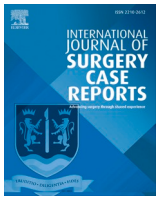
International Journal of Surgery Case Reports 91 (2022) 106708

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr



Case report

Challenges in diagnosing an extraosseous Ewing sarcoma: A case report

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ARTICLE INFO

Keywords:
Extraosseous Ewing sarcoma
Soft tissue
Surgery
Cancer
GIST

ABSTRACT

Introduction: Ewing sarcoma is a highly malignant and rare tumour of bones and soft tissue. It may occur at any age, but it is more common in children and teenagers.
Case report: We report a case of a 56-year-old woman with EES involving the right iliac fossa. Previous abdominal trauma with retroperitoneal hematoma, nonspecific symptoms and unusual age for EES have caused diagnostics difficulties. The first histopathological examination misdiagnosed tumour to be a GIST, and just after the second surgery the accurate diagnosis of EES was made.
Conclusions: The diagnosis of ES sometimes is complicated and delayed. Prompt detailed examination and imaging studies should be performed to people with long lasting pain without trauma and other nonspecific symptoms, especially followed by a palpable mass. The treatment of EES is multimodal.

1. Introduction

Ewing sarcoma (ES) is a malignant tumour composed of small, round cells. It affects people of all ages, but most common it is seen in children and teenagers [1]. ES can occur anywhere in the body: bone (skeletal ES) or soft tissue (extra skeletal, extraosseous ES) might be affected [1,2]. However, ES rarely develops in soft tissue [3,4]. Extraosseous ES (EES) composes 16–31% of all ES [2,5]. The most common sites of EES are chest wall, paravertebral region, extremities, buttocks and retroperitoneum [4]. It is associated with rapid growth and distant metastases [1,4,6]. Metastases of the tumour most commonly occur in the lungs and bones [4]. Patients with ES usually experience localised, intermittent or variable in intensity pain [3,4,7]. The pain may be followed by visible or palpable mass of the affected site [3,4]. When diagnosed advanced or metastatic disease, symptoms such as malaise, weakness, fever, anaemia, nonspecific signs of inflammation, weight loss may be observed [4]. Nonspecific symptoms may mimic other diseases and sometimes leads to a long delay in EES diagnosis. EES even might be mistaken with traumatic haematoma [7].

Ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI) or positron emission tomography–computed tomography (PET-CT) can be helpful in the diagnosis of EES. CT scan shows a heterogeneous ill-defined tumour [4], displacing surrounding tissues, with necrosis and/or calcification [8]. ES demonstrates heterogeneous, low signal intensity on T1-weighted MRI images and high signal intensity on T2-weighted images, due to haemorrhage and necrosis [8]. However, the definitive diagnosis of ES is confirmed by biopsy of the lesion with histological, immunohistochemistry, molecular pathology examination [1]. The treatment of EES is multimodal. Surgery and/or radiotherapy with chemotherapy are the treatment of choice for local disease [6]. Complete excision of the tumour with clear margins is essential whenever feasible [3]. When complete surgical removal is impossible then radiotherapy should be performed [1]. In recurrent or metastatic disease, systemic chemotherapy may be used for improving the survival [6].

In line with the CARE (Consensus-based Clinical Case Reporting Guideline) criteria, we report a case of a 56-year-old woman with EES involving the right iliac fossa [9].

2. Case report

56-year-old female was admitted to the Emergency Room (ER) because of severe pain in the right lower quadrant lasting for one day. She had an abdominal trauma six months ago. After that she felt intermittent mild-moderate pain in the right lower quadrant and groin, irradiating to the right leg every night. Her past medical history was

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https://doi.org/10.1016/j.ijscr.2021.106708
Received 26 October 2021; Received in revised form 9 December 2021; Accepted 14 December 2021
Available online 31 December 2021

significant for hepatitis B. She had no history of bleeding disorder.

Physical examination revealed tenderness in the lower right side of the abdomen. Blood laboratory findings were within normal limits. Ultrasound examination of the abdomen showed a mass in patient's right iliac fossa. A computed tomography (CT) scan of the abdomen was performed. It demonstrated a 7,6x11cm heterogeneous mass in the right iliac fossa displacing the uterus, urinary bladder, rectum with suspected retroperitoneal haematoma. No extravasation was observed (Fig. 1). The patient was admitted to the Department of Surgery for further examination and treatment. A laparotomy was performed by a surgeon consultant and an 8x10cm mass was found in the right iliac fossa. Retroperitoneum was opened and the mass, composed of old blood clots, was removed. Histological examination revealed blood clots mixed with high grade malignant mesenchymal tumour fragments, mostly compatible to malignant gastrointestinal stromal tumour (GIST) according to immunohistochemical reactions. Tumour cells were small to medium-sized, atypical, with light nuclei and eosinophilic nucleoli, and ill-defined, lightly eosinophilic cytoplasm. Multiple mitoses were found. On immunohistochemical investigation tumour cells were strongly positive for CD117, moderately positive for Plasmin (without Kappa/Lambda restriction) and negative for DOG1, CD31, CD34, smooth muscle actin, CD138, EMA, CK18, CD23, CD25, PLAP, S100P, CD10, BCL-2, Inhibin, anti-TLE markers.

The patient's postoperative course was complicated by severe anaemia (haemoglobin - 56 g/l), which was successfully managed conservatively by the transfusion of two units of red blood cells. The patient's recovery was otherwise uneventful. Her case was discussed at Multidisciplinary team (MDT) conference. It was decided to start neoadjuvant treatment with imatinib mesylate (Glivec, Novartis, Basel, Switzerland) due to GIST diagnosis. Two months after the surgery and the treatment with imatinib mesylate (400 mg daily) control pelvic - abdominal MRI scan was performed. It demonstrated a heterogeneous, well-circumscribed 5.6 × 3.7 cm size mass in the right iliac fossa (Fig. 2). The treatment with imatinib mesylate was extended. In total the patient received treatment with imatinib for five months. Then control abdominal MRI was performed. The tumour radiologically looked minimally downsized (4.5 × 3.5 cm). After that the patient again underwent surgical treatment. During the laparotomy a well-circumscribed, capsulated 5.7 × 5.6 cm tumour was found in the right iliac fossa (Fig. 3). The tumour was lightly attached to the urinary bladder and to the right external iliac artery and vein. The tumour was completely removed without injury of adjacent structures. Histologic examination showed a tumour composed of small to medium-sized atypical cells with light nuclei and eosinophilic nucleoli, ill-defined, scant, lightly eosinophilic cytoplasm (Fig. 3). Tumour cells were with multiple mitoses, arranged in solid and alveolar pattern with small necrotic areas. On immunohistochemical investigation tumour cells showed a strong positive reaction with CD117, CD99, BCL-2, slightly positive reaction with Synaptophysin and negative reactions for CD31, CD34, EMA, S100P, smooth muscle actin, CD10. EWSR1 (22q12) gene translocation was found. According to these findings, extraosseous Ewing sarcoma diagnosis was made. The patient's postoperative course was uneventful. The patient was referred for further outpatient oncological treatment.

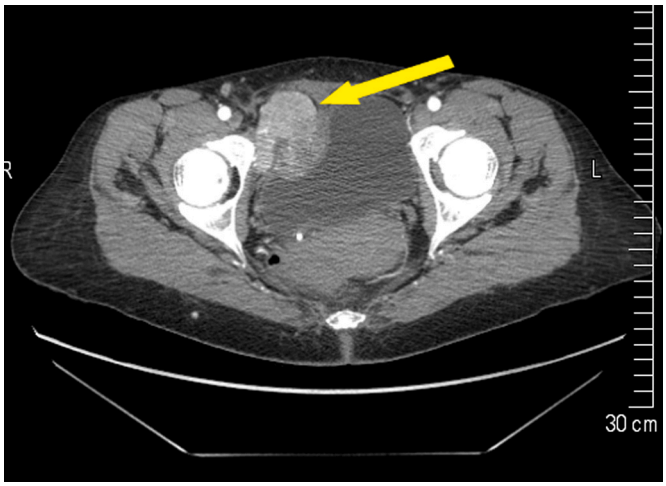

Fig. 1. CT scan showing a heterogeneous mass in the right iliac fossa.

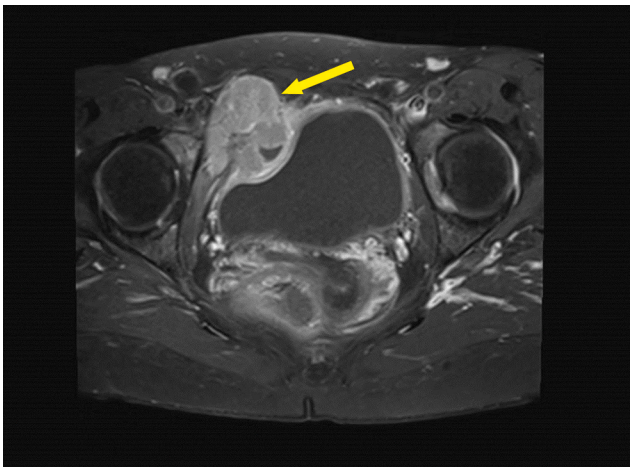

Fig. 2. MRI demonstrating a tumour in the right iliac fossa.

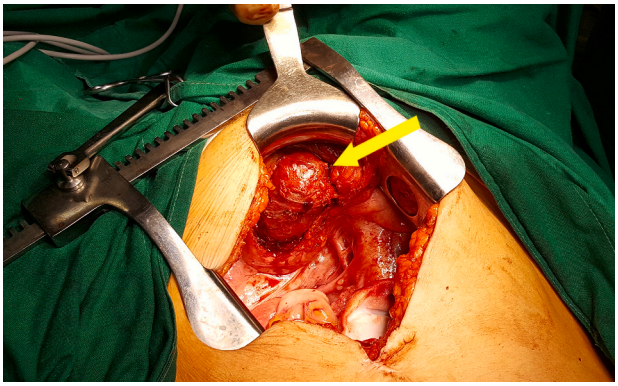

Fig. 3. Tumour in the right iliac fossa was observed.

3. Discussion

ES is an aggressive tumour often appearing in childhood and during the teen years [1]. It can develop in any part of the body [1,2], however, extraosseous localisation is rare [3,4]. ES has a tendency for rapid growth and a high incidence of distant metastases [1,4,6]. Symptoms and signs of ES are nonspecific and may include localised, intermittent or variable in intensity pain [3,4,7], visible or palpable mass of the affected site [3,4], malaise, weakness, fever, anaemia, signs of inflammation, weight loss, etc. [4].

The diagnosis of ES is complicated. Nonspecific symptoms may mimic other diseases and sometimes leads to delayed diagnosis. Ultrasound, CT scan, MRI or PET-CT scan can be used for diagnosis. However, imaging findings are nonspecific [3]. The definitive diagnosis of ES is confirmed by biopsy of the lesion [1]. Histologically this type of tumour is composed of small round cells [2,4], positive for CD99 [1–3] and often PAS positive [4]. ES is associated with gene EWSR1 located in chromosome 22 and FLI-1 located in chromosome 11 mutations [10].

We have experienced diagnostic difficulties as well. Our patient was

at unusual age for this disease and suffered nonspecific symptoms. Nonspecific heterogenous mass on radiological imaging, previous abdominal trauma with retroperitoneal hematoma have caused diagnostic difficulties. Moreover, during primary histological evaluation, malignant GIST diagnosis was made. Just after the second surgery, histological, immunohistochemical and genetic examination of surgical material, EES diagnosis was confirmed.

Other papers also describe difficulties of diagnosing EES due to lack of specificity of symptoms and radiological findings [11,12]. Challenging in diagnosis as well can be related to EES possibility to masquerade as a benign mass [13].

The treatment of choice for local EES is surgery and/or radiotherapy with chemotherapy [6]. Complete excision of the tumour with clear margins is essential whenever feasible [3]. Surgical treatment may be used to resectable metastatic tumours as well. Radiotherapy is used when the tumour cannot be removed completely during the primary surgery [1,14]. If after radiotherapy the tumour became resectable, surgical treatment may be used [14]. However, radiotherapy is associated with late side effects of high-dose radiotherapy, especially with second malignancy [6].

Chemotherapy plays an important role of EES treatment [6]. Usually, combination of several different types of drugs is used [14–16]. High dose chemotherapy [17], targeted therapy [18] and immunotherapy [19] also play a role in ES treatment.

The prognosis is overall poor [11]. However, EES overall outcomes are better compared with osseous ES [2]. Five-year overall survival for patients with ES is 61.5–70% [2,20].

Although, further studies in this area are needed to develop optimal treatment for EES [21].

4. Conclusions

The diagnosis of EES sometimes is complicated and delayed. Prompt detailed examination and imaging studies should be performed to people with long lasting pain without trauma and other nonspecific symptoms, especially followed by a palpable mass. The treatment of EES should be multimodal. When tumour is unresectable or surgical material margins are positive, then radiotherapy may be an option. Our case report shows that EES may require repeated surgical treatment and can be easily mistaken with other types of tumours.

Learning points

- The diagnosis of EES sometimes is complicated and delayed.
- EES though being a rare entity should be kept in the differential of retroperitoneal mass in children and adults.
- High index suspicion of EES is advisable when dealing with patients with long lasting pain or haematoma without trauma, and other nonspecific symptoms followed by a palpable mass.
- The treatment of EES should be multimodal. However, further studies in this area are needed to develop standardized EES treatment.

Sources of funding

None.

Ethical approval

Ethical approval was not required in the treatment of the patient in this report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

Not applicable.

Guarantor

Lina Pankratjevaite, Hassan Ali Eskandarani, Paulius Lizdenis and Zilvinas Saladzinskas are the guarantors of this submitted article.

CRediT authorship contribution statement

Lina Pankratjevaite – contributes to the study concept and design, data collection and writing the paper.

Hassan Ali Eskandarani – writing the paper.

Paulius Lizdenis - writing the paper.

Zilvinas Saladzinskas – critically revised article.

Declaration of competing interest

The authors declare no conflicts of interest.

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