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CASE REPORT

Ewing Sarcoma presenting as a gluteal mass in adult woman: Diagnostic approach and its challenges

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Abstract

Introduction: Sarcomas of the Ewing family of tumours are aggressive neoplasms occurring in bone and soft tissue of mostly children and young adults. It usually affects male more than female with peak incidence 10 to 15 years of age, and rarely encountered in adults especially in more than 40 years old. It is an aggressive, rare tumour with a tendency toward recurrence after resection and early metastasis. *Case Report:* We reported a rare case of Ewing Sarcoma in a 62-year-old woman who had an unusual clinical presentation. She had right painless buttock swelling only for a month. Magnetic resonance imaging (MRI) revealed soft tissue sarcoma originated from right gluteal muscle. The diagnosis of Ewing sarcoma (ES) was made in a limited diagnostic material in an initial tru-cut biopsy, followed by an excision supported by immunohistochemistry (IHC) and Fluorescent In-Situ Hybridization (FISH). *Discussion:* The purpose of this study is to document ES in an adult woman and its diagnostic challenges in histopathologic perspective.

Keywords: Ewing sarcoma, gluteal mass, adult, diagnostic challenge

INTRODUCTION

Ewing sarcoma (ES) is a malignant tumour of unknown origin characterised by primitive small round cells without obvious differentiation. Recently, Ewing sarcoma and primitive neuroendocrine tumour (PNET) have been unified into a single category named Ewing Sarcoma Family Tumours (ESFT) as they shared clinical, morphological, biochemical and molecular features. The peak incidence is between 10 to 15 years of age. However, 30 percent of cases arise in children under the age of 10, and another 30 percent are in adults over the age of 20.[1,2] The patients typically present with localised pain and swelling and the most common locations are the pelvis, axial skeleton and femur. Although overt metastatic disease is found in fewer than 25 percent at the time of diagnosis, most of the cases are presumed to have a subclinical metastatic disease because of 80 to 90 percent of patients who underwent local therapy alone had a history of relapsed. Thus, systemic chemotherapy has become an important component of the patients' treatment.[3]

CASE REPORT

A 62-year-old Malay woman, who presented with one-month history of right painless buttock swelling following a history of fall. The swelling was initially about the size of an egg, slowly increased in size. Neither signs of inflammation nor neurological deficit were detected. Her ambulatory function was not affected. Physical examination revealed she was afebrile, had a normal gait, and other systems were normal. The mass was about 5cm x 5cm, rounded, firm, non-mobile and non-tender, without skin changes or discharge. Magnetic resonance imaging (MRI) demonstrated soft tissue enhancing lesion with central necrosis arising from right gluteal muscle which measured 7x5 cm, without bony involvement. No intra-pelvic mass or

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lymphadenopathy.

An initial tru-cut biopsy of the mass revealed a limited diagnostic material consisted of a few tiny strips of tumour tissue with small round cell morphology and extensive necrosis. The limited immunohistochemical stains were done (EMA, LCA, CD34, S-100, Desmin and SMA) and none was positive. Glycogen was demonstrated by PAS/PAS-Diastase histochemical stains. In the difficulties of having viable tumour tissue, and having in mind this is an adult woman with soft tissue mass, an additional CD99 and FLI-1 stains were done and the pattern of positivity were pointed to the diagnosis of Ewing Sarcoma.

The patient underwent surgical resection. Intra-operatively it was a firm to hard mass arising from right gluteal maximus muscle. The gross examination revealed a well-circumscribed, lobulated cream tan tumour mass measured 6cm x 7cm x 8 cm (Fig. 1). Central cavitation filled with necrotic and hemorrhagic material was seen. Microscopically, it showed a highly cellular tumour, arranged in solid sheets and nests with small infiltrative clusters, embedded within the dense fibro-collagenous stroma. These cells are fairly monomorphic, small to medium-sized, exhibiting round to oval hyperchromatic nuclei, irregular nuclear membrane, with some show conspicuous nucleoli and scant eosinophilic cytoplasm. Homer-Wright rosettes were prominent. Mitoses, including those of aberrant type were easily seen (14/10 high power fields). The rhabdomyoblast was absent. The immunohistochemistry demonstrated a similar pattern with the tru-cut biopsy. The tumour cells were also negative for TLE-1, Synaptophysin and Chromogranin. The FISH analysis for EWSR1 gene using break-apart probe (VYSIS) demonstrated the presence of ESWR1 gene rearrangement (Fig. 2).

CT Thorax was performed a week later and reported to have multiple pleural based nodules, suggestive of metastasis. Currently, the patient had just completed third cycle of chemotherapy (Cyclophosphamide, Adriamycin, Vincristine / Ifosfamide and Etoposide) and clinically improved and stable.

DISCUSSION

Ewing sarcoma family of tumours (ESFTs) represent a family of malignant small round-cell neoplasms, in which generally originate in bone tissue, but they can occasionally originate in soft tissue, known as Extraskeletal Ewing sarcoma (EES), which constitutes 6% to 47% of all ESFTs and 1.1% of all malignant soft tissue tumours. Its morphological features are indistinguishable from Ewing sarcoma of bone which include IHC & molecular components with its osseous counterpart.[1,2]

The ES is considered as a childhood malignancy and it is rarely encountered in a female more than 40 years of age.[4] This is a rare case of EES in an adult woman. The usual extraskeletal sites of ES are the deep soft tissues of the lower extremities and paravertebral region. ES typically present with localised pain or swelling of a few weeks or months duration. The pain may be mild at first but intensifies fairly rapidly and it may be aggravated by exercise and is often worse at night.[3] A distinct soft tissue mass

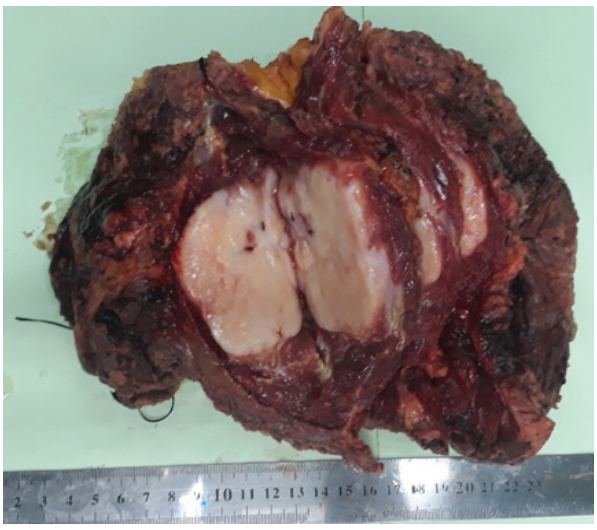

FIG. 1: A well-circumscribed solid cream tan tumour mass within the gluteal muscle measuring 6x7x8 cm.

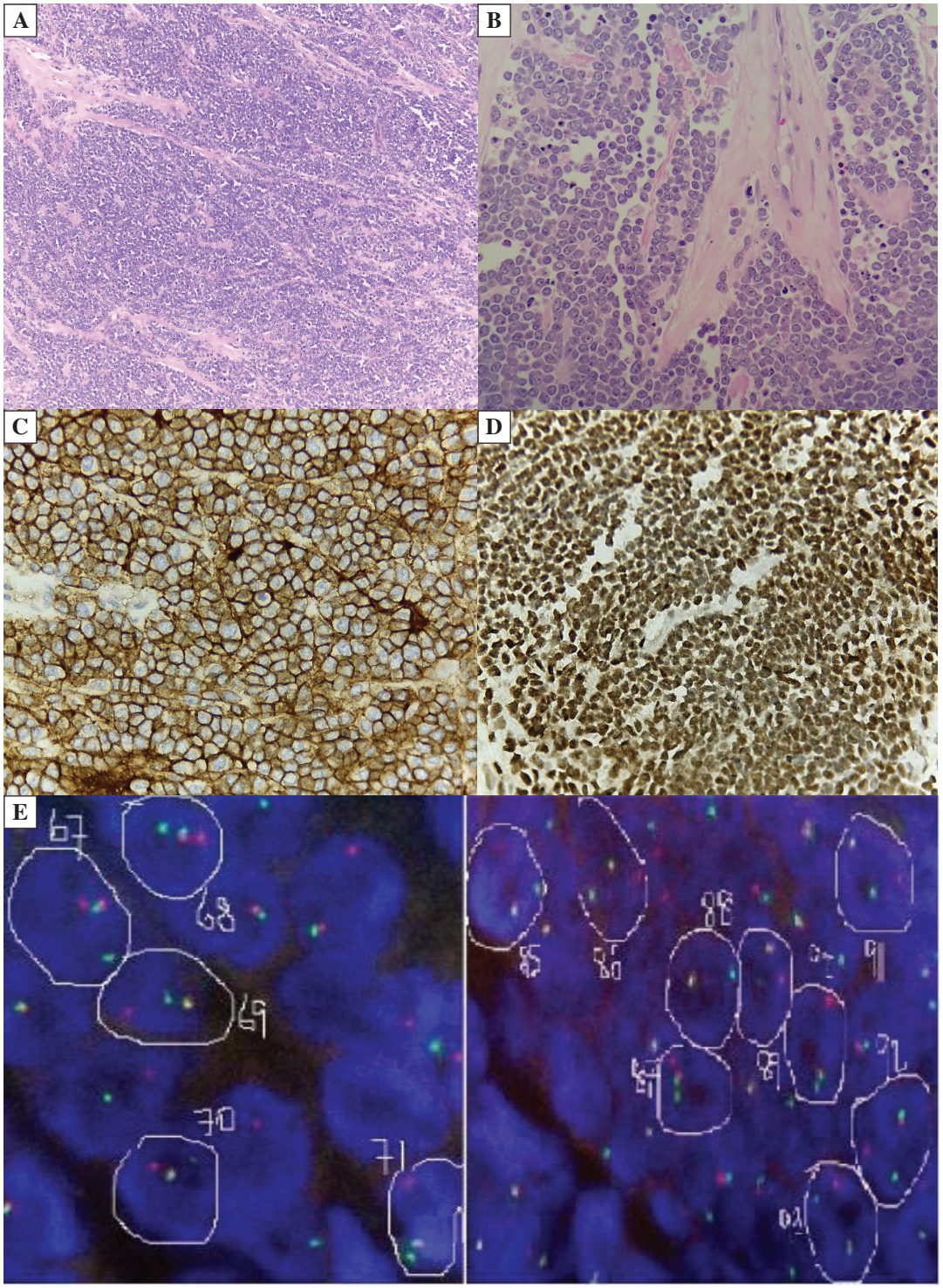

FIG. 2: (A) Sheets and clusters of small blue round cell tumours (H&E, x100) ;(B) Prominent Homer-Wright rosettes (H&E, x400). (C) CD99 immunohistochemistry showed diffuse intense membranous positivity (CD99, x400) and (D) FLI-1 immunohistochemistry with diffuse intense nuclear positivity (FLI-1, x400). (E) Fluorescence in situ hybridization (FISH) analysis for EWSR1 gene using break-apart probe (VYSIS), shows many nuclei with split signals consistent with presence of EWSR1 gene rearrangement.

can sometimes be appreciated. When present, it is usually firmly attached to the bone and tender to palpation.[18] More challenges will be faced by the pathologists when the soft tissue mass also invaded and involved the bone which can't be differentiated microscopically.

Its rarity, the histogenesis and differential diagnosis of the entities have been continuously caused problems in diagnostic pathology. It needs a very thorough workup especially in an unusual clinical context like this case. This unfortunate lady presented with painless buttock mass for a month after a history of fall. A short duration of presentation in an adult_woman, with small round cell morphology, obviously need a comprehensive workup to rule out other possible differential diagnoses which included lymphoma, metastatic undifferentiated /small cell carcinoma, neuroendocrine carcinoma, poorly differentiated synovial sarcoma, small cell liposarcoma and rhabdomyosarcoma which might tally with the radiological findings of right gluteal muscle mass. The ES will be down on the list of the differential diagnoses due to the unusual age of presentation. The initial biopsy itself was limited due to very minimal viable tumour cells were available for assessment rendered more challenges to the diagnosis. In such circumstances, a careful interpretation with relevant immunohistochemistry played a crucial role in order to reach or at least narrow down the diagnosis.

The immunohistochemistry which is widely available in routine diagnostic use, give valuable complementary information to rule out the differentials, though many of them are also shared immunoreactivity with other tumours and non-specific. It is important to exclude other non-sarcomatous tumours and then determine the line of mesenchymal differentiation. In an unusual clinicopathological context such as in our case, the integration of molecular pathology into the routine diagnosis is indicated to detect the translocation, not only for diagnostic confirmation but also for prognostication and further management.

CD99 strong diffuse membranous expression by immunohistochemistry is seen in approximately 95% of ES.[4] However, CD99 is not related to any gene products of specific translocation found in ES, and not specific for ES. CD99 immunoreactivity can also be seen in other tumours such as lymphoblastic lymphoma(73 -93%), almost all mesenchymal chondrosarcoma, 10-25% of rhabdomyosarcoma and also in synovial sarcoma.[4] However, it is important to see the typical strong diffuse membranous immunoreactivity pattern in ES which is not seen in other tumours in appropriate morphological features.

EWSR1-FLI-1 fusion genes are found in 85% of ES cases.[4,5] This finding of genetic alterations has led to the development of new antibody FLI-1 immunohistochemistry which is more specific but less sensitive for ES. With a combination of both CD99 and FLI-1 immunoreactivity, in an appropriate clinical and histologic context, that should be sufficient to allow a confident diagnosis of ES and exclude other small round cell tumour differentials.

In this case, we had proceeded with molecular analysis to confirm the diagnosis of ES (in an excised specimen) and had proven to have ESWR1 gene rearrangement by FISH analysis. Molecular studies of cytogenetic analysis and molecular assays have rapidly become the standard for confirming the diagnosis. The translocation t(11;22)(q24;q12) is the most common and leads to the formation of the EWS-FLI1 fusion protein, can be detected by reverse transcription-polymerase chain reaction (RT-PCR) and FISH.[5] Dagher R *et al*. analysed 58 ES cases by (RT-PCR) testing and found 45 out of 58 had (EWS)-FLI type 1 translocation.[6]

Our patient is an adult patient who had a large gluteal muscle mass as a primary tumour and had evidence of lung metastasis on follow up based on CT thorax done a week after diagnosis was made. The earlier CXR did not detect any evidence of metastasis. This indicates that most probably the micrometastasis had already set in which only detected by CT Scan of Thorax after the diagnosis was made. The children's oncology group reported that the detection of micrometastatic disease at initial diagnosis by flow cytometry or RT-PCR is not associated with outcome in newly diagnosed paediatric age patients with Ewing sarcoma.[7] However, it was a vice versa finding by Elizabeth HB *et al*. among adult ES age more than 26-year-old, with evidence of metastasis and extraskeletal in origin which showed adverse prognosis with 5-year survival rate (SR) is almost 0%.[8] It also true for ES of the bone in which the 5-year SR was dropped from 55% (without metastasis) to 21% (with metastasis), and lung metastasis has an overall better prognosis compared with bone metastasis or combination of both lungs and bone metastasis.[9]

CONCLUSION

ESFT is a rare type of tumour that occurs in bones and as well as soft tissues. It remains a diagnostic challenge especially in an unusual clinical context. Clinical correlation, imaging studies and tumour morphology are the key roles in the diagnosis, involving a multidisciplinary team. The interpretation of immunohistochemistry stains is crucial in guiding the diagnosis followed by molecular testing to confirm the diagnosis in difficult cases.

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