EWING'S SARCOMA IN A 52 YEAR-OLD WOMAN WITH LEG PAIN

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INTRODUCTION

Ewing Sarcoma (ES), often referred to as Ewing's sarcoma family tumors (ESFTs), is the second most common primary sacral tumor. ES are aggressive tumors with a tendency toward recurrence and pronounced proclivity toward early hematogenous metastasis to lungs and bone. In 90% of cases, ESFTs cells harbor the translocation t(11;22)(q24;q12), and in the remaining 10% of cases the variant translocation is t(21;12)(22;12). Although peak incidences are between the ages of 10 and 20 years, patients at younger or older age account for almost 30% of the cases.

CASE PRESENTATION

CHIEF COMPLAIN:
Right thigh pain

HISTORY OF PRESENTING ILLNESS:
A 52-year-old woman presented with a two week history of pain in her right posterior thigh radiating to the knee. No constitutional symptom was present.

PHYSICAL EXAMINATION:
The strength, sensory function, range of motion and reflexes were normal.

INITIAL DIAGNOSTIC IMPRESSION:
The initial diagnostic impression was hamstring tendonitis. Despite anti-inflammatory medication and physical therapy the pain persisted. On subsequent reassessment, a radicular component was present.

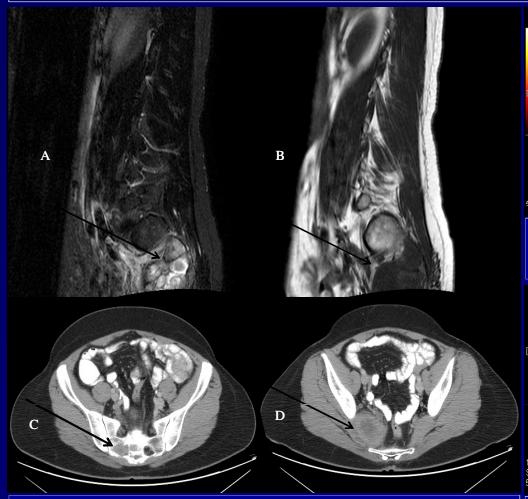
INVESTIGATIONS AND FINAL DIAGNOSIS:
• Lumbar spine MRI and CT scan demonstrated an irregular shaped complex right presacral mass with thick enhancing wall and central necrosis extending into right S2 neural foramen associated with lytic bone destruction.

• Pathologic evaluation revealed a small, round blue cell neoplasm suggestive of a primitive neuroectodermal tumor positive only for vimentin and CD 99. Fluorescence in-situ hybridization analysis was positive for the Ewing Sarcoma locus transformation (22q12).
• Staging workup with a PET/CT did not demonstrate abnormal area of uptake and the tumor staged as III T2b, N0, M0.

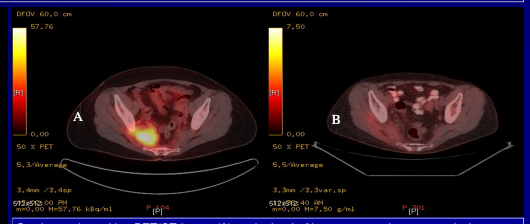
TREATMENT:
There was significant response after four cycles of therapy with Vincristine, Adriamycin, Cytoxan with, Mesna rescue alternating with Ifosfamide and Etoposide (IE). The involvement of S1 and S2 nerve roots represented a significant surgical challenge. As a result, the patient received radiation followed by thirteen additional cycles of chemotherapy. Post treatment CT demonstrated a near complete resolution with minimal residual infiltrates. PET imaging demonstrated normalization of FDG uptake within the pelvic mass.

POST-TREATMENT COURSE:
6 weeks post adjuvant chemotherapy the patient presented with acute shortness of breath. PET-CT demonstrated areas of increased FDG uptake within bilateral pulmonary hila and a new mass in the lower lung confirmed on biopsy to be a recurrent ES. The patient passed away within one month.

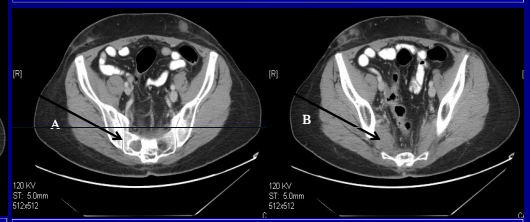
IMAGING STUDIES AND IMMUNOHISTOCHEMICAL SLIDES:



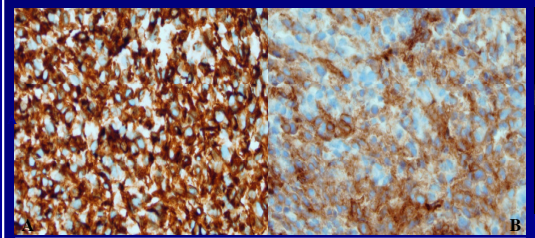
MRI lumbar spine shows an irregular shaped right presacral mass with heterogenous STIR hyperintensity (A) and T1 hypointensity (B).
CT of the pelvis shows a complex mass with thick enhancing wall and central necrosis extending into right S2 neuroal foramen with lytic bone destruction (C). The mass was 6x5x6 cm in size and compressed the right piriformis muscle posteriorly (D).



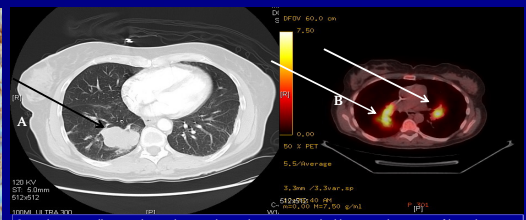
Staging workup with a PET/CT, image (A), at the level of lower sacrum demonstrated a large fluorodeoxyglucose (FDG) avid uptake within the sacral mass measuring approximately 5.8 cm. After four cycles of chemotherapy and radiation therapy a repeat PET/CT (B) showed normalization of FDG uptake within the pelvic mass.



Post treatment CT of pelvis demonstrated a near complete resolution of the mass with minimal residual infiltrative soft tissue.



A core needle biopsy of the mass revealed a small, round blue cell neoplasm suggestive of a primitive neuroectodermal tumor. Immunohistochemistry stains were strongly positive only for vimentin (A) and CD 99 (B).



6 weeks post adjuvant chemotherapy the patient presented with acute shortness of breath.
CT scan of the chest showed a new mass within right lower lung zone measuring 6 cm (A) representing interval development of metastatic disease.
PET-CT demonstrated area of increased FDG uptake within both pulmonary hila (B).

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DISCUSSION

➢Tumors of the pelvis continue to demonstrate a worse prognosis compared with other sites. Whether this is related to the increased difficulty in local therapy is unclear. Morbidity limits both primary surgery and radiation therapy as dose proximity to critical deep structures.

➢Although most cases of ES present as localized disease, overt metastases can develop rapidly. Microscopic metastatic disease has been postulated to exist even at the time of presentation, but its spread held in check by, as of yet unidentified, factors secreted by the primary tumor. When the primary tumor is removed or irradiated, the loss of the putative suppressive factors may permit the metastases to grow.

➢Treatment of adult patients follows the same principles as that of younger patients. However, tolerability of therapies in adults are taken into account when transferring treatment protocols conceived for patients of age above 30 years.

➢Poor prognostic factors include tumor ≥ 8 cm, pelvic primary, presence of metastasis, and age > 15 at the time of diagnosis. Older patients with sarcoma also have higher risk for thromboembolism.

➢ The recent intergroup study suggested that addition of IE to the traditional regimens may confer a local control benefit.

➢ Current studies show that, following achieving remission in patients with nonmetastatic ES, 30-40% of these patients will still develop recurrence of local or metastatic disease. Most of these studies report a time range of 2-10 years between commencing treatment and development of recurrence.

CONCLUSIONS

➢This case emphasizes the importance of timely establishing a correct diagnosis in patients whose symptoms fail to respond to conservative therapy so that targeted therapy can be started in order to optimizing the potential benefit from treatment. Because cancer is rarely in the differential diagnosis for a healthy active patient with leg pain, the average time from initial symptoms to actual diagnosis is about 8 months.

➢ The current case also illustrates complex issues with localized pelvic ES in an older patient who initially responded well to combined chemotherapy and radiation therapy with complete resolution of the tumor. Despite adequate control of the local disease, multimodal therapy did not appear to effect metastasis.

➢Although sarcomas are notorious for metastasis into lungs and bone, the utility of CT and MRI for detecting subclinical recurrence or metastases has not been established during the treatment or the follow up. Only the primary site is evaluated approximately every 10-12 weeks during therapy.

➢ The impact of chemotherapy on metastasis of ES patients older than age 30 is unclear. At this time, patient should be offered participation in a clinical trial when available.