Case Report

Pulmonary metastasis from desmoid tumor of the foot

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ABSTRACT

Extra-abdominal desmoid tumor is a rare tumor and only a few cases occurring in the foot have been reported. They are benign but locally aggressive, and wide local surgical excision is the treatment of choice owing to the high rate of recurrence in the lower extremities. Invasiveness into the surrounding soft tissue structures often makes wide excision difficult without compromise of function. A 30-year-old woman presented with gradually increasing swelling in the dorsal aspect of the right foot. This case had a large mass in the right foot with metastasis in lungs. Biopsy confirmed the diagnosis of extra-abdominal desmoid tumor of the foot.

Key words: Desmoid tumor, extra-abdominal, pulmonary metastasis

INTRODUCTION

Desmoid tumor, also known as aggressive fibromatosis or musculo-aponeurotic fibromatosis,[1] is a monoclonal fibroblastic proliferation arising in musculo-aponeurotic structures. Desmoid tumor has similarities with fibrosarcoma, hence classified as an aggressive fibromatosis.[2] Desmoid tumors arise from soft tissue fascia but do not metastasize and hence considered to be a locally infiltrative fibroblastic tumor. Bone involvement is very rare, invasion of soft tissue, muscles, neurovascular structures, and subcutaneous tissue being the most common. There have been only a few reported cases of bone involvement of the desmoid tumor.[2] The desmoid tumor usually originates from the abdominal fascia or musculo-aponeurotic structures.[3] They may arise from extra-abdominal sites, the most frequent sites being head/neck, shoulder, chest wall, thigh, and back.[3] Desmoid tumor involving the extremity is very rare. The microscopic feature of these tumors shows spindle-shaped cells in a collagenous matrix with a lack of pleomorphic, atypical, or hyperchromatic nuclei of malignancy.[4] They are locally invasive, and their propensity for recurrence after conservative resection is well documented. However, it usually does not metastasize to other parts of the body, hence considered to be a benign tumor.[4] We present a case of pulmonary metastasis in a patient with desmoid tumor of the foot.

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Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.164720

CASE REPORT

A 30-year-old lady presented to us with a swelling in her right foot for 10 years. It was initially small in size but progressed rapidly in last 6 months causing difficulty in walking. There was no history of similar swelling elsewhere in the body or similar disease in any of the family members. On examination, she had a 11 cm × 9 cm swelling with the bosselated surface on the dorsal aspect of her right foot. The skin was shiny with dilated overlying veins. The movement of the ankle joint was restricted. Radiograph of the foot showed large irregular sclerotic lesion with calcification involving all the tarsals and metatarsals [Figure 1]. Chest radiograph showed bilateral multiple cotton fluffy balls suggestive of metastasis [Figure 2]. Tru-cut biopsy of the

Cite this article as: Paramanandhan M, Kapoor A, Singhal MK, Kumar R, Kumar HS. Pulmonary metastasis from desmoid tumor of the foot. Clin Cancer Investig J 2015;4:658-61.

mass lesion was performed. Microscopically, spindle-shaped cells and collagen fibers arranged in ill-defined fascicles were visible [Figure 3]. On immunohistochemistry analysis, the cells stained strongly positive with vimentin and showed a variable reaction with smooth muscle actin. Staining for nuclear beta-catenin was also positive. Wide local excision of the mass was done. Gross appearance of the specimen was grayish-yellow with hard irregular surface. There were rare mitoses, but no signs of atypia were seen, confirming the diagnosis of extra-abdominal desmoid tumor. Infiltration of the bones was present. After the pathology report, a detailed search for other primary malignancy with pulmonary metastasis potential was performed. Mammography of bilateral breasts was normal. Ultrasound-guided fine-needle aspiration cytology from the lung lesion confirmed metastatic carcinoma. In view of pulmonary metastasis, palliative chemotherapy with ifosfamide and doxorubicin was given. However, the patient's respiratory symptoms gradually worsened and she succumbed after 5 months of diagnosis.

DISCUSSION

Desmoid tumor is classified as a benign disease, and it usually does not exhibit signs of metastasis, but it still has features of local infiltration and local recurrences.[5] The rate of recurrence can reach as high as 65%.[6] In accordance with its biological characteristics, WHO 2002 has classified desmoids-type fibromatosis as a tumor with the fibroblastic or myo-fibroblastic origin.[2] With respect to its biological status, is referred to as "the intermediate state," which falls in between benign and malignant (local infiltrative) tumors.[3] It is an aggressive, stage 3 (Enneking) benign neoplasm.[4] The site of origin is from muscle tendons, with myo-fibroblasts surrounded by collagen fibers.[5] Extra-abdominal fibromatosis is a difficult tumor in terms of recognition, recurrence, and infiltration of neighboring tissues.[6]

The most common age of presentation is between puberty and 40 years, with peak incidence being between 25 and 30 years of age.[3] It is uncommon in patients <10 years of age, but may be seen in <5% of patients. It is more common in women than men.[5] These lesions can appear in any part of the body, but have a predilection for the upper trunk which includes the upper arm (28%), chest wall/para-spinal (17%), and head/neck (10% to 23%). Other locations include the thigh (12%), knee (7%), buttock/hip (6%), and forearms (4%). The above case report is in accordance with the literature available, the patient in this discussion is a young female with a mass in the right foot. The only exceptional feature is that the site of the tumor is foot which is a rare site to occur. Extra-abdominal fibromatoses present as a painless, slow growing mass causing restriction of movement and invading the neurovascular bundle. Unusual presentations at the time of diagnosis include decreased range of motion,

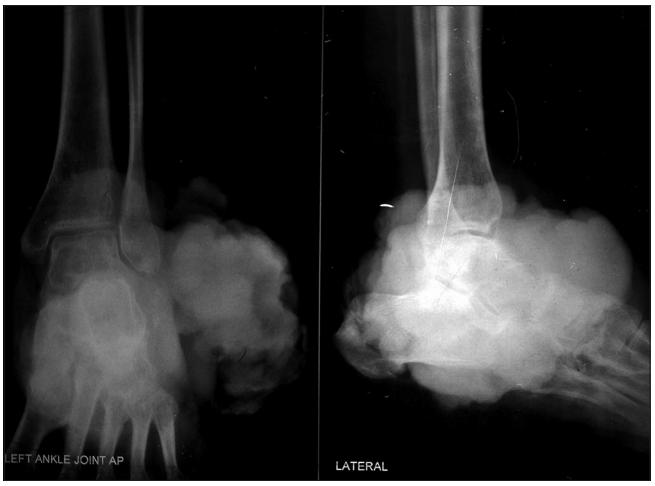

Figure 1: Radiograph of the foot showing large irregular sclerotic lesion with calcification involving all the tarsals and metatarsals

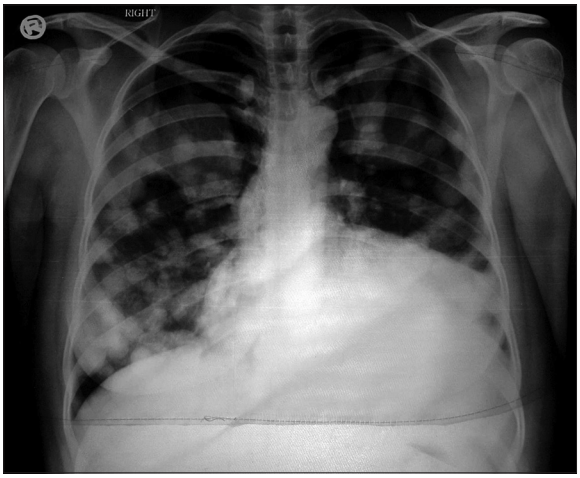

Figure 2: Chest radiograph showing bilateral multiple cotton fluffy balls suggestive of metastasis

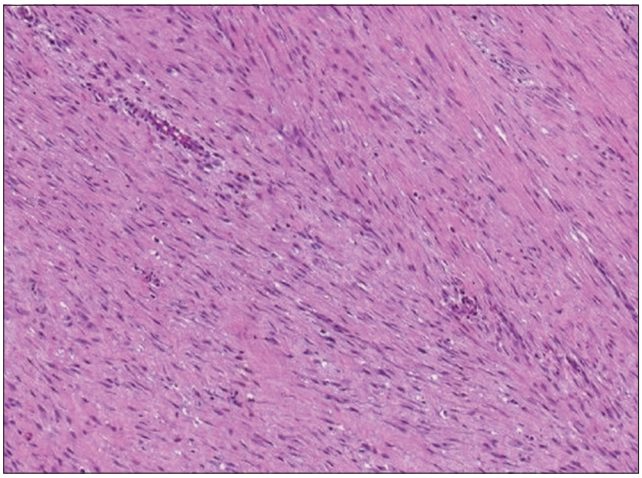

Figure 3: Histopatholgy showing spindle-shaped cells and collagen fibers arranged in ill-defined fascicles (H and E, ×100)

neurologic symptoms, and pain. The size of the tumor may vary from about 5 to 10 cm.[6] She presented with complaints of swelling of the right foot with the restriction of movements and difficulty in walking since 1-year. On examination, the patient had a swelling of 11 cm × 9 cm size.

Extra-abdominal fibromatoses grows along the planes of the fascia and can extend beyond the predominant mass. Endocrine factors have been hypothesized to play a role in the growth and development of these tumors. Solitary lesions are more common, but synchronous multicentric lesions are seen in 5–15% often in the same extremity (75–100%). Therefore, a soft tissue mass in the extremity of a previously diagnosed desmoid tumor should be regarded as a second desmoid tumor until proven otherwise.[7] Skeletal dysplasia is known to be associated with multi-centric fibromatosis.[5] The local recurrence rate varies from 19% to 77% (average 40%) and recurs within 2 years following resection.[6,8]

The typical histologic features are elongated spindle cells in bundles with collagen fibers in between, nuclei usually appear to be normal with slightly eosinophilic cytoplasm, a high degree of cellularity and mitosis is rare. In this case, the microscopy is consistent with the described features above. Electron microscopy reveals cells of fibroblastic derivation, with a range of organelle poor to organelle rich features, cytoplasmic microfibrils, and dilated RER.

Immunohistochemistry shows positivity for beta-catenin. Increased positivity is associated with an increase in relapses. Mutations in exon 3 of beta-catenin gene have been detected. Nuclear beta-catenin 89% with mutations in either CTNNB1 or APC germline positivity for phosphorylated SMAD 2/3 indicative of active transforming growth factor beta signaling. CTNNB1 mutations are detected in 66–84% of cases. Low level (0.87%) + nuclear expression of MCM7 (nuclear proliferative protein) and Ki-67 (19%). Lack of MCM2 and MCM5 proteins expression is consistent with the low mitotic activity of desmoid tumor cells. Beta-catenin is an important protein in the cell signaling pathway. In combination with other proteins, it controls the activities (expression) of particular genes, which help in cell differentiation and proliferation. One of a gene involved is the CTNNB1 gene which codes for the synthesis of beta-catenin protein.[9] Mutations in CTNNB1 gene forms a stable, abnormal beta-catenin protein which is not broken down when it is no longer needed. The protein accumulates in cells, where it continues to function in an uncontrolled way. The beta-catenin levels in the cell are also regulated by the proteins produced from the APC gene. Beta-catenin is broken down once its function is completed in the cell. This is carried out by the APC protein which binds to it. Mutations in the APC gene leads to a short APC protein that is unable to interact with beta-catenin.[10,11] This interferes with the breakdown of beta-catenin and accumulates in cells. Excess beta-catenin accumulated in the cell caused by either of the two mutations, promotes uncontrolled growth and proliferation of cells. This in turn leads to the growth of the tumor.

The differential diagnosis is mainly clinicopathologic. The common differential diagnoses are depicted in Table 1. The closest differential diagnosis being fibrosarcoma in which growth pattern is variable, and infiltration into surrounding structures is comparatively less while mitotic figures are usually higher. Another important differential is reactive fibrosis which is characterized by more variable growth pattern and focal hemorrhage.

Plain radiographs usually appear normal. Usually, two patterns of lesions are seen on a plain radiograph, one being a saucer-like cortical defect due to a lytic lesion in the center with peripheral sclerotic margins. The other variant is a frond-like periosteal reaction consisting of bony spicules invading the soft tissues.[12] Bone is rare, is seen in up to 6–37% of the cases.[13] The chances of bone involvement is higher in cases with multiple recurrences. In the case under discussion, a plain radiograph of the right foot showed irregular sclerotic lesions with calcification involving the tarsal and metatarsal of the right foot. As described earlier, it is a locally aggressive tumor, but a chest radiograph of the patient revealed bilateral multiple cotton fluffy appearance, indicating metastasis to the lungs. This is a very rare feature on presentation, as the patient was symptomless. Ultrasound study of the abdomen of pelvis gives a staghorn appearance due to extension into extra-abdominal regions between the subcutaneous nodules. Contrast enhanced computer tomography is usually nonspecific, the investigation of choice is magnetic resonance imaging of the involved part. It shows the exact location, infiltration into soft tissues. Fluorodeoxyglucose positron emission tomography scan is not preferred at the time of diagnosis, but has a role to assess the status of disease during the course of treatment and the response to chemotherapy.

Surgery is the treatment of choice. The aim of surgery is to have a complete excision of the tumor with negative margins,

Table 1: Important differential diagnosis of desmoid tumor

Differential diagnosis
Fibrosarcoma
Infantile fibrosarcoma
Reactive fibrosis
Solitary (malignant) fibrous tumor
Fibrous hamartoma of infancy
Leiomyoma (in the pelvic location)
Deep soft tissue leiomyoma in the foot
GIST in mesenteric location
Colonic malignancy in a submucosal location

GIST: Gastrointestinal stromal tumor

hence wide local excision is usually done. Amputations can also be done, depends on the site and extent of the disease. Positive margins following resection is reported to have a higher rate of recurrence, however margin positivity or negativity does not impact the rate of recurrences.[14] Postoperative radiotherapy is likely to have less chances of recurrence. Chemotherapy as a treatment in the form of oral sorafenib, imatinib (tyrosine-kinase inhibitors),[14] prostaglandin inhibitors, and anti-estrogen have been tried with limited success.[15] In our case, the patient presented with metastatic disease, hence could not be treated surgically.

CONCLUSION

Metastatic potential can be present in the extra-abdominal desmoid tumor. The authors would like to conclude with the note that complete work up of all patients are necessary even with known benign tumors in view of the unpredictable nature of the malignancy.

Acknowledgments

The authors would like to thank consultants in Department of Oncology, Dr. Ajay Sharma, Dr. N. Sharma, Dr. S. L. Jakhar, Dr. H. S. Kumar, and Dr. Surender Beniwal.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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