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CASE REPORT

An unusual cystic presentation of pelvic skeletal Ewing sarcoma: a case series

Giuseppe Francesco Papalia[1,2] · Sisith Ariyaratne[3] · Jerome Sison[1] · Guy Morris[1] · Sumathi Vaiyapuri[4] · Vineet Kurisunkal[1] · Rajesh Botchu[3]

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Abstract

Ewing sarcoma (ES) is the second most common primary malignant bone tumour in children and adolescents. About 14.5% of primary malignancies develop in pelvic bones, where they typically have worse prognoses than extremity or acral sarcomas. It usually presents with aggressive features on radiology scans, but may also present with different radiological characteristics. In this series, we describe rare appearances of pelvic skeletal Ewing sarcoma, with large extraosseous cystic component on imaging, defined by the presence of fluid-filled spaces in the extraosseous tumour lesion, which distinguishes it from the solid nature of conventional ES. We report 3 cases of cystic presentation of ES, with imaging features supporting diagnosis of a primary malignant bone tumour arising from the superior pubic ramus with associated massive intrapelvic solid and cystic mass. CT-guided biopsy provided diagnosis of ES, with large intrapelvic soft tissue and cystic component. These patients underwent neo-adjuvant chemotherapy and proton beam therapy with significant reduction in size of the solid components, while the cystic components remained relatively unchanged. Two patients underwent surgical resection of the tumour (navigated P3 internal hemipelvectomy and hemipelvis P2/P3 resection, respectively), and one patient died while on treatment. In both who underwent surgery, histology showed ES with margins clear and more than 99% of treatment-induced necrosis. To the authors' knowledge, this unusual presentation of pelvic ES is described for the first time in the literature as a case series, with particular reference to atypical extraosseous cystic changes, along with the clinical and radiological characteristics, and their treatment.

Keywords Ewing sarcoma · Cystic tumour · Pelvic sarcoma · Case series

Introduction

Ewing sarcoma (ES) is a rare high-grade malignant primary bone tumour, characterised histologically by the presence of small round blue cells and exhibits a spontaneous genetic mutation determining EWSR1 rearrangement [1]. It is the second most common primary malignancy of bone that affects children and adolescents and arises from the cells in the bone or soft tissues [2]. It presents with aggressive radiological features, but may also present atypically [3]. About 14.5% develop in the pelvis. Despite significant improvements in treatment choices, pelvic bone sarcomas typically have worse prognoses than extremity or acral sarcomas [4]. In fact, pelvic sarcomas frequently manifest later, with higher volumes and metastases [5]. Wide surgical margins are challenging to obtain when resecting pelvic tumours because of their proximity to important nerves and blood vessels and the complexity of the pelvic bone anatomy. The 5-year disease-specific survival ranges from 41 to 66% for pelvic Ewing sarcoma [6]. Due to its aggressive nature, current treatments for ES require a multimodal approach consisting of neoadjuvant chemotherapy, followed by local control with surgical resection and/or radiotherapy (RT) [7]. Surgical options are represented by internal hemipelvectomy followed by endoprosthetic or allograft/autograft reconstruction and hindquarter amputation in cases of critical

✉ Giuseppe Francesco Papalia
g.papalia@policlinicocampus.it

1 Department of Orthopedic Oncology, Royal Orthopedic Hospital, Birmingham, UK

2 Research Unit of Orthopaedic and Trauma Surgery, Fondazione Policlinico Universitario Campus Bio-Medico, Via Alvaro del Portillo, 00128 Roma, Italy

3 Department of Musculoskeletal Radiology, Royal Orthopedic Hospital, Birmingham, UK

4 Department of Pathology, Royal Orthopedic Hospital, Birmingham, UK

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neurovascular involvement [8]. Surgical treatment is then followed by adjuvant multiagent chemotherapy [9]. There is also a significant incidence of both short-term and long-term complications following pelvic surgeries. The mortality and morbidity for such pelvic procedures account for 2–5% and 50%, respectively [10]. The common complications include wound dehiscence or necrosis, deep infection, aseptic loosening, dislocation, and mechanical failure of the implants. In certain situations, based on the clinical evaluation of the patient, the use of RT for local control may be preferred over surgery. In this series, we report 3 cases of a rare presentation of ES, characterised by the presence of a large cystic extraosseous component, defined by the presence of fluid-filled spaces in the extraosseous component of the tumour lesion. This aspect distinguishes it from the solid nature of conventional ES. The aim of this study is to describe this unusual presentation of these rare tumours, with analysis of the clinical and radiological characteristics, along with the management of these lesions. To the authors' knowledge, this case series represents the first description in literature of pelvic Ewing sarcoma presenting in this manner.

Case presentation

Case 1

A 15-year-old male presented with pelvic pain and preliminary radiographs supporting a diagnosis of a primary malignant bone tumour arising from the right superior pubic ramus with compression of the right external iliac vein. Initial MRI at presentation showed an osseous lesion demonstrating low to intermediate T1 and high T2 signal. There was a large associated mixed solid and cystic extraosseous mass centred in the pelvis, measuring 10.4 cm in maximum diameter. The solid components demonstrated intermediate signal on T1 and T2 weighted sequences, and fluid components were hyperintense to muscle on both T1 and T2, suggesting a haemorrhage/proteinaceous content within. Positron emission tomography (PET) revealed a markedly fluorodeoxyglucose (FDG) avid lesion (Fig. 1a–d), arising from the right superior pubic ramus (Fig. 1e), and a CT chest showed pulmonary metastatic disease. There was no metastatic disease elsewhere. A CT-guided biopsy of the intraosseous component of the suprapubic mass was performed, which revealed a diagnosis of Ewing sarcoma with a large intrapelvic soft tissue component. In particular, Haematoxylin and Eosin (H&E) stained histological examination showed cyst wall consisting of solid sheets of small round cells (Fig. 2a), while immunohistochemistry showed diffuse membrane positivity with CD99 (Fig. 2b). Fluorescence in situ hybridisation (FISH) analysis showed EWS gene re-arrangement, consistent with a diagnosis of ES. The patient started neo-adjuvant chemotherapy: synchronously the pulmonary metastases resolved, and the solid component of tumour has responded well but the cystic component remained, causing bladder outflow obstruction. Therefore, he started pre-operative proton beam therapy (PBT) 3 months later (after cycle 9 of chemotherapy). Post chemotherapy (Fig. 3a–c) and PBT (Fig. 4a–c), the solid components demonstrated significant reduction in size, with the overall size of cystic components remaining relatively unchanged. At 6 weeks post radiotherapy, he underwent a navigated right-sided P3 internal hemipelvectomy. Histology showed marginal excision of Ewing sarcoma with margins clear and more than 99% necrosis. Then, he underwent adjuvant chemotherapy and whole lung irradiation. At the last follow-up (at 7 months), he did not feel any pain or discomfort from his pelvis or right hip, and he walked very well and started running.

Case 2

A 36-year-old male presented with pelvic pain. Preliminary radiograph and CT showed a massive intrapelvic mass originating from the right superior pubic ramus, without evidence of metastatic disease. MRI at presentation demonstrated an intermediate T1 and high T2 signal lesion within the right superior pubis. This was associated with a large mixed solid and cystic extra-osseous component extending into the pelvis, with a maximum diameter of 16.2 cm. The cystic component was hypointense to skeletal muscle on T1, with no significant enhancement with gadolinium contrast; the solid components showed low T2 signal, with heterogeneous mild peripheral enhancement on post gadolinium contrast sequences (Fig. 5a–d). There was involvement of the right superior pubic ramus (Fig. 5d). H&E stain from CT-guided biopsy specimens showed solid sheets of malignant small round blue cells (Fig. 6). FISH analysis showed EWS gene rearrangement, consistent with a diagnosis of ES. The patient underwent pre-operative radiotherapy with a view for limb salvage surgery. Unfortunately, the patient died while on treatment.

Case 3

A 12-year-old male presented with left groin pain and left lower limb swelling. MRI demonstrated a lesion involving the left anterior acetabulum and superior pubic ramus, demonstrating low T1 signal and intermediate to high short tau inversion recovery (STIR) signal. There was an associated extraosseous solid and cystic mass in the left inguinal region with a maximal diameter of 5.6 cm. The cystic component was hyperintense on fluid sensitive sequences. The solid component demonstrated low to intermediate signal on both T1 and T2. The lesion was in close contact with

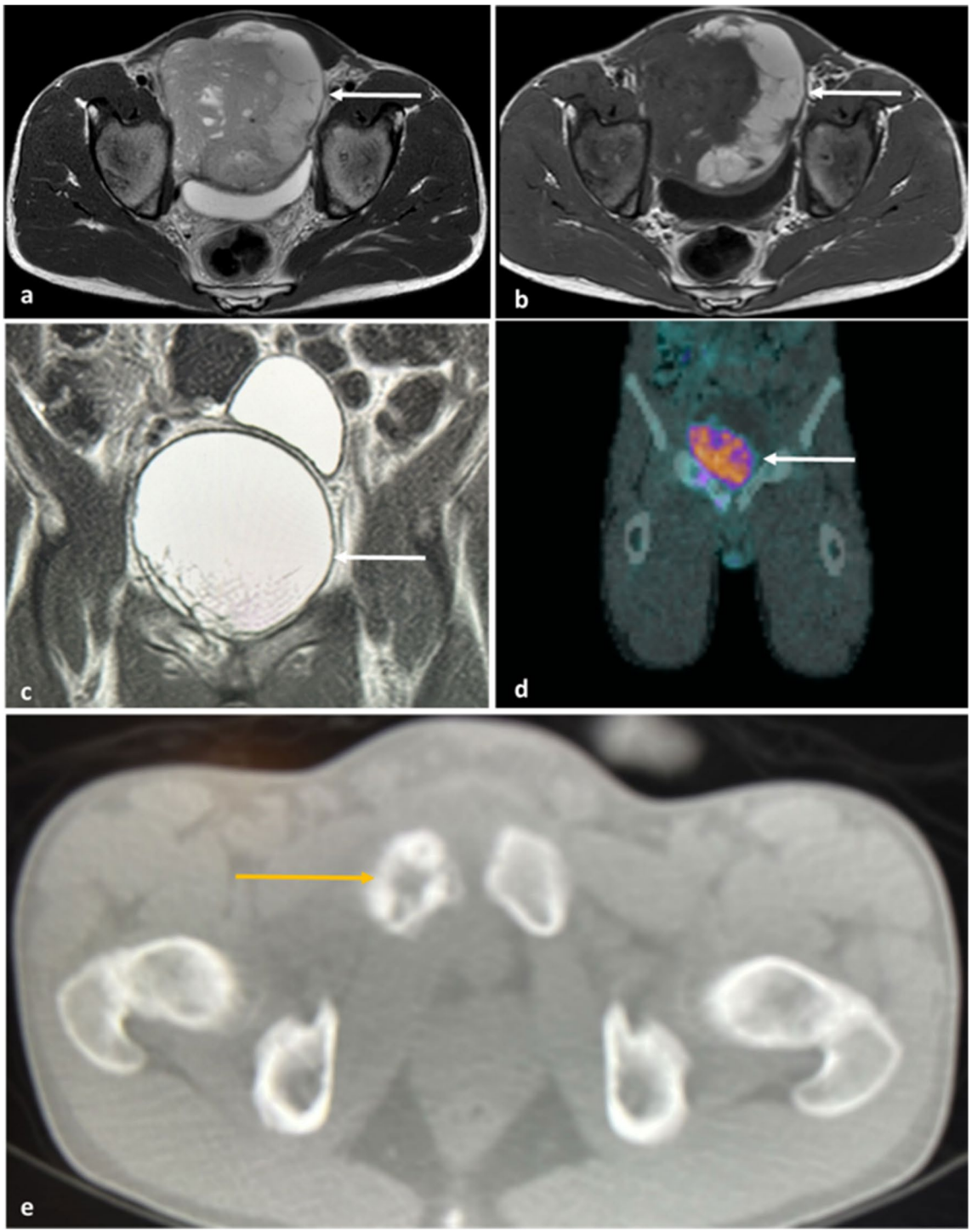

Fig. 1 Axial T2 (**a**), axial T1 (**b**), coronal T2 (**c**) and coronal fused PET CT (**d**) images demonstrating a large complex, mixed solid and cystic lesion in the pelvis with internal septa; the lesion is markedly FDG avid (*white arrows*). Axial CT bone window image (**e**) shows origin of the lesion in the right superior pubic ramus (*yellow arrow*). Increased FDG uptake also seen in the right superior pubic ramus on PET

the neurovascular bundle, resulting in an acute presentation with vascular compression due to venous congestion. A fluid–fluid level was present in the cystic component suggesting intralesional haemorrhage (Fig. 7a–d). After 2 weeks, a CT guided biopsy of the lesion was performed along with aspiration of the cystic component. The histology

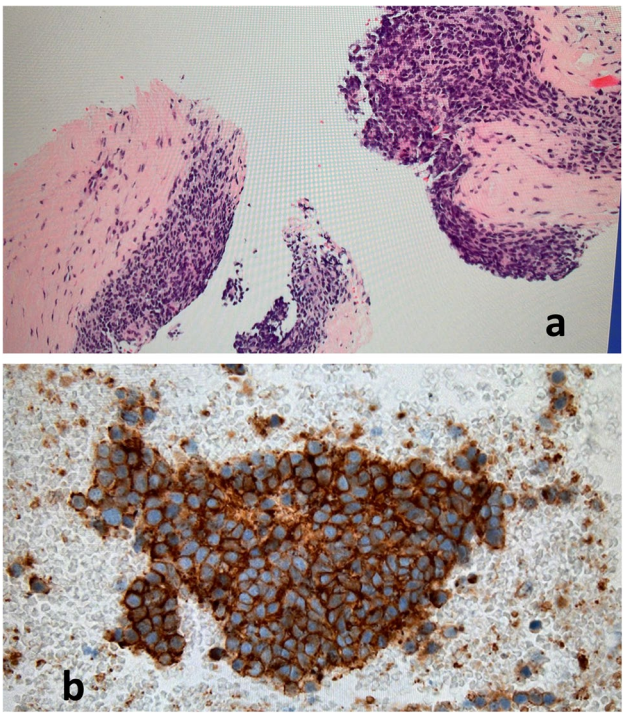

Fig. 2 Haematoxylin and eosin (H&E) stain histological examination shows cyst wall consisting of solid sheets of small round cells (**a**). Immunohistochemistry shows diffuse membrane positivity with CD99 (**b**)

showed a small round blue cell tumour. H&E stain histological examination showed haemorrhagic cyst wall consisting of clusters of malignant small round blue cells (Fig. 8). FISH analysis showed EWS gene rearrangement. Therefore, the diagnosis Ewing sarcoma arising from the anterior column left hip was made. The venous compression improved following aspiration of the cystic component. Initial CT chest was clear of metastatic disease. The patient underwent neoadjuvant chemotherapy with a dramatic response on follow-up MRI pelvis (moderate decrease of left superior pubic ramus Ewing sarcoma). Unfortunately, chemotherapy was repeatedly interrupted due to prolonged neutropenia and Clostridium difficile colitis. Once the bowel symptoms have resolved, pre-operative proton beam therapy was administered for 6 weeks. MRI post-PBT (Fig. 9a, b) demonstrated residual signal change in the adjacent pelvic and adductor muscles. After patient optimization, surgery was carried out 12 weeks following the end of PBT. A navigated resection was planned to excise the post-PBT volume only. The patient underwent left hemipelvis P2/P3 resection involving the left superior pubis ramus, anterior column left hip, followed by GraftJacket reconstruction (Regenerative Tissue Matrix) [11]. Postsurgical changes are demonstrated in the region on the final scan (Fig. 10a, b). Histology proved specimen of Ewing sarcoma showing over 99% of treatment-induced necrosis. The patient attended intensive physiotherapy following surgery. Finally, at 9-month follow-up, he did not feel any pain in his pelvis or left hip, and was mobilising.

Discussion

Ewing sarcoma can either present as osseous (intraosseous and periosteal) or extraosseous lesions. These tumours can have a variable morphology on CT, but usually appear aggressive, with permeative bone loss and pronounced periosteal reaction and sclerosis [12, 13]. Extraosseous solid soft tissue extensions are often seen, best delineated on MRI. The MRI signal characteristics of Ewing sarcomas are usually non-specific, with intermediate signal on T1 weighted sequences and intermediate to high signal on fluid sensitive sequences. The solid components can enhance following contrast [14].

While cystic appearances of extra-skeletal Ewing sarcoma are fairly well described in the literature [15, 16], significant cystic change within the extraosseous components of Ewing sarcoma of bone is not well described in the literature to the best of our knowledge, and as such, this can present

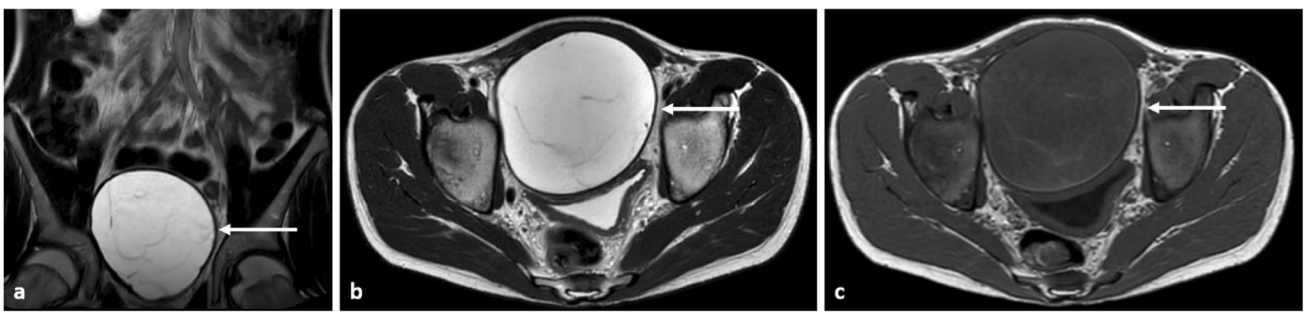

Fig. 3 Coronal T2 (**a**), axial T2 (**b**), and axial T1 post contrast (**c**) images of the same lesion 4 months later post chemotherapy. Note the large cystic component is still present (*white arrows*), possibly due to this representing necrosis. However, the solid component has substantially diminished

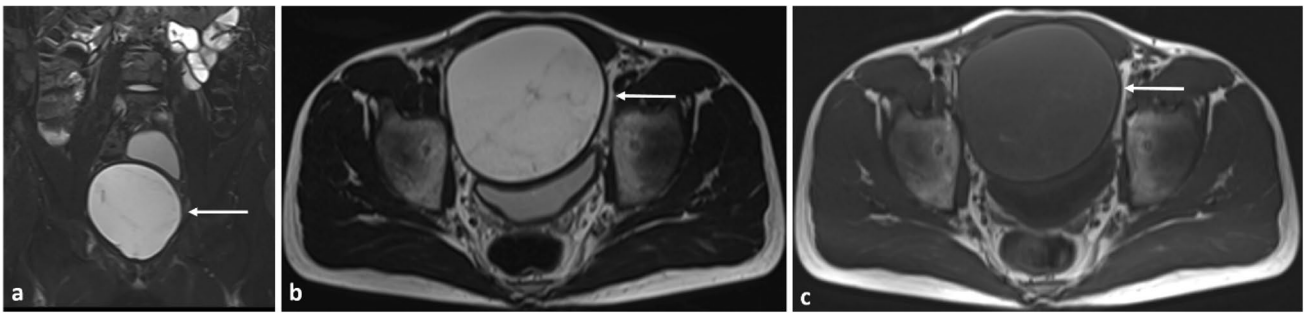

Fig. 4 Coronal T2 STIR (**a**), axial T2 (**b**) and axial T1 post contrast (**c**) images 6 months after initial presentation and post additional treatment with proton beam therapy. The size of the lesion and cystic component largely remains unchanged (*white arrows*). The enhancing septations also appear less conspicuous, suggesting further response

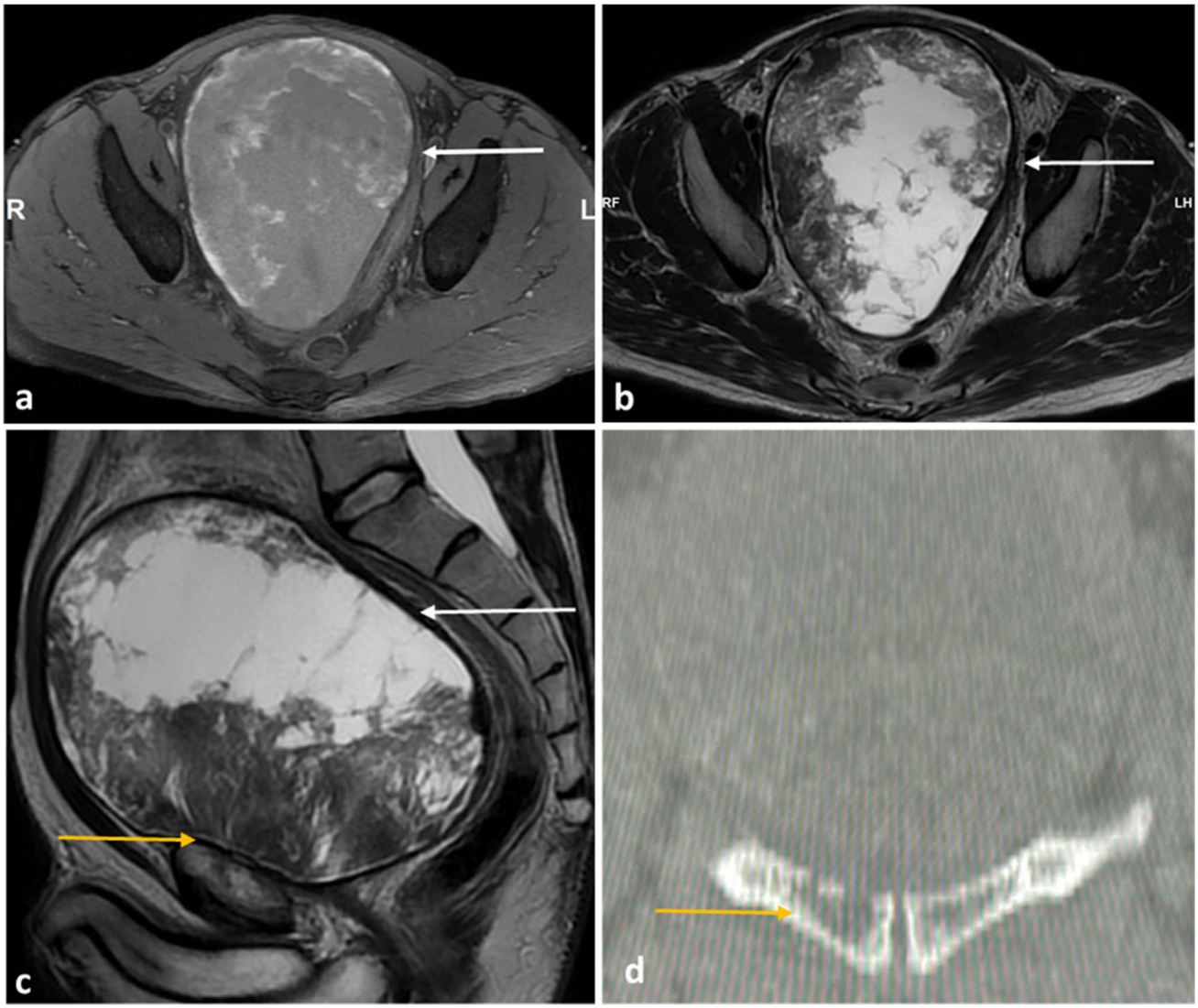

Fig. 5 Axial fat saturated T1 post contrast (**a**), axial T2 (**b**) and sagittal T2 (**c**) images demonstrating a large complex mixed solid and cystic tumour within the pelvis (*white arrows*), arising from the right pubis (*yellow arrow*, **c**). The solid components demonstrate enhancement on the post contrast sequence. Coronal CT bone window image (**d**) shows a lytic lesion in the right superior pubic ramus (*yellow arrow*, **d**) in keeping with an intraosseous tumour. There is significant displacement and compression of the adjacent pelvic viscera including the bladder

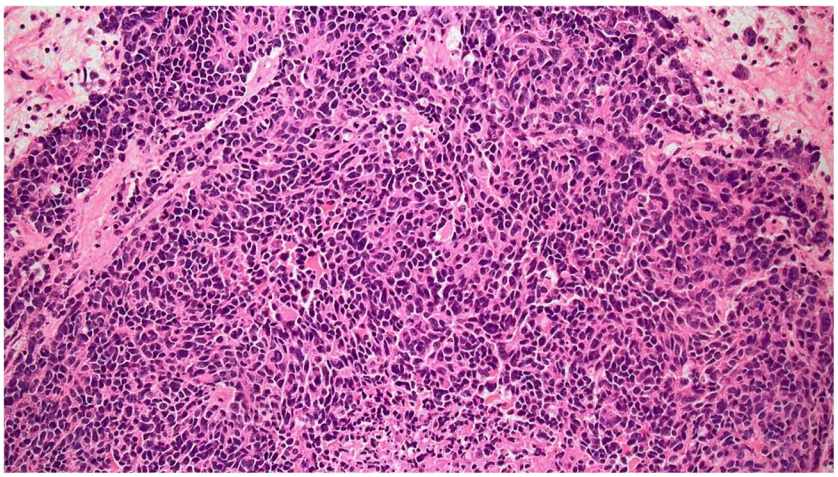

Fig. 6 H&E stain shows solid sheets of malignant small round blue cells

a diagnostic dilemma. These are not true cysts in a purely histopathological sense, i.e. are not fluid cavities lined by epithelial membranes, but rather appear "cystic" on imaging, particularly MRI. This could be sometimes due to a combination of necrosis and haemorrhage and/or proteinaceous content (noting in Case 1, the cystic component was T1 hyperintense suggesting haemorrhage).

Several reports of ES of bone presenting as cystic lesions are also described in the literature; Maheshwari et al. [17] described the case of a 27-year-old male with a pathologic fracture through a simple bone cyst-like lesion in the left distal tibial metaphysis. The fracture healed conservatively, but 1 year later, due to worsening pain, the lesion was curetted and grafted with allograft. Histology later revealed this to be Ewing sarcoma of bone. Papagelopoulos et al. [18] reported the case of a 14-year-old girl with imaging features suggestive of a benign cystic lesion of the left femoral head and neck. However, biopsy and molecular analysis revealed a diagnosis of Ewing sarcoma. These case studies however describe the cystic appearance of the primary intraosseous component of the ES, rather than the extra-osseous component which we describe here. Moreover, the cystic appearing extra-osseous component can be the dominating feature of the lesion in some cases, with the primary intra-osseous component being less conspicuous as was seen in our series. This can lead to difficulty distinguishing between an osseous malignancy such as Ewing sarcoma and other cystic neoplasms of the pelvis. It is important to carefully evaluate the adjacent bone so as not to miss this important diagnostic clue, as several other primary soft tissue malignancies, such as adnexal neoplasms in females, mucinous tumours and peritoneal mesothelioma can resemble them [19, 20]. Therefore, biopsy and histopathological examination are essential to establish the diagnosis of these sarcomas which have such peculiar radiological characteristics.

Treatment of Ewing sarcoma is usually a multimodal approach consisting of chemotherapy, RT, and surgery. Individualised treatment plans are developed focusing on factors such as tumour's size, location, and presence of metastasis. Moreover, the cystic nature of these tumours can also have important implications with regard to percutaneous image guided biopsy and surgical planning. The neo-adjuvant chemotherapy showed great results, leading to the resolution of pulmonary metastases and a significant reduction of the volume of the solid component of tumour. However, the cystic component seemed to have a lower response. This may be explained by the fact the cystic component is the result of necrosis and not active tumoral tissue. After chemotherapy, the most recent therapeutic schemes involve the use of PBT instead of conventional RT. PBT allows for further tumour shrinkage, with the ability to plan the excision for post-PBT volume only. In fact, wide excision of the tumour could be impossible due to the proximity of nerves, vessels, and pelvic organs. Therefore, internal hemipelvectomy, with or without reconstruction, allows for obtaining good clinical results, providing tumour excision with margins clear. Given the aggressive nature of Ewing sarcoma, the presence of extraosseous cystic components can increase the risk of tumour spillage during surgical resection, potentially increasing the likelihood of local recurrence.

On their most recent follow-up, patients in Case 1 and Case 3 are clinically well with no evidence of recurrences. The authors are confident about the strategic management plan provided for these patients, from their 1st presentation

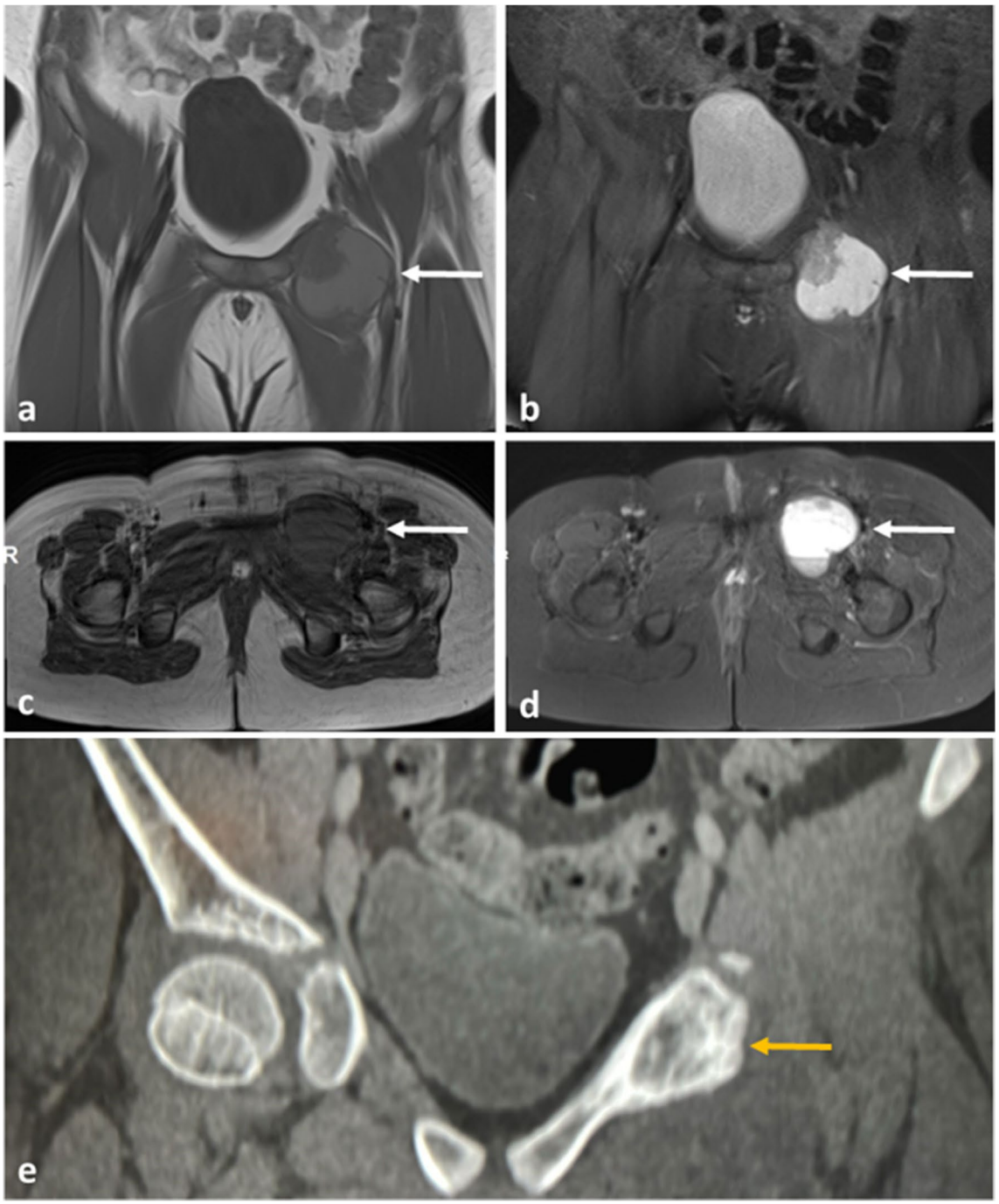

Fig. 7 Coronal T1 (**a**), T2 STIR (**b**), axial T1 (**c**) and axial T2 STIR (**d**) images demonstrating a mixed solid and cystic lesion in the left inguinal region, in close contact with the neurovascular bundle (*white arrows*). Layering fluid level is noted on the axial images. The lesion arises from the left anterior acetabulum and superior pubic ramus. Coronal CT bone window (**e**) demonstrates osseous origin of the lesion with involvement of the left superior acetabulum and superior pubic ramus (*yellow arrow*)

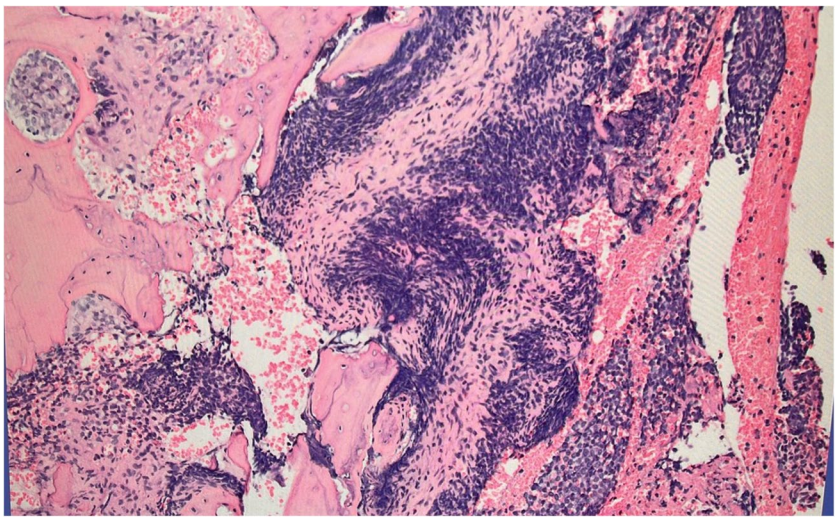

Fig. 8 H&E stain histological examination shows haemorrhagic cyst wall consisting of clusters of malignant small round blue cells

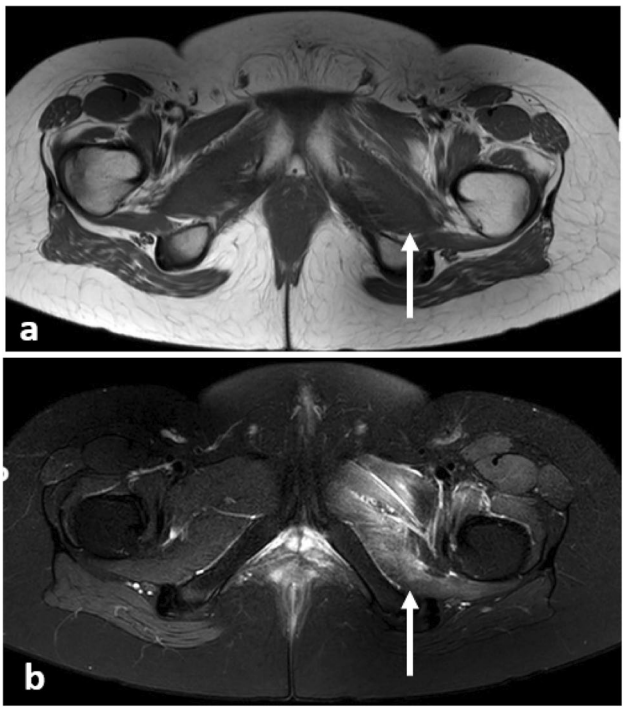

Fig. 9 Axial T1 (**a**) and T2 STIR (**b**) images of the lesion post CT guided biopsy and aspiration and proton beam therapy. There is residual signal change in the adjacent pelvic and adductor muscles (*white arrows*)

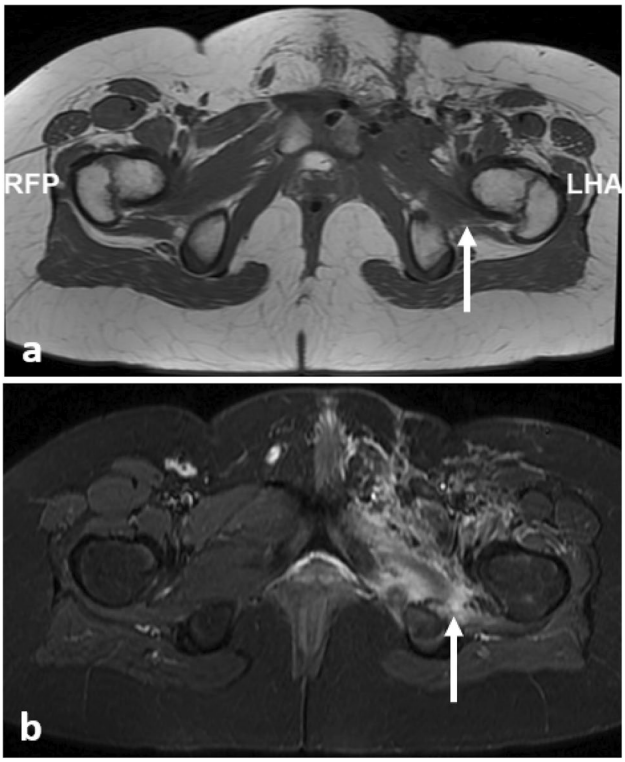

Fig. 10 Axial T1 (**a**) and T2 STIR (**b**) images post resection. Signal abnormality is noted in keeping with post-surgical change (*white arrows*). The left superior pubic ramus has also been resected

in the clinic, through the dilemma surrounding the radiologic and tissue diagnosis, the systemic and surgical treatment, and their ongoing sarcoma surveillance. We are hopeful that this case series can educate other institutions on the diagnosis and treatment of these unusual presentations of Ewing sarcoma of bone.

Declarations

Ethical approval All procedures performed in the study were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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