PICTORIAL REVIEW OF EXTRAOSSEOUS EWING’S TUMOR: A SINGLE CENTER EXPERIENCE

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Abstract
Purpose: Ewing’s Family tumour is an extremely rare tumour, with annual incidence rates among Caucasian children less than 21 years being in the range of 2-3 cases per million in the U.S. There are mainly three subtypes including Ewing’s sarcoma of bone, extraosseous Ewing’s tumour and Peripheral primitive neuroectodermal tumour (PPNET). Although extremely rare, this study represents a review of various types of cases and the significance of imaging including its baseline and post treatment response radiological characteristics. There are a very few cases of extraosseous Ewing’s sarcoma in current literature with variable spectrum of tumour site and there imaging characteristics.

Material and Methods: Electronic records were retrospectively reviewed from 01-05-2011 to 01-05-2016 with patients who were diagnosed as histologically proven Ewing’s sarcoma. Number of patients, gender and baseline CT/MRI findings for staging were reviewed.

Results: A total of 568 patients with diagnosed Ewing’s Sarcoma were analysed out of which 15 patients had extraosseous type of Ewing’s Sarcoma. Out of which only 8 patients had baseline imaging available including tumours arising from occipital region, orbit, anterior mediastinum, anterior abdominal wall, mesentery, kidney, prostate gland and presacral region.

Conclusion: Extraosseous Ewing’s sarcoma is a rare entity and can involve a wide array of soft tissue organs. Cross sectional imaging with CT and MR has a key role in pre and post treatment assessment.

Keywords: Ewing’s sarcoma, extraosseous Ewing’s, Peripheral primitive neuroectodermal tumour. MRI, CT

Introduction:
Ewing Family Of Tumour is an extremely rare tumour, with annual incidence rates among Caucasian children less than 21 years being in the range of 2-3 cases per million in the U.S. There are mainly three further types comprising Ewing sarcoma of bone, extraosseous Ewing tumour and Peripheral primitive neuroectodermal tumour (PPNET). Most arise in the second decade of life, primarily among Caucasian children [1]. Although extremely rare, this study represents annual review of various types of cases and the significance of imaging including its baseline and post treatment response radiological characteristics. There are a very few cases of extraosseous Ewing’s sarcoma in current literature with variable spectrum of tumour site and there imaging characteristics. Presently, the diagnosis of this type of tumour is becoming recognized.

Materials and Methods:
Electronic records were retrospectively reviewed from 01-05-2011 to 01-05-2016 with patients who were diagnosed as histologically proven Ewing’s sarcoma. Number of patients, gender and baseline CT/MRI findings for staging were reviewed. Toshiba Aquillion 64 slice CT and Phillips Ingenia 1.5T Phillips were used for image acquisition. Patient had tumour cells on Haematoxylin-eosin staining with immunohistochemical staining positive for vimentin and CD99. Molecular genetic studies by polymerase chain reaction (RT-PCR) or FISH to detect chromosomal translocation, such as t(11;22)(q24;q12) which is positive in 88–95% of ES/PNET cases (Figure 1).
Figure 1: Histopathological slides

(A) Haematoxylin-eosin staining; ×10. Left: tumour cells closely packed together. Right: capsule

(B) Immunohistochemical staining; vimentin-positive cells

(C) Immunohistochemical staining; CD99-positive cells; ×20.

Results:

A total of 568 patients with diagnosed Ewing’s Sarcoma were analysed out of which 15 patients had extra osseous type of Ewing’s Sarcoma (Table 1). Out of which only 8 patients had baseline imaging available. 10 patients had age of less than 30 years whereas 5 patients had an age of more than 30 years. There was female predilection with male/female ratio of around 2:3 (Table 2).

Table 1:

<table>
<thead>
<tr>
<th>Site</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbit</td>
<td>1</td>
</tr>
<tr>
<td>Kidney</td>
<td>1</td>
</tr>
<tr>
<td>Mesentery</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal wall</td>
<td>2</td>
</tr>
<tr>
<td>Pelvic cavity</td>
<td>1</td>
</tr>
<tr>
<td>Scalp</td>
<td>4</td>
</tr>
<tr>
<td>Uterus</td>
<td>2</td>
</tr>
<tr>
<td>Prostate gland</td>
<td>1</td>
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</table>

Table 2:

<table>
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<th>Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>10</td>
<td>10</td>
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</tbody>
</table>

Discussions:

Patients with contained disease have expected 5-year overall survival rates of about 70% due to substantial evolution in both radiotherapy and chemotherapy during the past 4 decades [3,4,5]. Disease relapse and distant metastases presents worst outcome with decline of survival rates of less than 25 % in 5 years [6]. Extraosseous (EO) Ewing’s sarcoma is generally seen in the lower extremities and the paravertebral region. It has also been reported to arise in the GIT [7], kidney [8], uterus [9] and other infrequent sites [10–12]. Imaging is worthwhile for local spread,
resectability and metastases. The diagnosis is founded on immunohistochemistry and molecular pathologic findings. Image-guided biopsy plays an imperative role in determining preoperative diagnosis. Once Ewing’s sarcoma has been diagnosed, multimodal treatment is indicated. Despite all treatment choices, prognosis is poor. It is an aggressive form of tumour which arises in young age. Most of the tumours presented as bulky masses arising from various sites; most common site was root of the mesentery and second most common site was the pelvic cavity. These were solid encapsulated masses with moderate heterogeneous enhancement and mass effect on the surrounding structures with no obvious encasement of the vessels, any overt locoregional lymphadenopathy or osseous involvement.

CASE 1 - Metastatic Occipital Scalp Ewing sarcoma: (Figure 2)
A 31 year old female presented to us with three and a half years history of left occipital region swelling. Initially pea-sized and asymptomatic, but gradually increased in size and became painful and associated with headache, heaviness of left arm and dizziness and fainting.

Figure 2: A, B & C T2-Weighted axial MRI through the thoracic spine shows T2 hyperintense, heterogeneous, metastatic, soft tissue para spinal masses causing spinal cord compression. (D) Post gadolinium T1-Weighted axial view of the brain shows a heterogeneous primary left occipital scalp tumour.
CASE 2 Prostate gland: (Figure 3)
A 43 year old male presented with history of haematuria for one year and acute urinary retention two months back. CT and MRI showed prostate is replaced by heterogeneous lobulated soft tissue extending into the prostatic urethra with no evidence of distant metastases. Afterwards histopathology report favouring small round blue cell tumour.

Figure 3: A. Contrast enhanced CT pelvis showed an expansile, heterogeneously enhancing mass which has completely replaced the prostate gland parenchyma. B. Post chemo/XRT coronal T2 coronal, axial and sagittal T2- weighted sequences shows significant decrease in the tumour bulk involving the prostate gland. No locoregional lymphadenopathy noted.
Case 3 - Kidney: (Figure 4)
A 4 year old boy developed acute right flank pain, low-grade fever and vomiting. No past history of haematuria or significant medical problems recorded. Imaging showed poorly marginated right kidney lesion on ultrasound consistent neoplasia. A staging CT scan of the abdomen was then executed revealing a large infiltrative mass replacing almost whole of kidney, abutting the inferior surface of the right hepatic lobe with no evidence of distant metastases. Diagnosis of Ewing’s sarcoma was confirmed by fluorescence in situ hybridization (FISH) technique, which showed translocations involving the EWS locus (EWSR1 gene rearrangement). Renal PNET occurs predominantly in young adults and has a tendency to be extremely aggressive. The CT and MRI findings will show large masses mimicking Wilms tumour and less likely neuroblastoma.

Case 4 - Orbit: (Figure 5).
A 6 year girl with 3 month complaint of right proptosis came to our hospital for further examination and management. Past history was negative for any medical problems, especially no complaint of thyroid or renal abnormality. No significant family or developmental history noted. Primary extrasosseous Ewing’s sarcoma of orbit is very uncommon and less than 5 % of cases of Ewing’s sarcoma originate from anyplace in the calvarium. Following table shows total number of extrasosseous Ewing’s sarcoma cases that has been reported in present literature (Table. 3).

Figure 5:

Figure 4: A staging contrast enhanced CT scan of the abdomen revealed a large infiltrative hypodense mass replacing almost whole of kidney, abutting the inferior aspect of the right lobe of the liver with no evidence of distant metastases.
Case 5 - Abdominal Wall: (Figure 6)
A 21 year old girl presented with swelling on left lumbar region for about 8 months. Swelling gradually increases in size. Ultrasound abdomen revealed a solid heterogeneous mass in left flank. (Figure 6) Excision biopsy histopathology favour Ewing’s sarcoma. Contrast enhanced CT chest abdomen and pelvis showed a primary tumour in left lower abdominal wall. This was associated with surrounding fat stranding and thickening of overlying skin; the deeper abdominal muscles including transversus abdominis appear intact without any obvious infiltration into the properitoneal fat. This was not associated with any radiologically significant abdominopelvic lymphadenopathy. No pulmonary or mediastinal nodal metastases were reported. Histology revealed a packed, lobular shape of uniform small round malignant blue cells. The individual cells had round-to-ovoid small nuclei with fine chromatin and scanty vacuolated cytoplasm. Immunohistochemistry analysis shows CD99 positive membranous cells. PNET/Ewing’s sarcoma was expected diagnosis. She was given 6 cycles of chemotherapy which showed partial response with more than 70 % regression in tumour size. At multidisciplinary team conference, after pathological and radiological correlation, patient was referred to surgery for excision and tranversus abdominus muscle flap. According to the American Joint Committee on Cancer (AJCC) classification, patient was staged as a PT1bN0M0 extrasosceous Ewing’s sarcoma. She is currently in complete remission for 24 months and continues with a regular active life.

Case 6 - Pelvic Cavity: (Figure 7): A 4-year old child came to us with generalised weakness, irritability and constipation. On ultrasound there was a large pelvic mass with bilateral hydrenephrosis. The differential includes rhabdomyosarcoma versus germ cell tumour. A contrast CT of the chest abdomen and pelvis demonstrated an approximately 10 x 7cm heterogeneous mixed isoattenuating soft tissue mass in the presacral region. The lesion was displacing the pelvic viscera compressing the adjacent structures and involving the whole pelvic cavity. No bony involvement was seen.
Figure 7: A post biopsy contrast enhanced spiral CT of the chest abdomen and pelvis demonstrated heterogeneous mixed iso attenuation soft tissue mass in the presacral region. The lesion was displacing the pelvic viscera compressing the adjacent structures and involving the whole pelvic cavity.

CASE 7 Mediastinum: (Figure 8 A&B)
A 20-year-old man presented with hoarseness of voice, sore throat, recurrent chest discomfort, low grade fever and weight loss since 3 months. Physical examination revealed a palpable mass in the left posterior neck and axilla. Chest radiograph showed superior mediastinal widening with right upper lobe collapse and right pleural effusion. Subsequently computed tomography thorax confirmed a large anterior mediastinal solid mass with central areas of necrosis, demonstrating mass effect on the great mediastinal vessels, especially the SVC and the right pulmonary artery. (Figure 8 A&B)

Figure 8: (A) Chest radiograph showed superior mediastinal widening with right upper lobe collapse and suspicion of right pleural effusion.

Figure 8: (B) Subsequently computed tomography thorax confirmed a large anterior mediastinal solid mass with central areas of necrosis, demonstrating mass effect on the great mediastinal vessels, especially the SVC and the right pulmonary artery.
### Table 3: Orbital extraosseous Ewing’s sarcoma in the literature

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Sex</th>
<th>Chief complaint(s)</th>
<th>Year published</th>
<th>Site and extent of tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Harbert &amp; Tabor</td>
<td>19</td>
<td>M</td>
<td>Visual loss, Proptosis</td>
<td>1950</td>
<td>Orbit</td>
</tr>
<tr>
<td>2 Yamada &amp; Takahashilo</td>
<td>61</td>
<td>M</td>
<td>Visual loss, proptosis</td>
<td>1957</td>
<td>Orbit</td>
</tr>
<tr>
<td>3 Alvarez Berdecia et al.</td>
<td>6</td>
<td>M</td>
<td>Headache, Proptosis</td>
<td>1979</td>
<td>Orbit, cranial fossa</td>
</tr>
<tr>
<td>4 Howard &amp; Lundll</td>
<td>14</td>
<td>M</td>
<td>Painful swelling over nasal bridge</td>
<td>1985</td>
<td>Sinuses, Orbit, cranial fossa</td>
</tr>
<tr>
<td>5 Woodruff et al</td>
<td>6</td>
<td>M</td>
<td>Visual loss; headache</td>
<td>1988</td>
<td>Sinuses, Orbit, cranial fossa</td>
</tr>
<tr>
<td>6 Tewari et al.</td>
<td>10</td>
<td>F</td>
<td>Painful proptosis</td>
<td>1993</td>
<td>Orbit, cranial fossa</td>
</tr>
<tr>
<td>7 Fiorillo et al.</td>
<td>7</td>
<td>M</td>
<td>Painless lower orbital swelling</td>
<td>1996</td>
<td>Orbit</td>
</tr>
<tr>
<td>8 Fiorillo et al.</td>
<td>22</td>
<td>F</td>
<td>Facial swelling</td>
<td>1996</td>
<td>Orbit</td>
</tr>
<tr>
<td>9 Dennis S.C, Lam Chi K Li</td>
<td>2</td>
<td>M</td>
<td>Bilateral proptosis</td>
<td>1998</td>
<td>Sinuses, Orbit, cranial fossa</td>
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<tr>
<td>10 Current case</td>
<td>6</td>
<td>F</td>
<td>Painless unilateral proptosis</td>
<td>2016</td>
<td>Sinuses, Orbit, cranial fossa</td>
</tr>
</tbody>
</table>

**CASE 8 - Root of Mesentery:** (Figure 9)

A 6 year old boy has 2 months history of fever, abdominal pain and distention. Physical examination shows a tense and firm palpable mass in the left upper aspect of the abdomen. Sonographic evaluation revealed a well encapsulated abdominal mass occupying the whole peritoneal cavity with study in Doppler mode revealed no blood flow. Subsequently, abdominal CT confirmed an isoattenuating mass with epicenter within the small bowel mesentery. It measured 20 x 17 x 12 cm. (Figure 9). Tumour was encapsulated, partially solid/cystic and had few calcifications. The lesion was displacing compressing the adjacent pancreas from which is not clearly separated. There was indentation into the adjacent stomach and lesion all around the left sub hepatic space. There were no internal calcific foci. It was difficult to exclude some necrotic component within this lesion but no gross macroscopic fat attenuation seen. There was no invasion of the splenoportal venous system or IVC. Aorta remains reasonably well clear of this tumour process as are both the kidneys.

![Figure 9: Abdominal computed tomography of 6 year old boy which confirmed an isoattenuating mass with epicentre within the small bowel mesentery. It measured 20 x 17 x 12 cm.](image)

**Conclusion:**
Extraosseous Ewing’s sarcoma (ESS) is an exceptionally rare tumour with nonspecific features. This tumour is diagnosed as cumulative correlation between radiology and histopathology analysis. Recent advances in diagnostic and interventional radiology are valuable for evaluating respectability, biopsy guidance and tumour response to treatment.
References:


