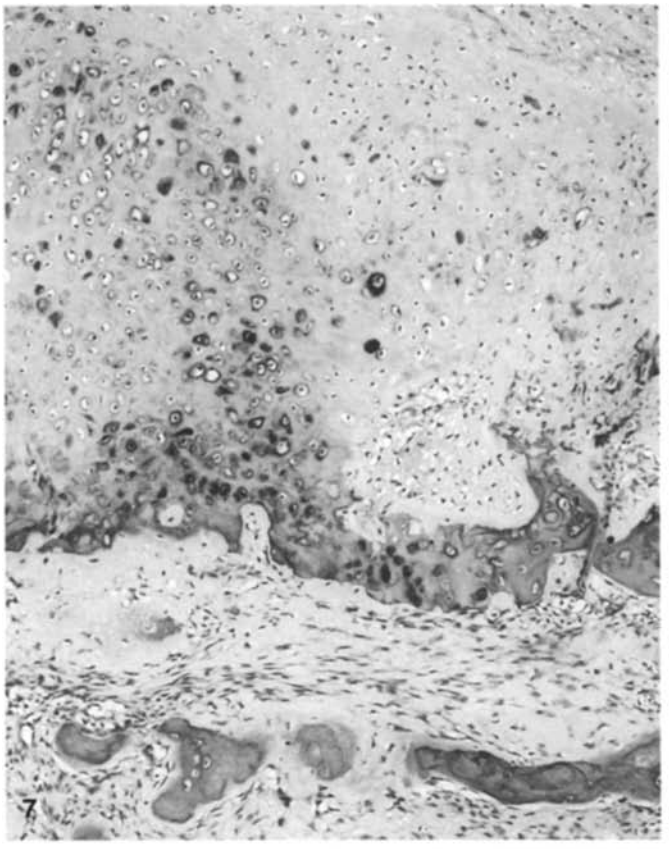
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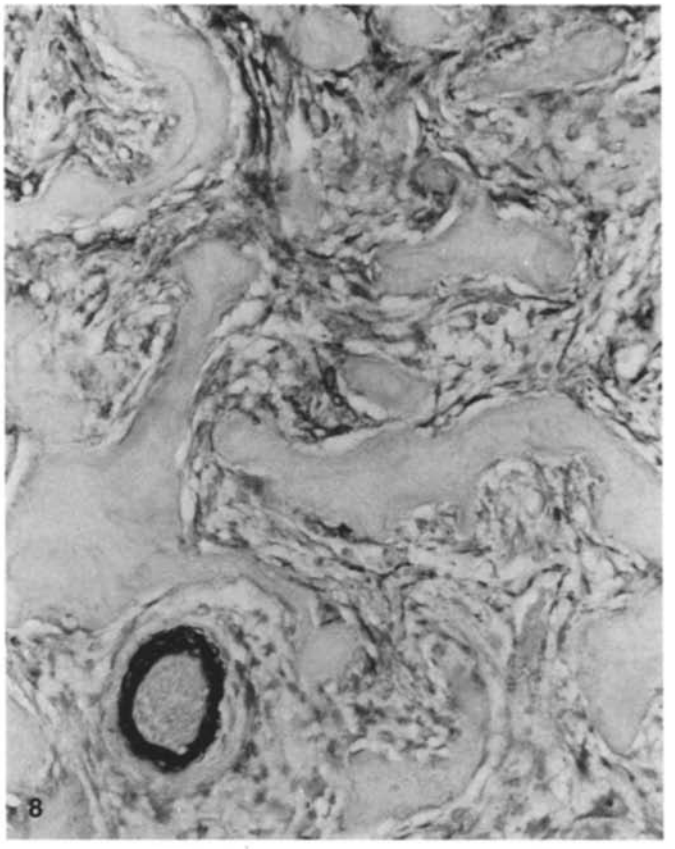
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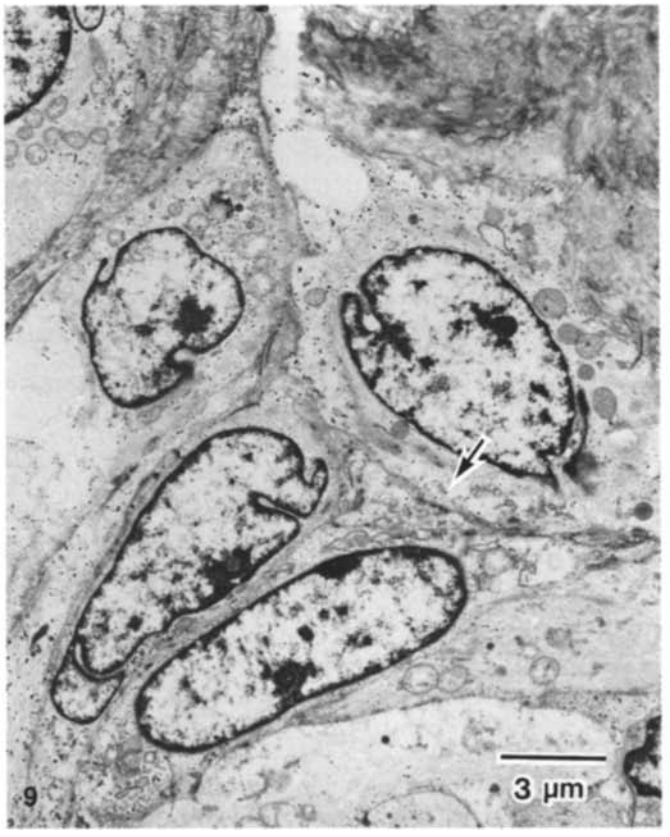
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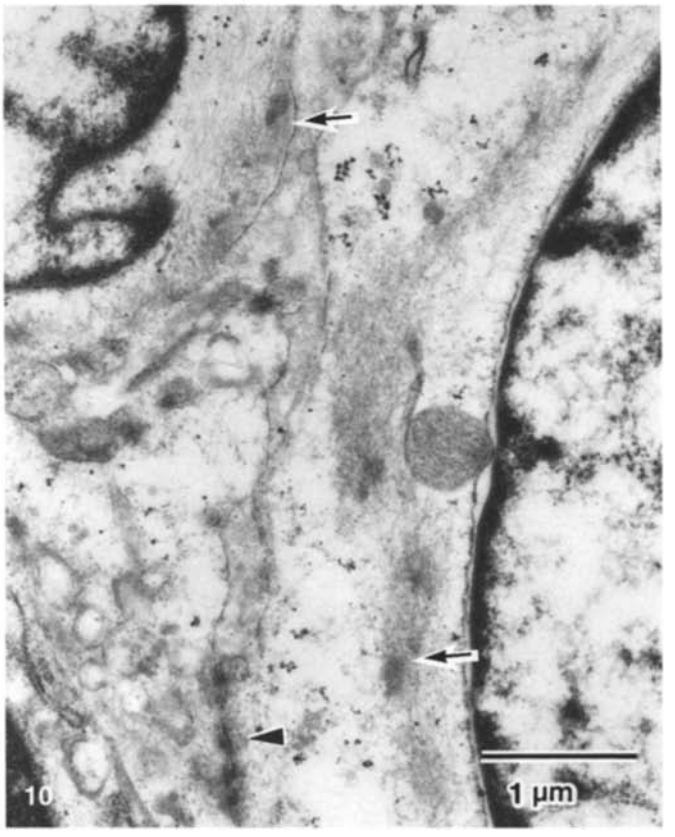
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mosome-like junctions (Fig. 10). The cytoplasm of several tumour cells also possessed fine filaments with dense foci, compatible with myofibroblasts (Fig. 10).

Discussion

Osteosarcoma of the phalangeal and metacarpal bones is extremely rare; only seven such cases have been reported. Several of these reported osteosarcomas were secondary, arising after irradiation or as a complication of Paget's disease [1, 2]. Our patient had no history relevant to the lesion or evidence of Paget's disease. Recently, Mirra et al. reported the first sclerosing variant of primary osteosarcoma of a phalanx of the toe. They concluded that this osteosarcoma has an intermediate biological malignancy potential, somewhere between high-grade and low-grade osteosarcoma [7]. The tumour in the present case was fibroblastic with an irregularly shaped but mature bone formation. A greater number of less atypical nuclei were present in this tumour than in the one described by Mirra et al., suggesting that it was a low-grade osteosarcoma, that is, an IWDO.

Radiographs revealed intramedullary osteolytic lesions with irregular calcifications and cortical degradation. These findings suggest either a chondrosarcoma or osteosarcoma and are rare among fibrous dysplasias or enchondromas. Thus, radiological analysis appears to be a very effective method of diagnosing this type of tumour.

Histologically, IWDO resembles parosteal osteosarcoma, desmoid tumours and fibrous dysplasia [6]. However, parosteal osteosarcoma differs considerably in its radiographic features, including shape and location [11, 12]. Intraosseous desmoid tumours also differ considerably from the present tumour in many respects, including the lack of bone formation and substantial desmoplasia [4, 13]. The tumour in our patient resembled fibrous dysplasia, but the presence of intramedullary permeation, soft tissue invasion, focal hypercellularity and nuclear atypia indicated otherwise. Furthermore, the typical woven bone pattern of fibrous dysplasia was very rarely observed, the major bone formation being appositional.

Similarly, the ultrastructural findings did not suggest fibrous dysplasia. The tumour cells showed evidence of nuclear pleomorphism and few intracytoplasmic organelles, suggesting that they were somewhat poorly differentiated. In addition, fibrous dysplasia usually include many fibroblastic cells with abundant rough endoplasmic reticulum and large Golgi apparatuses, implying osteoblastic differentiation [3]. There were, however, several similarities in myofibroblastic differentiation between the two types of lesion [3]. Positive immunohistochemical staining of smooth muscle actin indicated that the tumour in the present case had the same myofibroblastic cell differentiation as that seen in an ultrastructural study of fibrous dysplasia [8]. The bone tumour antigens, osteocalcin and osteonectin, were recognized as in other reported cases [5, 9], confirming that this was a bone forming tumour. The MIB1 (Ki-67) labelling index was between those of chondroblastoma and giant cell tumour [10]. This lesion would thus be likely to possess an enhanced ability to proliferate.

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◀ **Fig. 7** Cartilage differentiation in the dorsal portion was predominantly hyalinous with myxoid-type foci

Fig. 8 Weak but definitely positive immunohistochemical staining of smooth muscle actin in the tumour cells. Note the strong positivity in the vascular wall

Fig. 9 Ultrastructurally some tumour cells were attached to the bone matrix (*upper right*) with cell junctions (*arrows*) and exhibited odd invaginations of the nuclear membrane

Fig. 10 Higher power view of the arrowed area of Fig. 9. Some tumour cells possessed fine intracytoplasmic filaments with dense areas (*arrows*) and desmosome-like junctions (*arrowheads*)

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