Bilateral adrenal metastases and metastatic subcutaneous deposit in the chest wall from osteosarcoma of the mandible: utility of ¹⁸F-FDG-PET

Abstract

Adrenal gland involvement as well as metastatic subcutaneous nodule from skeletal osteosarcoma are two extremely rare and unusual manifestations in the natural history of the disease. We herein report a 45 yr old female with both these uncommon occurrences, having large bilateral adrenal metastases and a metastatic subcutaneous nodule in the chest wall arising from osteosarcoma of the mandible. Our fluorine-18 fluorodeoxyglucose-positron emission tomography study provided all information needed about the disease status in a single examination. It is noteworthy that osteosarcoma of the jaws, thought to be relatively less aggressive compared to its counterpart in long bones, can occasionally give rise to widespread metastases, including atypical sites. A systematic review of the existing literature aiming to explore the patients’ characteristics and clinical behavior of adrenal metastases from osteosarcoma, including the present case, was carried out.

Description of the case

A 45 years old lady presented with a history of right-sided jaw swelling of six months duration. An orthopantomogram revealed the presence of a well-defined lytic lesion in the horizontal ramus of the right mandible with an associated soft tissue mass. The right mandibular canal appeared to be involved by the lesion. Evidence of caries was noted in the left 1st lower molar tooth and the left 2nd upper molar tooth. A chest roentgenogram revealed a large well-defined mass posteriorly in the lower lobe of the left lung. No evidence of any cavitation or calcification was seen. Computer tomography (CT) scan of the mandible showed an osteolytic lesion involving the body of the right half of the mandible, with involvement of the root of the first molar tooth and erosion of the alveolar margin and the buccal cortex (Fig. 1). Abnormal enhancing soft tissue was seen within the lesion extending into the buccal space. Biopsy from the posterior 1/3rd of the alveolar lesion proved it to be primary osteoclast-rich osteosarcoma of the mandible with an overabundance of osteoclasts and paucity of tumour osteoid. The tumor cells were positive for vimentin and negative for CK, EMA, S100, SMA, desmin, HMB45 and CD34 on immunohistochemistry. Tranaxial helical spiral CT scan of the thorax and abdomen performed in contrast dynamic mode showed a large mass of 7.5 X 6.3 cm in the left lung lower lobe with calcification touching the pleura and erosion of the left 5th rib. Bilateral large adrenal metastatic lesions were noted (right 5.3X4.5 cm and left 8.2 × 6.2 cm). She was started on neoadjuvant chemotherapy and was referred for fluorine-18 fluorodeoxyglucose-positron emission tomography (¹⁸F-FDG-PET) (Fig. 1a, b and c) 8 days after receiving last chemotherapy for evaluation of disease status. Focus of increased ¹⁸F-FDG uptake was noted in the right hemimandible corresponding to the site of the primary. Varying degree of diffuse ¹⁸F-FDG uptakes was also noted in the bone marrow of the vertebrae, humerii, pelvis, ribs and proximal femora along with spleen. This was most likely related to the recent administration of granulocyte-macrophage colony stimulating factor (GM-CSF) 8 days prior to the ¹⁸F-FDG-PET. Heterogeneous ¹⁸F-FDG uptake was seen in the left lung lower zone corresponding to the CT described mass in that area. Heterogeneous ¹⁸F-FDG uptakes were also noted in both the
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Figure 1. CT scan of the mandible showing an osteolytic lesion involving the body of the right half of the mandible, with involvement of the root of the first molar tooth and erosion of the alveolar margin and buccal cortex. Abnormal enhancing soft tissue is seen within the lesion, which extends into the buccal space.

Discussion

Skeletal osteosarcoma is the most common primary malignant neoplasm of the bone of mesenchymal derivation, predominantly occurring in the metaphysis of the long bones of adolescents, young adults and affects males slightly more often than females. In the United States, the incidence of osteosarcoma is 400 cases per year [1]. Metastatic spread is the single most important prognostic factor. Osteosarcoma tends to have early hematogenous metastases. The lung is overwhelmingly the most common site of metastases for skeletal osteosarcoma. The mainstay of therapy is removal of the lesion. Limb-sparing procedures are carried out to preserve function. More than 80% of patients subsequently develop recurrent disease that usually presents as pulmonary metastases treated with “surgery-only” approach [2, 3]. This is due to the fact that most patients have micrometastatic disease at diagnosis. Therefore, the use of adjuvant chemotherapy is critical for the treatment of patients with osteosarcoma. Neoadjuvant chemotherapy has been used to facilitate subsequent surgical removal by shrinking the tumor, treating distant metastases present at diagnosis and also works as an important risk parameter. Patients who have a good histopathologic response to neoadjuvant chemotherapy (>95% tumor cell kill or necrosis) have a better prognosis.

Adrenal metastases from skeletal malignancies are rare and those from osteogenic sarcoma more so, with only 3 cases reported previously in the literature [4-6]. The patients’ characteristics and the clinical details of individual cases are mentioned in Table 1. In the 4 reported cases (including the present one), there does not seem to be any age predilection. While the patients in the first two reports were in their second decade, the cases reported by Kpodonu et al (2005) and that in the present study were in their fourth and fifth decade of age respectively [6]. All the previous reports except the present one have been reported in males (male to female ratio 3:1). In all the previous reports the primary site was in the long bones, essentially reflecting the overwhelmingly common occurrence of osteosarcoma in the extremities of long bones and the relatively aggressive behaviour of

<table>
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<td>Potepan et al [1]</td>
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<td>10 yrs/Male</td>
<td>Left proximal tibia</td>
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<td>Kpodonu et al [3]</td>
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<td>Present study</td>
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<td>45 yrs/Female</td>
<td>Right side of the mandible</td>
<td>Bilateral large adrenal masses detected at diagnosis along with pulmonary and subcutaneous metastasis.</td>
<td>Left lung lower lobe mass, metastatic subcutaneous nodule in the left anterior chest wall</td>
<td>2# neoadjuvant chemotherapy at the time of 18F-FDG-PET</td>
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Figure 2a. $^{18}$F-FDG-PET coronal images, showing increased $^{18}$F-FDG uptake in the right hemimandible (corresponding to the site of the primary), left lung lower zone and both adrenal glands (arrows). Areas of photopenia are seen interspersed in the heterogeneous $^{18}$F-FDG uptake in the metastatic pulmonary and adrenal lesions reflecting necrosis. The right adrenal shows evidence of more necrosis compared to the left. Diffuse $^{18}$F-FDG uptake is noted in the spleen and bone marrow of the vertebrae, humeri, pelvis, ribs and proximal femora related to the recent administration of GM-CSF 8 days prior to the $^{18}$F-FDG-PET study. Another tiny intense focal $^{18}$F-FDG uptake is observed in the left anterior chest wall.

Figure 2b and 2c. $^{18}$F-FDG-PET (MIP images) triangulated over the metastatic adrenal glands (upper panel) and the subcutaneous nodule in the left anterior chest wall (lower panel) respectively (arrows).
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these compared to the osteosarcoma of the jaws [7-9]. Osteosarcoma of the jaws tends to occur at an older mean age and its prognosis is believed to be better than that arising in other sites [7]. Lower mitotic activity and lesser degree of cellular anaplasia in osteosarcomas of the jaws are the two factors implicated to be responsible for their different clinical and biologic characteristics and for favorable prognosis compared to those of osteosarcomas of the long bones [8]. Overall there is a lesser tendency for osteosarcomas of the jaws to metastasize than for osteosarcomas of the long bones [9]. This is, to the best of our knowledge, the first report of osteosarcoma of the jaws metastasizing to both adrenal glands irrespective of the site of the primary. In the previous 3 reports there has been unilateral adrenal metastasis. The metastatic deposit into the subcutaneous tissue at a site distant from the site of primary osteosarcoma is also hitherto unreported. With the improved outcome with multimodality management and increased survival of patients with osteosarcoma, these atypical metastatic sites are likely to be increasingly encountered in practice.

Bibliography

7. Sciubba JJ, Fantasia JE, Kahn LB. Tumors and cysts of the jaws (3rd series), Atlas of Tumor Pathology, Armed Forces Institute of Pathology, Bethesda, MD. 1999; 181.