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Case Report

OSTEOSARCOMA IN A PATIENT WITH CRANIAL FIBROUS DYSPLASIA: A CASE REPORT

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SUMMARY – Fibrous dysplasia is a benign fibro-osseous lesion which rarely undergoes malignant transformation, frequently after radiotherapy. Osteosarcoma is the most common malignancy arising in fibrous dysplasia. We report a case of 67-year-old female patient with osteosarcoma developing in long lasting fibrous dysplasia without prior radiation. The patient underwent surgery with postoperative chemotherapy. She developed two relapses over the course of four years after the initial therapy. With this case, we want to underline the importance of noticing any significant change in the otherwise unremarkable course in patients with fibrous dysplasia.

Key words: *Fibrous dysplasia; Malignant transformation; Osteosarcoma; Radiotherapy*

Introduction

Fibrous dysplasia (FD) is a benign fibro-osseous lesion in which normal bone is replaced by proliferation of fibrous connective tissue and immature osseous tissue[1-5]. Long bones of the extremities and craniofacial bones are typically affected[6-8]. The disease presents in a monostotic or polyostotic form and typically occurs in childhood, causing pain, swelling and deformity[7,9,10]. The disease itself usually subsides by adulthood[3,4,6,10]. Malignant transformation of FD is rare. The overall risk of malignant transformation is estimated at less than 1%, but seems to be higher in the polyostotic form of disease, especially in patients with McCune-Albright and Mazabraud syndrome[4,6,9-14]. Past history of radiotherapy is frequently encountered in these patients and radiotherapeutic treatment appears to be an important predisposing factor for malignant transformation in FD[3,6,9,12,15,16]. However, a number of cases of spontaneous transformation of FD have been reported in recent years[2-5,9,12,14,17-20]. Although the incidence of malignant change is low, some reports consider FD as a premalignant bone lesion[15,21]. Malignant transformation occurs with similar frequency at all ages and in both sexes[16]. A persistently high level of alkaline phosphatase is a common finding in these patients, even in adults[1,3,4,16]. Osteosarcoma is the most frequent neoplasm, followed by fibrosarcoma, chondrosarcoma, and malignant fibrous histiocytoma[1,3,6,12,18,19]. In the craniomaxillofacial region, tumors are most often located in the maxilla and mandible, whereas involvement of the calvarium is rare[2,3,9]. The overall prognosis of this disease is poor[3,9,10,19,22].

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Case Report

We report a case of a 67-year-old female patient with a history of skull deformity in the left forehead and parietal region, which lasted from childhood and had been previously diagnosed as a polyostotic form of FD. However, in the last 6 months, she noticed moderate enlargement, especially in the left part of the frontal bone. Twelve years prior to the mentioned enlargement of the frontal bone, the patient had been treated surgically and with chemotherapy for breast carcinoma, which included 5-fluorouracil, Adriamycin and cyclophosphamide. The patient had no history of radiation therapy. The current symptoms had worsened, in particular because the tumor mass was compressing the left orbit with its content.

Radiology

Multi-slice computed tomography (MSCT) and magnetic resonance (MR) were performed to show a widespread lesion which matched FD (Figs. 1 and 2) on the left side of the cranium, involving the frontal, parietal and partly occipital, sphenoid and zygomatic bone. An area measuring approximately 4.5x3.5 cm showed cystic degeneration of the left part of the frontal bone and showed significant enlargement compared to MSCT performed 6 months earlier. At that time, cystic degeneration measured only 1.5 cm in greatest diameter. Surgical treatment was recommended because of the clinically evident growing asymmetry of the skull.

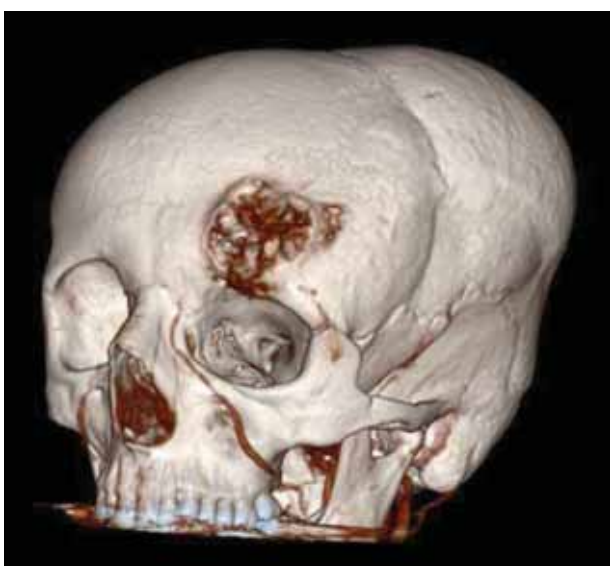

Fig. 1. Involvement of the left part of the frontal bone, left parietal bone and partly sphenoid bone (multi-slice computer tomography).

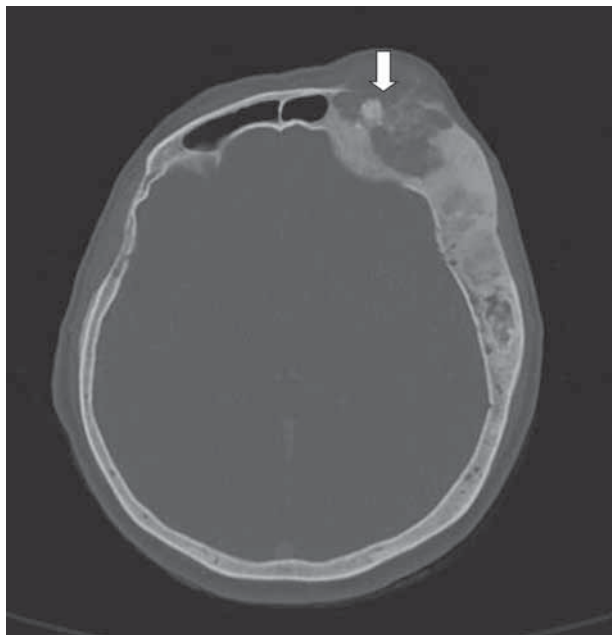

Fig. 2. Computed tomography showing fibrous dysplasia with the area of cortical destruction (arrow).

Surgery

The bicoronal flap approach was performed and complete left side of the skull was exposed, with evident osteodysplastic bone deformity in the left frontal, parietal, temporal and partly occipital region. A defect of approximately 20 mm in diameter in the left frontal region, filled with a grayish mass was identified, which was later histopathologically diagnosed as osteosarcoma. The surrounding periosteum was also excised with the remaining bone deformity of the left side of the skull being shaved and modeled with a high-speed burr in order to obtain symmetry of the skull. After obtaining definitive pathology results as described above, a reoperation was indicated. Considering the suspected multicentric nature of the osteosarcoma in this case, complete removal of the tumor was not possible because it would have included hemicraniectomy. Consequently, the supraorbital portion of the left frontal bone was removed with exposure of the underlying dura. The left side of the frontal sinus was explored with no evidence of disease, so the sinus was obliterated with a fat graft taken from the abdominal wall. The remaining part of the left skull was modeled with a high-speed burr. The postoperative period was uneventful. No adjuvant surgical treatment was indicated and conventional chemotherapy was administered.

However, the patient had two relapses within four years of the initial surgery, with the frontoparietal parts of the skull bone being remodeled and replaced with bone cement and covered with microvascular muscle lobe and skin transplant. Subsequently, she underwent radiotherapy. Since then, her condition has been unchanged.

Histopathology

Histologically, the resected tissue consisted of bone with changes that corresponded to the previously known polyostotic FD, which involved the left part of the frontal bone, left parietal bone, and partially left sphenoid and zygomatic bone. The majority of the material was pure FD consisting of bland fibroblastic proliferation surrounding irregular trabeculae of woven bone with only focally present osteoblastic rimming and visible Sharpey fibers from trabeculae into adjacent stroma (Fig. 3).

Transition area showing typical FD with a more cellular stroma composed of atypical spindle cells was around one locus where it progressed into osteosarcoma with moderate pleomorphism and increased mitotic activity, consistent with low grade osteosarcoma (Fig. 4). Histologically, all the relapses exhibited the same picture.

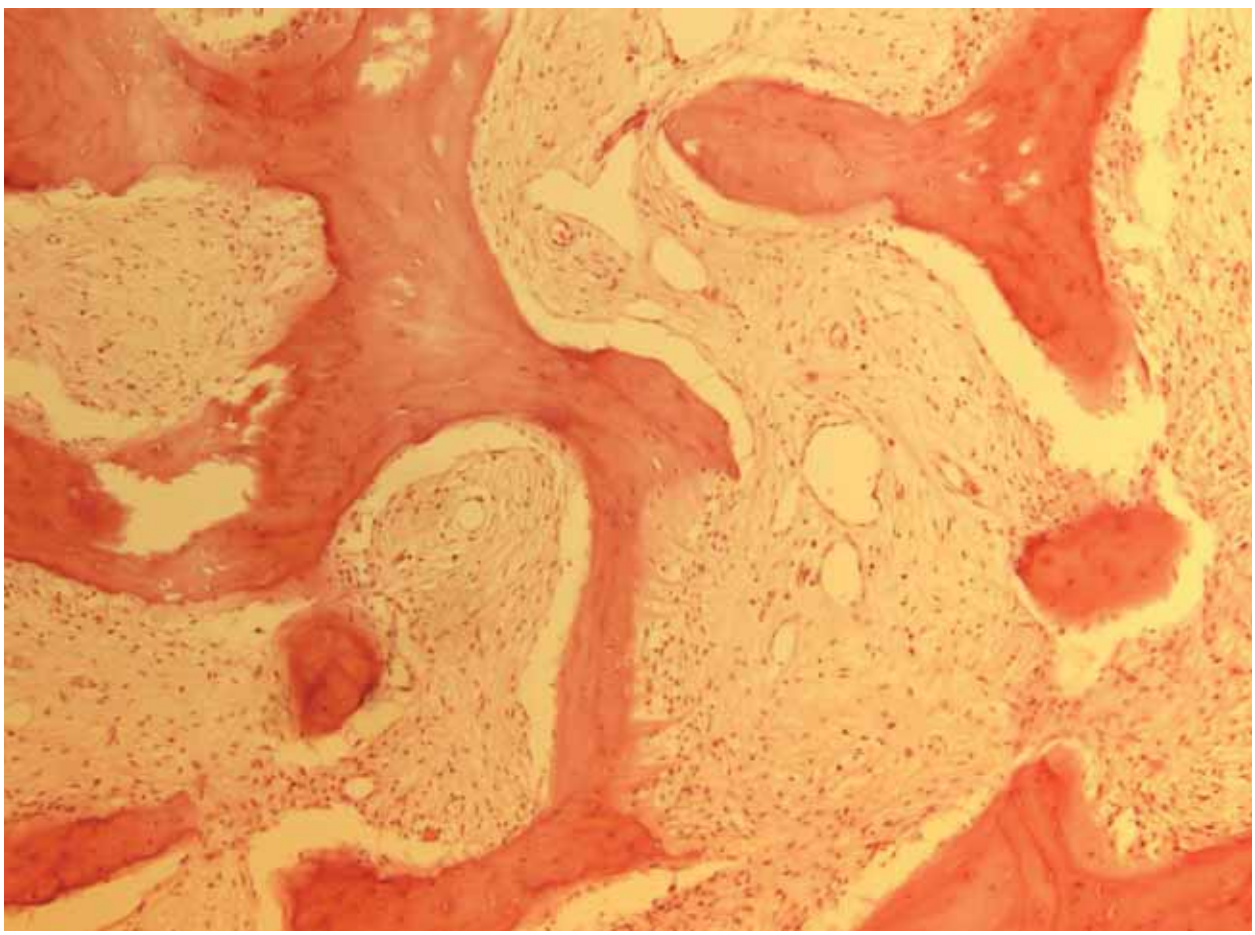

Fig. 3. Fibrous dysplasia with visible Sharpey fibers (hematoxylin and eosin stain, magnification X100).

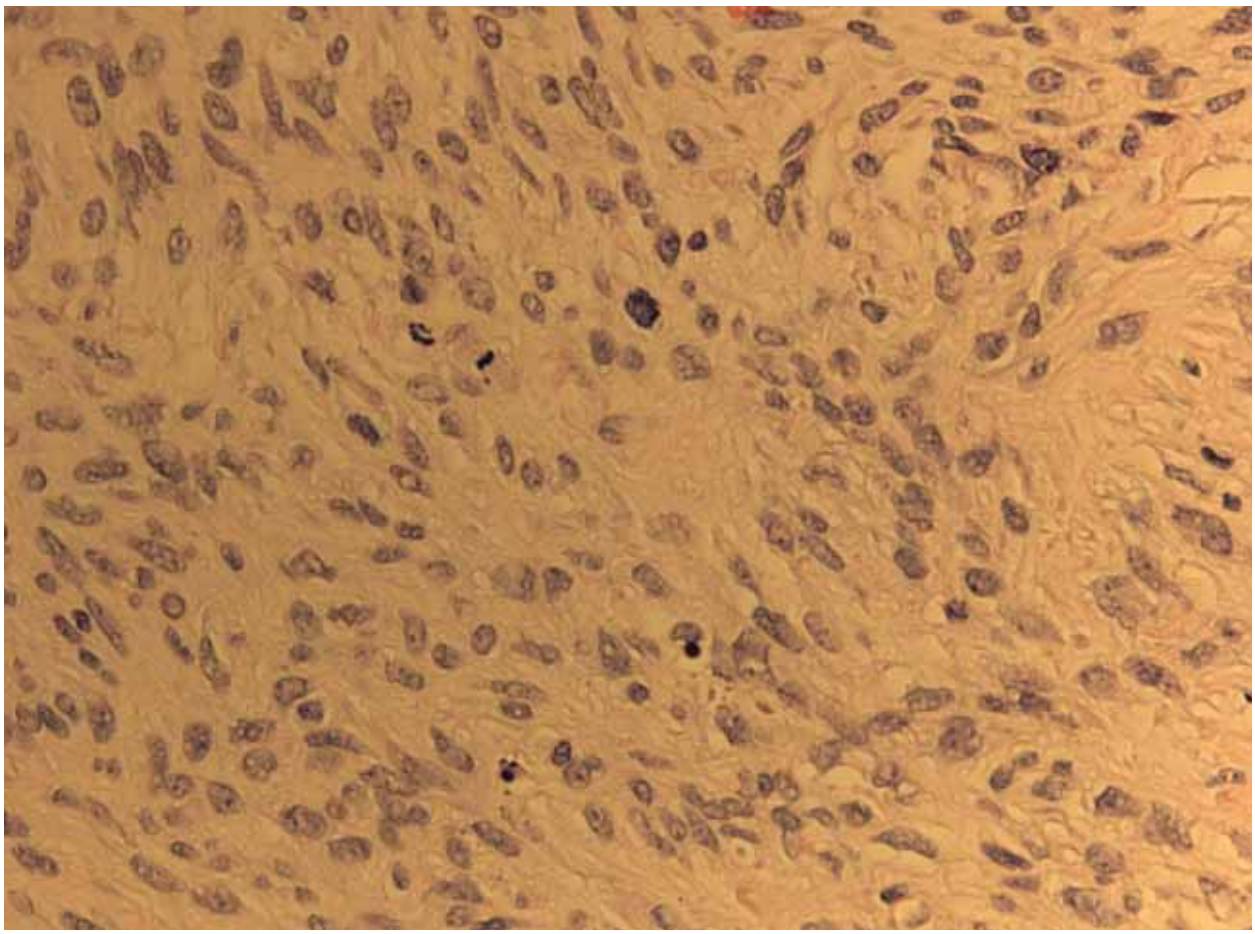

Fig. 4. Osteosarcoma with visible pathologic mitotic figures (hematoxylin and eosin stain, magnification X400).

Discussion

The first well documented case of spontaneous malignant transformation of FD was reported by Coley and Stewart in 1945[23]. Reis *et al.*[2] described a case very similar to ours, where a patient with long-standing craniofacial polyostotic FD and no history of prior radiation therapy developed spontaneous right temporal bone osteosarcoma. A case of a 59-year-old female with cranial polyostotic FD and osteosarcoma developing without prior radiation has also been reported by Mardekian and Tuluc[17]. A review showing 10 patients with malignant transformation of monostotic FD by Qu *et al.*[4] in an 8-year period reported no previous radiation. Sun *et al.*[19] also report on 10 cases of spontaneous osteosarcoma in a group of patients with craniomaxillofacial FD. A systematic review of all published cases of spontaneous malignant transformation of craniomaxillofacial fibro-osseous lesions has been recently performed by Wagner *et al.*[5]. Patients with FD predominated (96.2%), with a higher frequency of polyostotic form of disease. The mean age at the time of malignant transformation was 38.11 years and the mean period from initial diagnosis to malignant transformation was 18.2 years. The 3-year survival rate was 51%. Similar systematic reviews were published by Li *et al.*[22] and Cheng *et al.*[3]. However, their studies also included patients with a past history of radiotherapy (33% and 39.5% of patients, respectively). The overall results were similar to those reported by Wagner *et al.*[5], with few exceptions, i.e., slightly lower mean patient age in the study by Li *et al.*[22] and predominance of monostotic FD in the study by Cheng *et al.*[3]. It is also worth mentioning that prior radiotherapy is associated with malignant transformation of FD, while according to the study by Li *et al.*[22], it does not affect the overall

survival of patients. A case of a 72-year-old male developing osteosarcoma on the basis of polyostotic FD of the knee without prior radiation, with detailed overview of chromosomal changes, has also been reported[18]. This particular case is interesting because it emphasizes the very likely role of genetic mutations in malignant transformation in FD patients.

Patients with FD should be followed-up for life in order to detect the possible malignant transformation as early as possible and maximize their therapeutic response[5,9,10,21]. Radiological screening once a year is advised, and patients must be educated to seek prompt medical attention upon experiencing a sudden change in the quality or severity of their symptoms[6,17]. The most common symptoms of sarcomatous change are painless swelling, pain and local numbness[3,14,19,20,22]. Early radiological signs of malignant transformation in FD are moth-eaten or cystic areas of osteolysis, cortical destruction, and formation of a soft tissue mass[1,4,12,19]. Radical resection is primary treatment of choice if the tumor location is suitable for surgical excision[3,4,9,14]. In the craniomaxillofacial region, complete removal is sometimes limited by the presence of vital neurovascular structures and such patients can undergo postoperative radiotherapy and/or chemotherapy[3,19,22]. This was the case in our patient, who developed two relapses in four years after the initial diagnosis.

Hereby, we contribute this case to other rare cases of malignant transformation of FD without previous radiation. However, in this particular case, it is also unclear whether chemotherapy the patient had received 12 years earlier had any influence on malignant transformation of FD. Considering that malignant alteration of FD without previous radiation is rare, it is possible that chemotherapy in this case could have been a triggering factor for osteosarcoma genesis. At the end, we would also like to emphasize the importance of changes in the clinical course of FD, as well as changes in radiological imaging features among the complex radiological findings in this entity.

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Sažetak

OSTEOSARKOM U BOLESNICE S FIBROZNOM DISPLAZIJOM: PRIKAZ SLUČAJA

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Fibrozna displazija je benigna fibrozno-koštana bolest koja rijetko maligno alterira. Osteosarkom je najčešća maligna neoplazma koja nastaje na podlozi fibrozne displazije. Prikazujemo slučaj 67-godišnje bolesnice s dugogodišnjom dijagnozom fibrozne displazije iz koje se razvio osteosarkom, bez prethodne radioterapije. Bolesnica je liječena kirurškim zahvatom s poslijeoperacijskom kemoterapijom. Unutar četiri godine od spomenute terapije razvija dva recidiva bolesti. Prikazom ovog slučaja želimo naglasiti važnost uočavanja bilo kakve značajnije promjene u inače neupadljivom tijeku bolesti kod bolesnika s dijagnozom fibrozne displazije.

Ključne riječi: *Fibrozna displazija; Maligna transformacija; Osterosarkom; Radioterapija*