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The development of osteosarcoma following radiotherapy for fibrous dysplasia

Radyoterapi uygulanan fibröz displazili bir olguda osteosarkom gelişimi

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Fibröz displazi (FD) zemininde sarkom gelişmesi nadirdir ve polyostotik olgularda dönüşüm daha sıktır. Bu yazıda, polyostotik FD tanısından 28 yıl sonra sol tibiasında osteosarkom gelişen 41 yaşında bir erkek hasta sunuldu. Osteosarkom FD nedeniyle uygulanan radyoterapiden 20 yıl sonra gelişmişti. Diz üstü amputasyon yapılan hasta ameliyattan sekiz ay sonra öldü. Bu olguda radyoterapinin FD tedavisinde yarar sağlamadığı görüldü ve sarkom gelişmesinin radyoterapiyle ilişkili olabileceği düşünüldü.

Anahtar sözcükler: Tibia neoplazileri; kemikte fibröz displazi/patoloji/komplikasyon; fibröz displazi, polyostotik/komplikasyon; osteosarkom/komplikasyon/radyografi.

Sarcoma arising from fibrous dysplasia (FD) is rare and it is more common in polyostotic type. In this case report, we present a 41-year-old male patient who developed osteosarcoma of the left tibia 28 years after the initial diagnosis and 20 years after radiation therapy for FD. He underwent above-knee amputation, but died eight months after surgery. This case suggests that radiotherapy has no beneficial effect in the treatment of FD and that it may be associated with the development of sarcoma.

Key words: Tibial neoplasms; fibrous dysplasia of bone/pathology/complications; fibrous dysplasia, polyostotic/complications; osteosarcoma/complications/radiography.

Fibrous dysplasia (FD) is a benign bone disorder thought to arise from a structural error or a developmental error, in which health bone is displaced by fibrous tissue; and the cause is not yet fully known [1,3]. More than a hundred cases with sarcoma on FD grounds have been reported till today[3-7]. Transformation to sarcoma in polyostotic type FD is more frequent [4,5,7-9]. Frequency of occurrence is osteosarcoma, fibrosarcoma, and chondrosarcoma, respectively [4,5]. Effect of radiotherapy on sarcoma in patients with fibrous dysplasia is controversial [4,5,10].

In this paper, a case with osteosarcoma occurring 28 years later than the diagnosis of FD is reported.

Case report

A thirteen-year old male applied to our hospital with pain in the left hip following an unimportant falling down. He did not have such complaints till then. Upon finding that there was a fracture in the upper end of the femur in the radiological examination, fixation was performed with open reduction and Jewett type plate. The patient was diagnosed with FD in the biopsy taken in the operation. All the skeletal system of the patient was examined, and similar radiographic characteristics were found also in pelvis, tibia, scapula, 6th to 10th ribs, and olecranon, in addition to the lesion in the upper end (Figure 1a, b). There were wide-spread café au lait" spots in the

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body. No hormonal disorder could be determined in the patient. Fractures in the patient, who came to control visits regularly after the first application in 1973, occurring as results of minor falls (tibia: 1981; olecranon: 1991) were treated with plasters. In 1982, lesion in the left tibia was exposed to radiotherapy of 1400 rad in 1982. In June 2001, the swelling in the left tibia of the patient, who attended control visits with complaints like occasional pain, deformations, or limping when walking, rapidly grew in one week, and severe pain started in the same region. An open wound formed in the anterior-medial side of the left cruris. In the plain x-rays and magnetic resonance examinations, soft tissue involvement was found in left tibia (Figure 2a, b). In the whole body bone scintigraphy, prominent activity involvement was seen in the upper end of the left tibia (Figure 2c). The result of the "tru-cut" needle biopsy performed with the idea that sarcoma had been developed over FD was reported to be FD. Since it was an unexpected result, needle biopsy was repeated; however, result was the same. Upon this, open biopsy was performed on August 2001. To make be sure about the result, several samples were collected from different areas. Pathological diagnosis was aggressive, osteogenic type sarcoma (Figure 3a, b). Numerous parenchymal nodules were found in the anterior part of the upper lobe of the left lung and in the upper part of the lingual in the thoracic computerized tomography. Thoracic Surgery Clinic did not recommend surgical therapy. Neo-adjuvant chemotherapy was applied to the patient after consulting with Medical Oncology Clinic. It was planned to give ifosfamid (188 mg/m^2/day) for five days, and methotrexate in 1st and 28th days; however, upon the development of a deep pancytopenia and febrile neutropenia following the application in the 21st day, dosage of 28th day was cancelled, and amputation was performed in the upper part of the left knee. Multiple metastases were found in the follow-ups, and the patient died in the eighth postoperative month because of respiratory failure.

Discussion

Fibrous dysplasia can present with extensive skeletal deformities, color changes in the skin, as well as keeping its course without giving any signs 1. Pain is the most frequent complaint. Transformation into sarcoma is rare [1,4,5]. More than 100 cases have been reported still today [3-7,11-15]. Transformation rate into sarcoma from fibrous dysplasia is less than 1% 16. While this ratio is 0.5% in monocytic form, it reaches 4% in Albright syndrome3-5. The biggest study on fibrous dysplasia was performed in Mayo Clinic. In one thousand one hundred and twenty-two patients followed with the

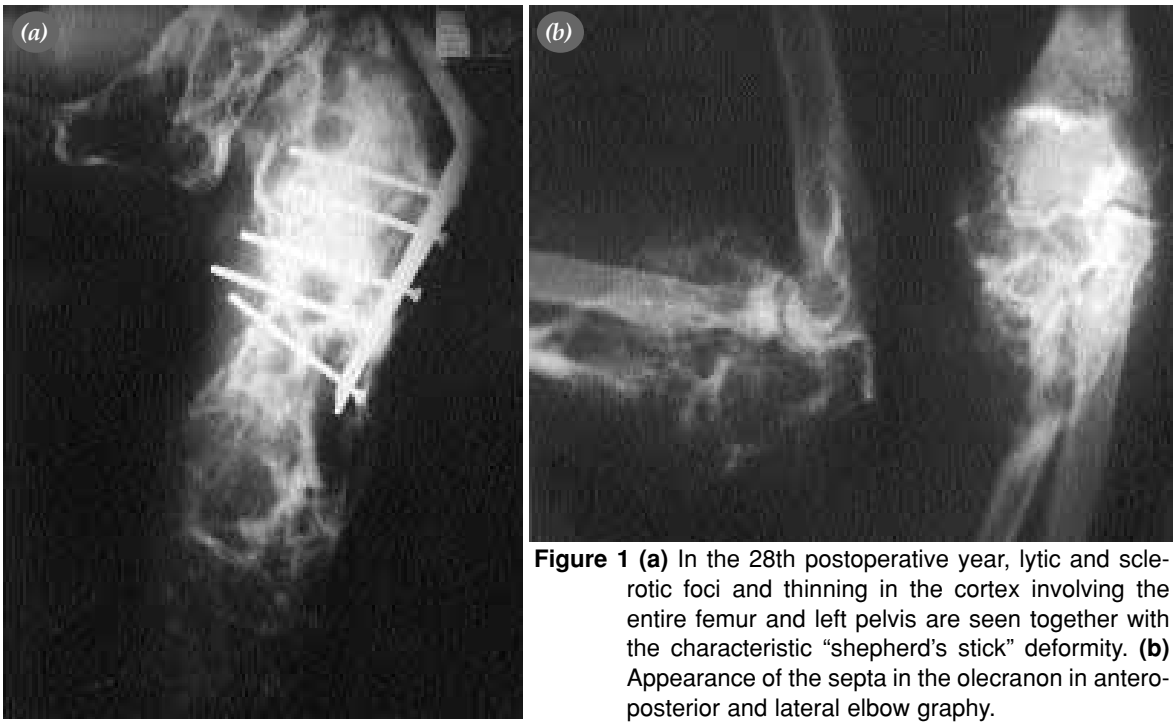

Figure 1 (a) In the 28th postoperative year, lytic and sclerotic foci and thinning in the cortex involving the entire femur and left pelvis are seen together with the characteristic "shepherd's stick" deformity. **(b)** Appearance of the septa in the olecranon in anteroposterior and lateral elbow graphy.

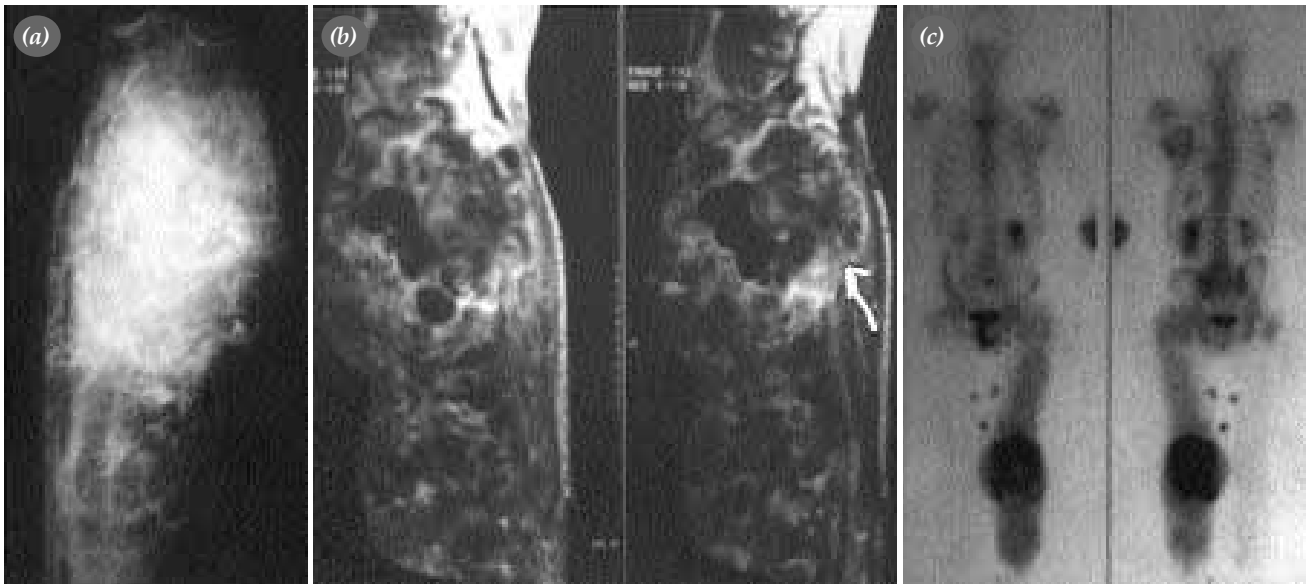

Figure 2 (a) Appearance of the widespread sclerotic and lytic foci with irregular borders involving the entire tibia and causing enlargement in the bone. **(b)** In the cross section of sagittal magnetic resonance imaging, extending of the lesion to soft tissue. **(c)** Distinctive involvement in the left tibia in whole body scintigraphy.

diagnosis of FD, 28 sarcomas were found (19 osteosarcomas, 5 fibrosarcomas, 3 chondrosarcomas, and 1 malign fibrous hystiocytomas), out of which nine were in polyostotoic form. In thirteen of these involvement of mandible and maxilla, and tibia were reported; and transformation ratio to sarcoma was found to be 2.5% 4. In our clinic, 28 patients were treated with the diagnosis of FD, out of which seven were in polyostotic form, and no sarcomas were encountered other than this case (3.5%). Role of radiotherapy in the transformation of FD into sarcoma is controversial [1,4,5,10]. While sarcoma may not develop in every case that radiotherapy has been applied, it is possible for sarcoma to develop in cases that radiotherapy has not been applied. In various studies it was reported that radiotherapy was applied in all the cases transforming into sarcoma; in 12 of 28 patients; and one of 15 patients 4,10. Application ratio for radiotherapy in cases transforming into sarcoma was 46% in the study of Mayo Clinic 4. Time period between radiotherapy and the development of sarcoma is average 19 years (distribution 3 – 52 years) 4. Yabut et al.5 reported that radiotherapy developed in 23 cases out of 83 cases they found in the literature, it was not applied in 46 cases, and there were no records regarding the issue for 14 cases. There is no definite evidence about the relation of radiotherapy with the development of sar-

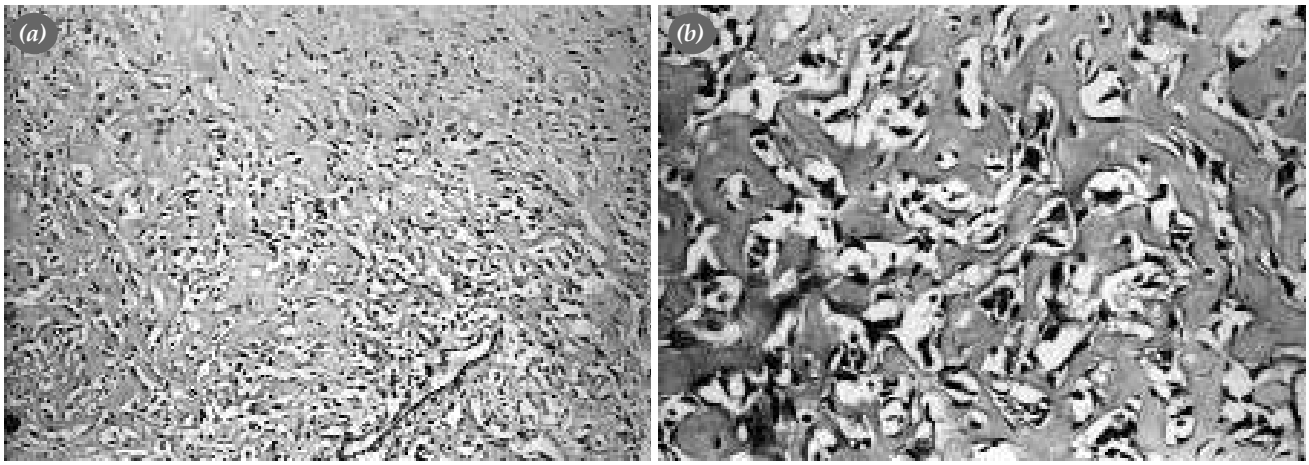

Figure 3 (a) Widespread, atypical osteoblastic cells forming irregular osteoid sections (H-E, x100). **(b)** Appearance of the atypical features in these osteoblasts in grater magnification (H-E, x200)

coma [1,4,5,10]. Contrary to this, developing of sarcoma in the region where radiotherapy was applied to, and lack of such development in areas where it was not applied (femur, scapula, olecranon, ribs) suggest that radioptherapy has an effect on the development of sarcoma in FD. Early diagnosis of sarcoma developing on FD is importants. Sarcoma is in an advanced stage in most of the patients in time of diagnosis 4. Signs develop rapidly in most of the patients. Severe pain, increase in the severity of pain, abrupt growing of the swelling, changes in the radiological appearances that are characteristic for FD, destruction in cortex, and particularly extension to the surrounding soft tissue should remind sarcoma 1. Advanced examinations must all means be performed in these patients. Collecting samples from a single localization can be misleading like in our case.

Sarcoma development risk must always be taken on mind in patients with fibrous dysplasia, and patients must be interrogated in terms of increases in pain and swelling.

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