Case Report

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Synchronous Multicentric Osteosarcoma Involving Mandible and Femur: A Rare Case Report

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Abstract

Synchronous multifocal/multicentric osteosarcoma (SMOS) is a rare variant of osteosarcoma with fewer than 100 well-documented cases in the medical literature. SMOS affecting the jaw is even rarer with only three cases involving the mandible reefing been reported. We report here a case of a 16-year-old mentally challenged girl with SMOS. Radiological examinations showed sclerotic lesions in the left distal femur and in right mandible without pulmonary metastasis. Histological examination showed osteoblastic-type osteosarcoma with chondroid differentiation. Despite high-dose chemotherapy the patient died after 6 months after the initial diagnosis. Immunohistochemistry revealed that p53 protein was positive in most of the tumor cells. The clinical course, radiological and histological appearance of the lesion indicated it was an SMOS rather than metastasis arising from a single osteosarcoma. This case could be regarded as powerful evidence to support the multicentric theory related to SMOS.

Keywords: Synchronous; Multifocal; Multicentric osteosarcoma.

Introduction

Most osteosarcomas (OSs) arise as a solitary lesion. More than one bone lesion of OS without pulmonary metastasis at the initial examination is designated as multicentric or multifocal osteosarcoma (MOS). Such a variant has been recognized since 1936[1], accounting for 1-2% of all OS.[2,3] The involvement of more than one bone naturally compounds therapists' problems[4] and the prognosis in this rare disease remains poor. Parham *et al.* reported that the median survival of their series was 12 months despite multi-agent chemotherapy, mainly high-dose methotrexate and cisplastin-doxorubicin.[5]

MOSs are classified into two types: synchronous and metachronous. The synchronous type is defined as multiple lesions that appear to develop within 6 months.[3] It is controversial whether the tumors have a true multicentric origin or merely represent bone-to-bone metastasis without pulmonary metastasis.[2,6,7-9] We report a case of a mentally retarded 16-year old girl with Synchronous Multicentric Osteosarcoma.

Case report

A 16-year old girl presented with complaints of pain and swelling over right cheek and left thigh simultaneously for 4 months with no other significant medical history. Local examination revealed right cheek swelling extending from angle of mandible to pre-auricular region measuring 10x8 cm and was

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Fig 1:X-ray skull and mandible- osteosclerotic lesion

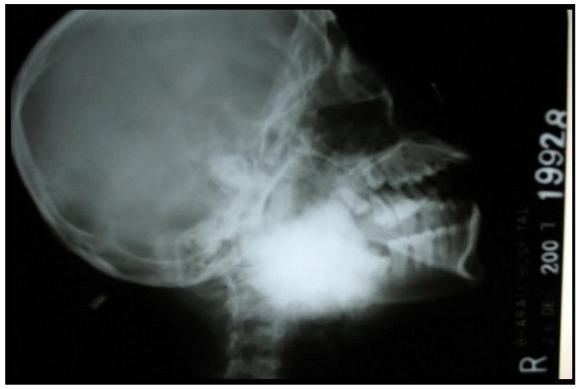
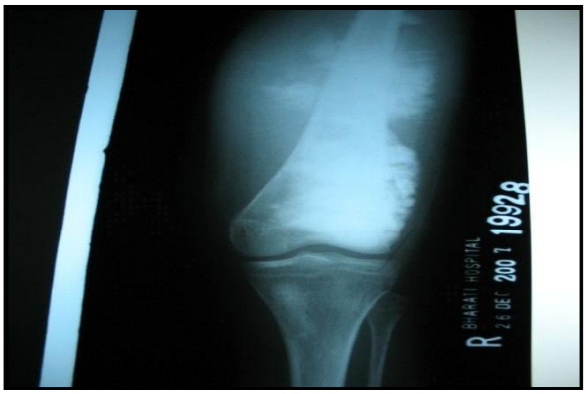


Fig 2: X-ray left leg A-P view- mass involving diaphysis, metaphysis and epiphysis of lower end of femur giving a "sunburst appearance"



tender, hard, immobile. The left thigh swelling measured 20x10 cm which was firm to hard, immobile. All the laboratory investigations and ultrasound of abdomen were normal. X-ray skull and mandible showed osteosclerotic lesion involving right cheek (Fig 1). X-ray left leg A-P view showed mass involving diaphysis, metaphysis and epiphysis of lower end of femur giving a classical "sunburst appearance" (Fig 2), but the x-ray chest was unremarkable. Both bone scan and PET- scan showed foci of involvement of left lower end of femur and right mandible, identified as showing extended uptake at both sites. Histpathological examination of biopsy specimen from both the sites showed osteoblastic-type of Osteosarcoma with chondroid differentiation. Immunohistochemical stain for p53 protein was positive in most of the tumor cells. So, these lesions were diagnosed as Synchronous Multicentric Osteosarcoma.

Fig 3: Photomicrograph (40X)- lace like tumor osteoid

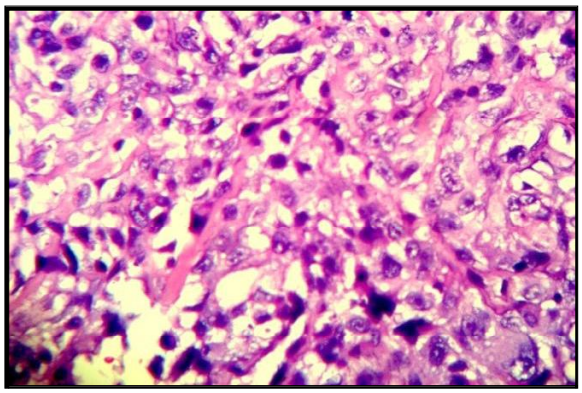


Figure 3 shows lace like tumor osteoid. There was tumor invasion in muscle also.

Discussion

In multifocal/multicentric osteosarcoma (MOS), the issue of whether the bone lesions are multifocal in origin or merely represent bone-to-bone metastases has been controversial. Initially, many authors proposed that MOS was caused by multiple primary tumors if the lungs were free of metastatic disease.[12,13] Later, Mahoney *et al* suggested that metachronous lesions that develop within a 24-month period were probably metastatic, whereas tumors that develop after longer intervals may be true multicentric.[8] Daffner *et al*. stated that MOS represents one extreme of a continuous scale of metastatic OS rather than multiple synchronous primary tumors.[7] Histology of the present case showed high-grade, sclerotic OS of osteoblastic type, consistent with the previous reports.[2,5,14, 15] To support the bone-to-bone metastasis theory, the following facts were noted: (a) one lesion was larger and more extensive than the other lesions in the majority of patients[11]; (b) bone metastases were found in 41% of all OS at autopsy[16]; and (c) an anatomical route was postulated in the vertebral venous plexus system connecting the extremities and spine without passage through the lungs to explain the absence of pulmonary metastasis.[2,17] In the present case, a larger lesion was noted in the left lower femur than in the other locations,

suggesting the primary, focus. Other lesions could be metastatic.

In most patients with usual OS, hematogenous metastasis is observed primarily in the lungs as randomly distributed nodular lesions. The present case did not show any metastasis to lungs. There is a possibility that specific mutations in tumor-suppressor genes are associated with multifocal osteosarcoma, since p53 mutations were found in all four patients with multifocal osteosarcoma[18], higher in usual osteosarcoma.[19] Consistent with this, most of the tumor cells in the present case were positive for p53 by immunohistochemistry. Papai *et al* examined the correlation between p53 expression and clinical prognosis and also response to therapy for conventional osteosarcomas and found that all patients who showed any kind of positive p53 expression were non-responders to chemotherapy.[20] Mutations of p53 gene may play an important part in pathogenesis and chemoresistance of MOS.[21] We need further analyses including clarification of the route of metastasis (hematogenous or lymphogenous) and genetic alterations in MOS.

Conclusion

Multifocal/Multicentric Osteosarcoma are rare they can occur in a synchronous or a metachronous fashion. Most of these Multicentric cases occur in children and tend to be radiographically densely sclerotic. These tumors are extremely aggressive and have poor prognosis.

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