

## PICTORIAL REVIEW OF EXTRAOSSEOUS EWING'S TUMOUR: A SINGLE-CENTRE EXPERIENCE

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### Abstract

**Purpose:** Ewing's family tumour is an extremely rare tumour, with annual incidence rates amongst Caucasian children <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 (ES) of bone, extraosseous (EO) Ewing's tumour and Peripheral primitive neuroectodermal tumour. 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 EO ES in the current literature with variable spectrum of tumour site and their imaging characteristics.

**Materials and Methods:** Electronic records were retrospectively reviewed from 1 May 2011 to 1 May 2016 with patients who were diagnosed as histologically proven ES. A number of patients, gender and baseline computed tomography (CT)/magnetic resonance imaging findings for staging were reviewed.

**Results:** A total of 568 patients with diagnosed ES were analysed, of which 15 patients had EO type of ES. Of these only 8 patients had baseline imaging available which included tumours arising from the occipital region, orbit, anterior mediastinum, anterior abdominal wall, mesentery, kidney, prostate gland and presacral region.

**Conclusion:** EO ES is a rare entity and can involve a wide array of soft tissue organs. A cross-sectional imaging with CT and MR has a key role in pre- and post-treatment assessment.

**Key words:** Computed tomography, Ewing's sarcoma, extraosseous Ewing's, magnetic resonance imaging, peripheral primitive neuroectodermal tumour

### Introduction

Ewing family of tumour is an extremely rare tumour, with annual incidence rates amongst Caucasian children <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 (ES) of bone, extraosseous (EO) Ewing tumour and peripheral primitive neuroectodermal tumour (PNET). Most ES arise in the second decade of life, primarily amongst Caucasian children.<sup>[1,2]</sup> Although extremely rare, this study represents an 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 EO ES in the current literature

with a variable spectrum of tumour site and their imaging characteristics. At present, the diagnosis of this type of tumour is becoming recognised.

### Materials and Methods

Electronic records were retrospectively reviewed from 1 May 2011 to 1 May 2016 with patients who were diagnosed as histologically proven ES. A number of patients, gender and baseline computed tomography (CT)/magnetic resonance imaging (MRI) findings for staging were reviewed. Toshiba Aquilion 64 slice CT and Philips Ingenia 1.5T Philips were used for image acquisition. The patient had tumour cells on haematoxylin-eosin staining with immunohistochemical staining positive for vimentin and CD99. Molecular genetic studies by reverse transcription polymerase chain reaction or fluorescence *in situ* hybridisation (FISH) to detect chromosomal

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translocation, such as t(11;22) (q24;q12) which is positive in 88–95% of ES/PNET cases [Figure 1].

**Results**

A total of 568 patients with diagnosed ES were analysed, of which 15 patients had EO type of ES [Graph 1]. Baseline imaging was available only for eight out of these fifteen patients. Ten patients had an age of <30 years, whereas five patients had an age of >30 years. There was a female predilection with male:female ratio of around 2:3 [Graph 2].

**Discussion**

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 four decades.<sup>[3-5]</sup> Disease relapse and distant metastases present the worst outcome with a decline of survival rates of <25% in 5 years.<sup>[6]</sup> EO ES is generally seen in the lower extremities and the paravertebral region. It has also been reported to arise in the gastrointestinal tract,<sup>[7]</sup> kidney,<sup>[8]</sup> uterus<sup>[9]</sup> and other infrequent sites.<sup>[10-12]</sup> 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 pre-operative diagnosis. Once ES has been diagnosed, multimodal treatment is indicated. Despite all treatment choices, the prognosis is

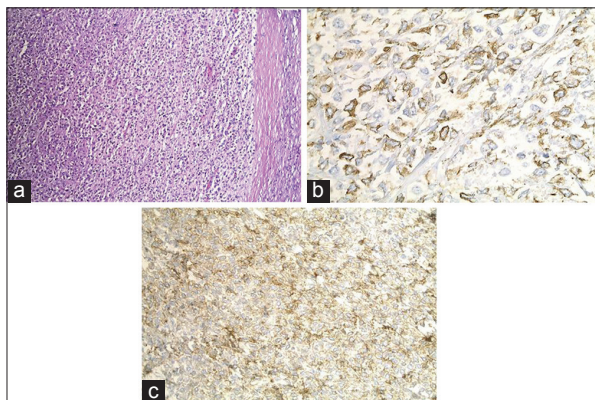
poor. It is an aggressive form of tumour which arises in young age. Most of the tumours presented as bulky masses arising from various sites; the most common site was the root of the mesentery and the second most common site was the pelvic cavity. These were solid encapsulated masses with moderate heterogeneous 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 ES [Figure 2]**

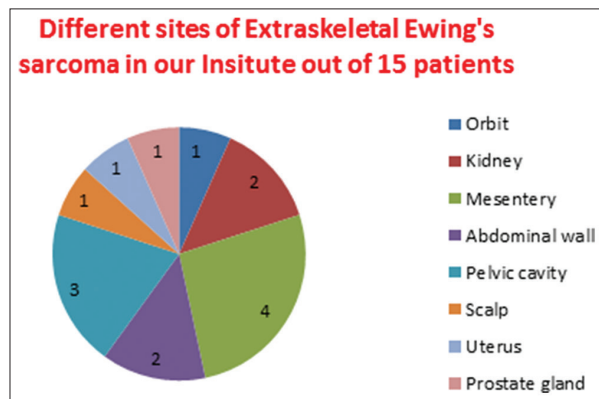
A 31-year-old female presented to us with 3½ years’ history of left occipital region swelling. Initially the swelling was pea-sized and asymptomatic, but gradually it increased in size and became painful and associated with headache, heaviness of left arm and dizziness and fainting.

**Case 2 - Prostate gland [Figure 3]**

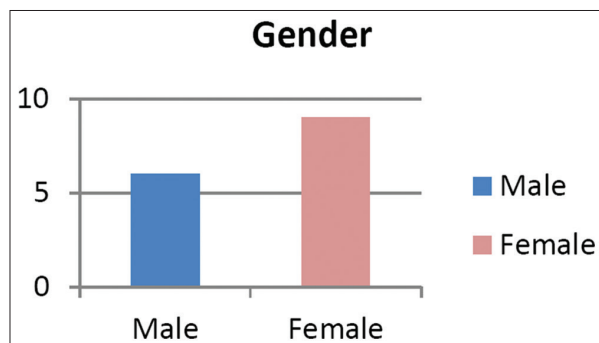
A 43-year-old male presented with a history of haematuria for 1 year and acute urinary retention 2 months back.



**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

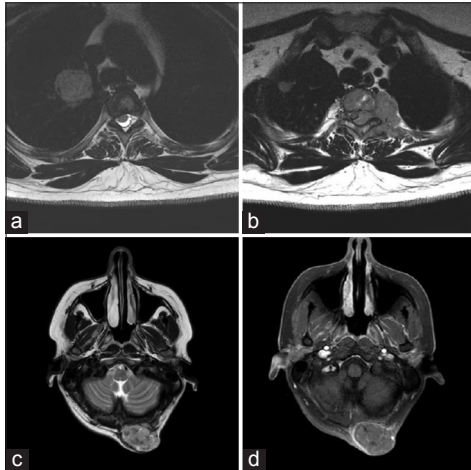


**Graph 1:** Sites of extraskelatal Ewing's sarcoma

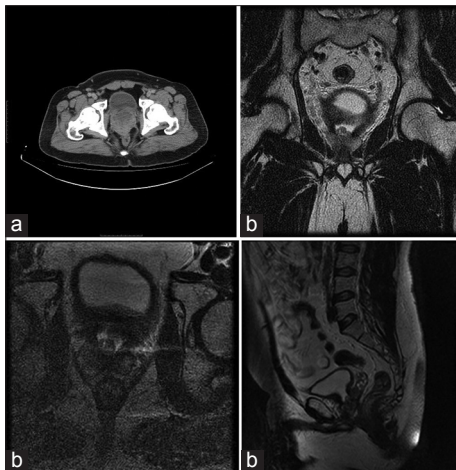


**Graph 2:** Male: Female ratio

CT and MRI showed that 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 2:** (a-c) T2-weighted axial magnetic resonance imaging through the thoracic spine shows T2 hyperintense, heterogeneous, metastatic, soft tissue paraspinal masses causing spinal cord compression. (d) Post-gadolinium T1-weighted axial view of the brain shows a heterogeneous primary left occipital scalp tumour



**Figure 3:** (a) Contrast-enhanced computed tomography pelvis (axial view) showed an expansile, heterogeneously enhancing mass which has completely replaced the prostate gland parenchyma. (b) MRI Post-chemo/XRT T2-weighted coronal, axial and sagittal sequences show a significant decrease in the tumour bulk involving the prostate gland. No locoregional lymphadenopathy noted.

### Case 3 - Kidney [Figure 4]

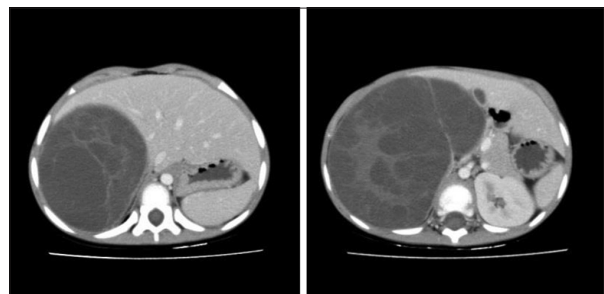
A 4-year-old boy developed acute right flank pain, low-grade fever and vomiting. No past history of haematuria or significant medical problems was recorded. Imaging showed poorly marginated right kidney lesion on ultrasound consistent neoplasia. A staging CT scan of the abdomen was then executed revealing a large infiltrative mass replacing almost whole of the kidney, abutting the inferior surface of the right hepatic lobe with no evidence of distant metastases. Diagnosis of ES was confirmed by 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. CT and MRI findings will show large masses mimicking Wilms' tumour and less likely neuroblastoma.

### Case 4 - Orbit [Figure 5]

A 6-year-old girl with 3 months' complaint of right eye proptosis came to our hospital for further examination and management. History was negative for any medical problems, especially no complaint of thyroid or renal abnormality. No significant family or developmental history was noted. Primary EO ES of the orbit is very uncommon and <5% of cases of ES originate from any place in the calvarium. Table 1 shows a total number of EO ES cases that have been reported in the present literature.

### Case 5 - Abdominal wall [Figure 6]

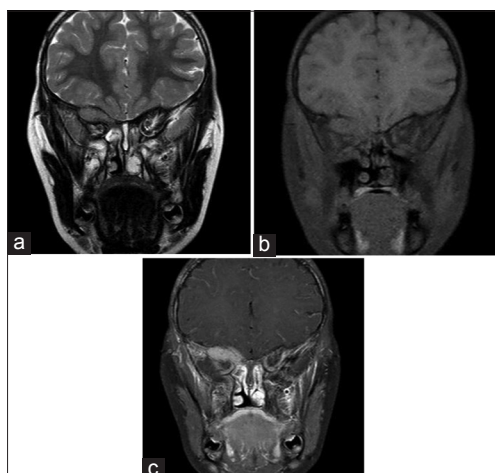
A 21-year-old girl presented with swelling on the left lumbar region for about 8 months. Swelling gradually



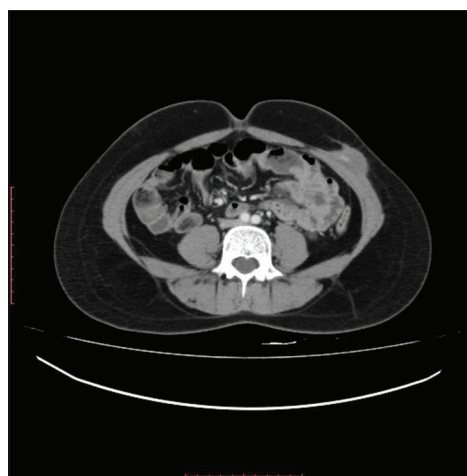
**Figure 4:** A staging contrast-enhanced computed tomography scan of the abdomen revealed a large infiltrative hypodense mass replacing almost whole of the kidney, abutting the inferior aspect of the right lobe of the liver with no evidence of distant metastases

increases in size. Ultrasound abdomen revealed a solid heterogeneous mass in the left flank [Figure 6]. Excision biopsy histopathology favours ES. Contrast-enhanced CT chest abdomen and pelvis showed a primary tumour in the 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 peritoneal 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/ES was expected a diagnosis. She was given six cycles of chemotherapy which showed partial response with >70% regression in tumour size. At multidisciplinary team conference, after pathological and radiological correlation, the patient was referred to surgery for excision and transversus abdominis muscle flap.



**Figure 5:** (a-c) Orbit targeted, pre-contrast, Fat-Sat, T1-weighted (T1WI) sequence shows a soft tissue right orbital mass which is isointense to grey matter. (a) Coronal T2-weighted, (b) pre-contrast coronal, (c) pre-contrast coronal T1WI



**Figure 6:** Contrast-enhanced computed tomography abdomen showed a primary tumour in the left lower abdominal wall which is a complex solid/cystic mass. 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 peritoneal fat. This was not associated with any radiologically significant abdominopelvic lymphadenopathy. No pulmonary or mediastinal nodal metastases were reported

**Table 1: Orbital extraosseous Ewing's sarcoma in the literature**

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



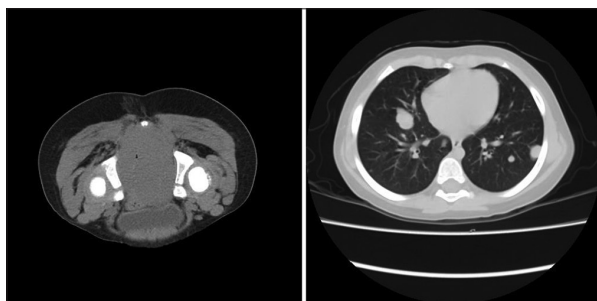
According to the American Joint Committee on Cancer classification, the patient was staged as a PT1bN0M0 EO ES. She is currently in complete remission for 24 months and continues with a regular active life.

#### 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 hydronephrosis. The differential includes rhabdomyosarcoma versus germ cell tumour. A contrast CT of the chest abdomen and pelvis demonstrated an approximately 10 cm × 7 cm 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.

#### Case 7 - Mediastinum [Figure 8a and b]

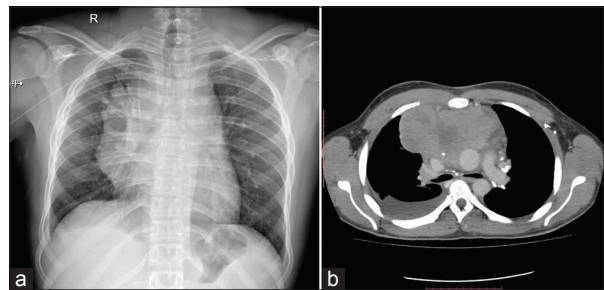
A 20-year-old man presented with hoarseness of voice, sore throat, recurrent chest discomfort, low-grade fever and weight loss for 3 months. Physical examination revealed a palpable mass in the left posterior neck and axilla. Chest radiograph showed superior mediastinal widening with the right upper lobe collapse and right pleural effusion. Subsequently, CT thorax confirmed a large anterior mediastinal solid mass with central areas of necrosis, demonstrating the mass effect on the great mediastinal vessels, especially the superior vena cava and the right pulmonary artery [Figure 8a and b].



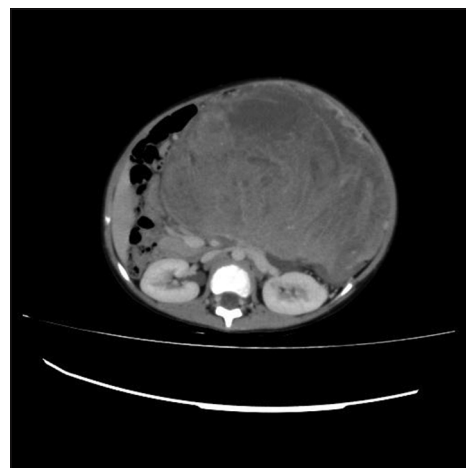
**Figure 7:** A post-biopsy contrast-enhanced spiral computed tomography of the chest abdomen and pelvis demonstrated heterogeneous mixed isoattenuation soft tissue mass in the presacral region. The lesion was displacing the pelvic viscera compressing the adjacent structures and involving the whole pelvic cavity

#### Case 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. Doppler mode revealed no blood flow. Subsequently, abdominal CT confirmed an isoattenuating mass with epicentre within the small bowel mesentery. It measured 20 cm × 17 cm × 12 cm [Figure 9]. Tumour was encapsulated, partially solid/cystic and had few calcifications. The lesion was displacing and compressing the adjacent pancreas and could not be clearly separated from it. There was indentation



**Figure 8:** (a) Chest radiograph showed superior mediastinal widening with right upper lobe collapse and suspicion of right pleural effusion. (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 superior vena cava and the right pulmonary artery



**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 cm × 17 cm × 12 cm

into the adjacent stomach and lesion all around the left subhepatic space. There were no internal calcific foci. It was difficult to exclude some necrotic component within this lesion but no gross macroscopic fat attenuation was seen. There was no invasion of the splenoportal venous system or inferior vena cava. Aorta remains reasonably well clear of this tumour process as are both the kidneys.

### Conclusion

EO ES is an exceptionally rare tumour with non-specific features. This tumour is diagnosed as a 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.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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