BJMS
Borneo Journal of Medical Sciences

CASE REPORT

Retroperitoneal Extraskeletal Ewing's Sarcoma in Adult

Cheong Kang Wei[1], Chandran Nadarajan[2]*

[1] Department of Radiology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[2] Department of Radiology, Hospital Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

*Corresponding author's email: drchandran@usm.my

Received: 10 September 2022

Accepted: 7 December 2022

Published: 31 January 2023

DOI: https://doi.org/10.51200/bjms.v17i1.3780

Keywords: *extraskeletal, retroperitoneal, Ewing's sarcoma*

ABSTRACT

Ewing's sarcoma is a highly malignant tumour of osseous or non-osseous origin, typically seen in the paediatric and adolescent age group. However, extraskeletal Ewing's sarcoma is an uncommon tumour. It could arise from the soft tissue in the paravertebral area, chest wall, head and neck, and retroperitoneum. Retroperitoneal extraosseous Ewing's sarcoma is even rarer, with only a few reported cases in the literature. We describe the radiologic findings of this rare retroperitoneal extraskeletal Ewing sarcoma manifested in an adult patient. Our patient is a 32-year-old gentleman who presented with abdominal pain and constitutional symptoms for two months. Imaging shows a retroperitoneal tumour with local infiltration. It was confirmed via histopathological analysis as retroperitoneal Ewing's sarcoma. We discussed the diagnostic strategy as well as the literature review of this rare disease.

INTRODUCTION

Ewing's sarcoma is a family of tumours which includes: osseous Ewing sarcoma (OES), extraskeletal Ewing sarcoma (EES), primitive neuroectodermal tumour, and Askin tumour (Murphey et al., 2013). Histologically, these tumours demonstrate crowded sheets of small round blue cells (García-Moreno Nisa et al., 2007). These lesions share the same karyotype abnormality, which is a non-random reciprocal

translocation between chromosomes 11 and 22 (t [11;22][q24;q12]). The 22q12 locus codes for EWS, while the 11q24 site codes for FL1, resulting in the EWS-FL1 fusion transcript typically seen in 85% to 95% of Ewing sarcoma (Murphey et al., 2013). Extraskeletal Ewing's sarcoma was first described by Tefft et al. in 1969 and characterized by Angervall and Enzinger in 1975 (Nishino et al., 2003). It is rare in comparison with Ewing sarcoma of bone and usually manifests in young patients, with 85% of cases detected between 20 months and 30 years old (Murphey et al., 2013). Clinically, these patients will present with pain and a large, rapidly growing soft tissue mass. The mass is often deeply seated. The commonly reported locations include the paravertebral region (32%), lower extremities (26%), chest wall (18%), retroperitoneum (11%), and pelvic region (11%) (Murphey et al., 2013). Retroperitoneal Ewing's sarcoma often presents late as the retroperitoneum is a large potential space allowing the tumour to grow to a substantial amount before symptom manifestation.

CASE PRESENTATION

A 32-year-old male patient presented with complaints of abdominal discomfort and vague pain at the left hypochondrium for two months. It was associated with significant loss of appetite, causing 15 kg weight loss within this period. Clinical examination revealed a mass over the left upper abdomen. The initial abdominal radiograph (Figure 1) shows an ill-defined soft tissue mass with no clear border at the left hypochondrium, displacing the adjacent small and large bowels. Ultrasound abdomen (Figure 2) showed a huge heterogeneous hypoechoic mass, predominantly solid with small cystic components occupying the left hypochondrium and lumbar region, extending to the epigastric region. Calcification or internal vascularity was not seen within this mass. Computed tomography (CT) scan of the abdomen (Figure 3) was performed for further evaluation, which showed a large heterogeneously enhancing lobulated mass at the left retroperitoneal region, measuring approximately 18.6 cm × 20.0 cm × 26.6 cm. There are areas of non-enhancing hypodensities within this mass, suggestive of the presence of necrotic components. It also displaced the abdominal aorta, inferior vena cava, and their tributaries laterally to the right side; however, these vessels remained patent. It causes a mass effect on the adjacent organs, including the left kidney, pancreas, and small and large bowels. However, no evidence of distal metastasis to the lung, bone and other solid organs is seen. In magnetic resonance imaging (MRI) imaging, the lobulated mass is heterogeneously hypointense on T1-weighted (T1W) images and hyperintense on T2-weighted (T2W) images with enhancement in post-Gadolinium images. There are areas within, which are hypointense on T1-weighted (T1W) images and hyperintense on T2-weighted (T2W) images with no enhancement post-Gadolinium (Figure 4), suggestive of the presence of necrotic component. It is not suppressed on spectral attenuated inversion recovery (SPAIR) sequence to suggest the presence of fat components within. It has no clear plane with the left kidney, pancreas, and left psoas muscle. However, there are no abnormal signal intensities to suggest infiltration. Ultrasound-guided biopsy of this mass was performed. Histopathology examination showed monomorphic small blue round cells displaying round to oval hyperchromatic to vesicular nuclei, fine chromatin and small inconspicuous nucleoli with scanty to clear cytoplasm. There is the presence of glycogen highlighted by PAS and PASD stain. Immunohistochemistry shows positivity of strong diffuse membranous CD99 and nuclear FLI-1. It is negative for CKAE1/AE3, CK7, CK20, Melan A, HMB45, Chromogranin A, Synaptophysin, CD45, CD56, CD34 and CD10. These features are in favour of Ewing's sarcoma. The EWSR1 gene molecular analysis was not performed for this patient, due to the unavailability of this analysis at the cytogenetics laboratory at Hospital USM. The treating oncology team was satisfied with the HPE report and radiological findings of the tumour to initiate chemotherapy.

This patient is currently undergoing neo-adjuvant chemotherapy comprising a combination of vincristine, doxorubicin, and cyclophosphamide before tumour resection. Subsequent follow-up CT and MRI studies show a good response to chemotherapy, as evident by the tumour's size reduction.

Figure 1
Abdominal radiograph showing an ill-defined mass (white arrows) at the left hypochondrium displacing the small and large bowel loops

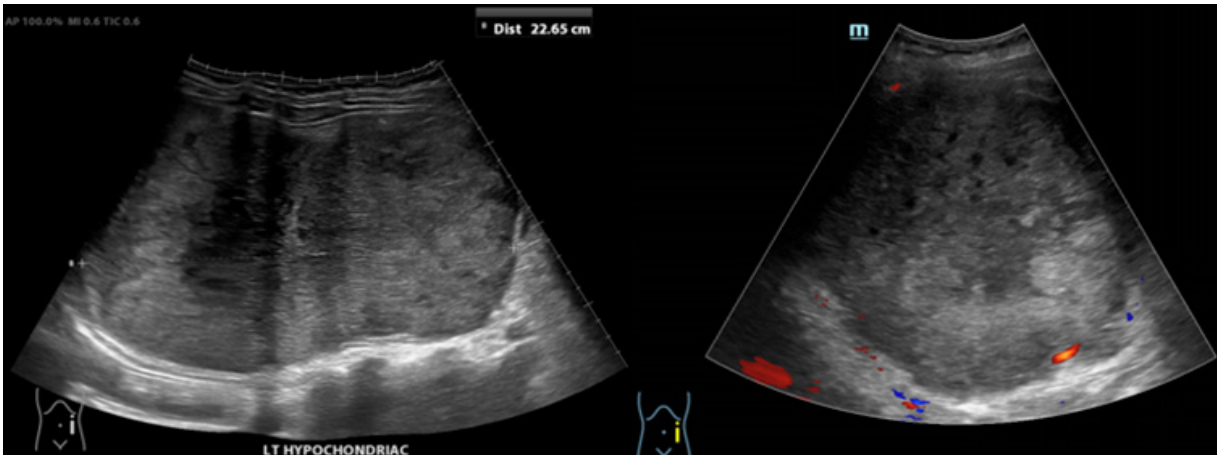
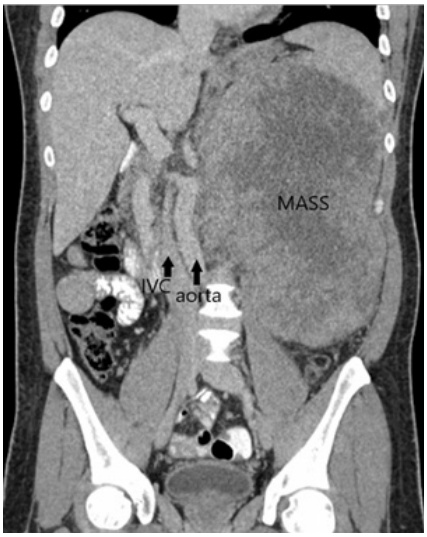


Figure 2 Ultrasound shows a retroperitoneal mass at the left hypochondrium. This mass is predominantly solid, with areas of necrosis within. No vascularity or calcification was seen within the mass.

Figure 3
A contrasted CT scan in coronal view showing a large soft tissue mass at the left retroperitoneal region. It causes a mass effect on the adjacent structures and displaces the inferior vena cava and the aorta to the right side. Areas of hypodensities that do not show contrast enhancement are in keeping with the necrotic component.



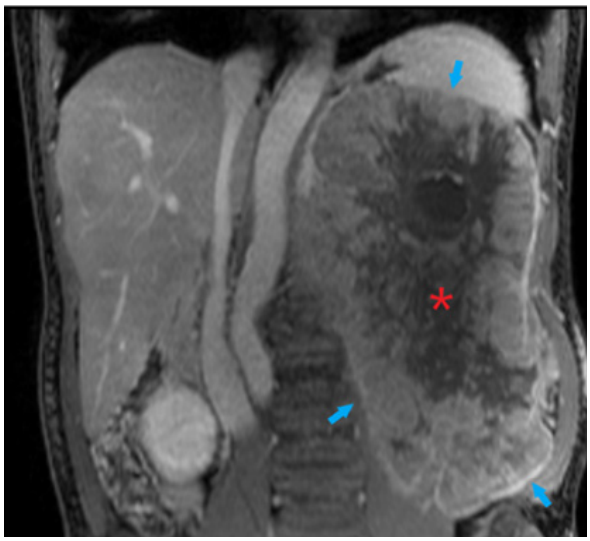


Figure 4
Post-Gadolinium coronal T1-weighted image showing the soft tissue component (blue arrows) demonstrating heterogeneous enhancement post-contrast. The non-enhancing region (labelled as *) within the mass represents the necrotic region.

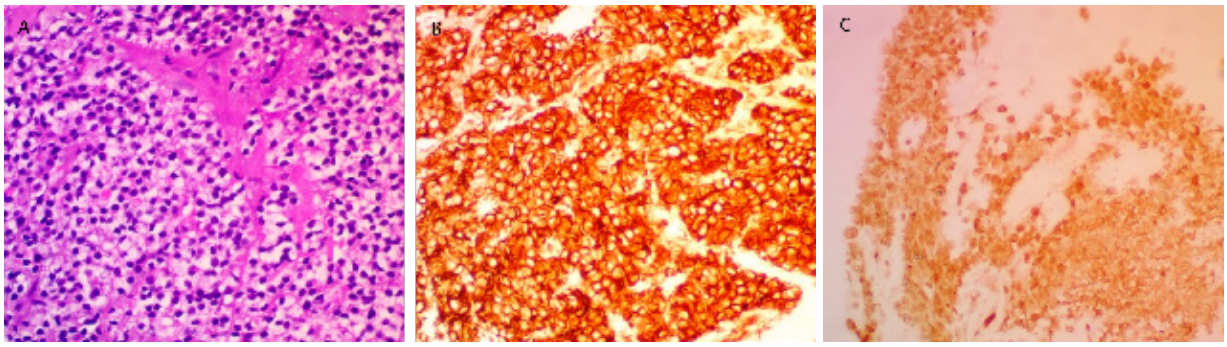


Figure 5 Histopathology examination showed monomorphic small blue round cells (A) displaying round to oval hyperchromatic to vesicular nuclei, fine chromatin and small inconspicuous nucleoli with scanty to clear cytoplasm. Immunohistochemistry shows positivity of strong diffuse membranous CD99 (B) and nuclear FLI-1(C).

DISCUSSION

OES is the second most common primary malignant tumour of bone in children and adolescents. EES is rarer compared to its osseous counterpart. The incidence of EES is 15% of that of OES. Only 11% of EES is seen in the retroperitoneal region (Murphey et al., 2013). Patients with retroperitoneal Ewing's sarcoma present with variable clinical manifestations. It depends on the size and site of the tumour as well as its invasion into adjacent structures. These tumours are made up of rapidly enlarging masses and commonly cause compression symptoms and abdominal pain, as in our patients. Often, a mass may be palpable on an abdomen examination (Javalgi et al., 2016). EES has been reported to have some different characteristics compared to OES as it does not have a predilection for male patients but rather is more equally distributed between both genders. Patients with EES are often slightly older by approximately 5 – 10 years, as in our patient. Meanwhile, OES is more common in the paediatric and adolescent age groups. EES also more commonly affects the trunk rather than the lower limbs (Murphey et al., 2013).

The initial diagnosis of EES is based on imaging modalities. In ultrasound, O'Keefe and colleagues reported that extraskeletal Ewing's sarcoma lesions are most frequently hypoechoic with anechoic areas within, likely to represent areas of necrosis. CT often demonstrates a soft tissue mass with similar

attenuation to the muscle (87% of cases). Areas of haemorrhage or necrosis can be seen within. MRI imaging is superior to CT for evaluating infiltration of the adjacent organs. MRI demonstrates a heterogeneous soft tissue mass with similar signal intensity to that of skeletal muscle on T1-weighted images (T1W) and intermediate to high signal intensity on T2-weighted images (T2W). Prominent contrast enhancement is seen in both CT and MR imaging (Murphey et al., 2013). Calcification and lymphadenopathy are rare, reported in less than 10% of the cases (Javery et al., 2011). It can displace, encase, or invade adjacent organs. However, unlike OES, it does not show osseous or marrow involvement (Murphey et al., 2013). Despite bulky disease at presentation, regional or distant metastases are uncommon (Javery et al., 2011).

Histopathology examination is essential for the definitive diagnosis of retroperitoneal Ewing's sarcoma. On histopathology, extraskeletal Ewing's sarcoma is similar to the classical Ewing's sarcoma of the bone. It shows closely packed small blue round cells arranged in sheets with round nuclei and indistinct nucleoli with a high nuclear-cytoplasmic ratio. Molecular analysis of these tumours demonstrates chromosomal rearrangements involving t(11;22) (q24; q12) (Javalgi et al., 2016).

Other more common primary retroperitoneal malignancies which should be considered as differentials include lymphoma, liposarcoma, undifferentiated pleomorphic sarcoma, leiomyosarcoma, and rhabdomyosarcoma (Mota et al., 2018). Lymphoma, the most common malignant retroperitoneal neoplasm, typically presents as a para-aortic mass encasing adjacent structures. Necrosis and calcifications are uncommon before treatment (Mota et al., 2018). Liposarcoma is the most common retroperitoneal sarcoma, affecting individuals in the fifth and sixth decades. On imaging, liposarcoma is a fat-containing lesion with multiple septa and enhancing soft tissue components. Meanwhile, undifferentiated pleomorphic sarcoma is a heterogenous lesion with a similar density to adjacent muscle, with enhancing soft tissue components and areas of calcification (Mota et al., 2018). Leiomyosarcoma is characterized by the presence of massive cystic components and the absence of fat or calcification within. It often shows the contiguous involvement of a vessel. Rhabdomyosarcoma is predominantly seen in the pediatric age group. It presents as an aggressive heterogeneous tumour with adjacent bone destruction (Mota et al., 2018).

EES is chemo and radiosensitive. Neoadjuvant chemotherapy is the standard of care before definitive surgery for localized disease. Chemotherapy consisting of vincristine, doxorubicin, and cyclophosphamide is used in most cases and has increased the long-term survival rate. This is followed by surgical resection of the primary tumour, which has been shown to improve local control and survival more than radiotherapy (García-Moreno Nisa et al., 2007).

CONCLUSION

Although rare, extraskeletal Ewing's sarcoma should be considered in young adults presenting with a large heterogeneous mass in the retroperitoneum. Imaging allows for early detection of these tumours, and histopathology examinations confirm the diagnosis. MRI imaging is essential for preoperative planning and evaluating response to treatment.

CONFLICT OF INTEREST

The authors have no competing interest to publish this case report.

CONSENT

Written consent was obtained from the patient to publish this case report. A copy of the written consent is available for review by the Chief Editor.

ACKNOWLEDGEMENTS

The authors would like to thank the Director General of Health Malaysia for the permission to publish this case report.

REFERENCES

García-Moreno Nisa, F., López Quindos, P., García Teruel, D., & Beni Pérez, R. (2007). Extraosseous retroperitoneal Ewing's sarcoma. *Clinical and Translational Oncology*, *9* (6), 404 – 405. https://doi.org/10.1007/s12094-007-0074-8

Javalgi, A. P., Karigoudar, M. H., & Palur, K. (2016). Blue cell tumour at an unusual site. Retroperitoneal Ewing's sarcoma. *Journal of Clinical and Diagnostic Research*, *10* (4), ED21 – ED22. https://doi.org/10.7860/JCDR/2016/18302.7618

Javery, O., Krajewski, K., O'Regan, K., Kis, B., Giardino, A., Jagannathan, J., & Ramaiya, N. H. (2011). A to Z of extraskeletal Ewing sarcoma family of tumours in adults: Imaging features of primary disease, metastatic patterns, and treatment responses. *American Journal of Roentgenology*, *197*, (6). https://doi.org/10.2214/AJR.11.6667

Mota, M. M. D. S., Bezerra, R. O. F., & Garcia, M. R. T. (2018). Practical approach to primary retroperitoneal masses in adults. *Radiologia Brasileira*, 51 (6), 391 – 400. https://doi.org/10.1590/0100-3984.2017.0179

Murphey, M. D., Senchak, L. T., Mambalam, P. K., Logie, C. I., Klassen-Fischer, M. K., & Kransdorf, M. J. (2013). From the radiologic pathology archives: Ewing sarcoma family of tumors: Radiologic-pathologic correlation. *Radiographics*, *33* (3), 803 – 831. https://doi.org/10.1148/rg.333135005

Nishino, M., Hayakawa, K., Minami, M., Yamamoto, A., Ueda, H., & Takasu, K. (2003). Primary retroperitoneal neoplasms: CT and MR imaging findings with anatomic and pathologic diagnostic clues. *Radiographics*, *23* (1), 45 – 57. https://doi.org/10.1148/rg.231025037

Ulusan, S., Koc, Z., Canpolat, E. T., & Çolakoglu, T. (2007). Radiological findings of primary retroperitoneal Ewing sarcoma. *Acta Radiologica*, *48* (7), 814 – 818. https://doi.org/10.1080/02841850701408244