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A pelvic mass 21 years after a Wilms tumour: late recurrence or new tumour?

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Abstract

Introduction: Late Wilms tumour (WT) recurrences are rare events with poorly understood pathogenesis. They could be induced by previous chemo- and radiotherapy regimens, which can also prompt a rhabdomyomatous differentiation. Prostatic embryonal rhabdomyosarcoma (PER) is an extremely rare disease in adults, with an aggressive behaviour and abysmal prognosis. Radio-induced PER have been described.

Case description: We report the case of a 29 years old man, with a history of WT, diagnosed with a symptomatic prostatic mass. Blastemic elements were shown at the transrectal biopsy, suggesting the possibility of a late WT recurrence. After laparoscopic resection, an unexpected pathologic diagnosis was reached: PER.

Conclusion: We retrace and analyse the diagnostic and therapeutic path of the case that represents a mixture of two different conditions which might be unrelated or intertwined in a causal relationship. Among the differential diagnosis of a prostatic mass, the possibility of a prostatic sarcoma should not be overlooked, in presence of blastemic elements, even in a patient with a WT history.

Keywords

Wilms tumour, prostate embryonal rhabdomyosarcoma, radiotherapy-induced, sarcoma

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Introduction

Wilms tumour (WT) is one of the most common solid malignant neoplasms of the kidney in childhood, typically diagnosed in children <5 years of age. Despite the good response to multimodal therapy, consisting in surgery, chemotherapy and in selected cases radiotherapy, up to 20% of patients experience a relapse, especially in the first 2 years after the primary diagnosis. On the contrary, late recurrences, defined as more than 5 years after the initial diagnosis, are extremely rare and their pathogenesis is poorly understood. The lung is the most common site of relapse, whereas pelvic relapses are rare, occurring in about 10% of cases.[1] To our knowledge, no reports have been published on prostate late WT recurrences. The differential diagnosis of a prostatic mass in these cases could be challenging, especially when the pathology reveals a highly undifferentiated tumour. Can this tumour be considered a late relapse of the primary WT, possibly induced by chemo-radiotherapy, or could it be, on the other hand, a 'de novo' growth? We describe the unusual case of a periprostatic mass discovered in a young adult 21 years after the diagnosis of the primary WT.

Case description

In 1992, a 10-years old patient was diagnosed with a 12-cm WT of the right kidney invading the vena cava, for which he underwent radical nephrectomy (stage II) and adjuvant chemotherapy and radiotherapy. Two years later, he developed

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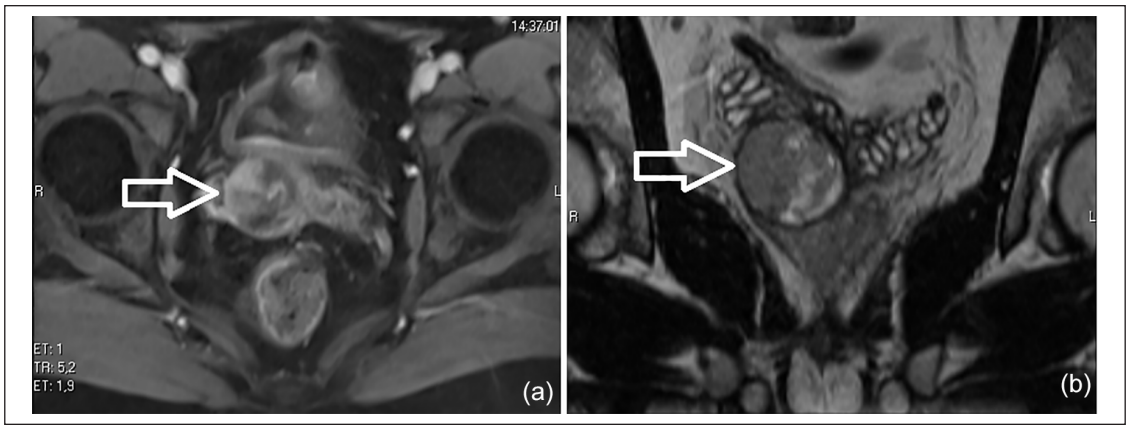

Figure 1. (a, b) CT scan showed a necrotic mass of 34 mm in contact with the prostate and the right seminal vesicle.

lung metastases treated with further chemotherapy including intensification with PBSC infusion, which achieved a complete response. The patient maintained a healthy status in the years after treatment, without evidence of relapse. Twenty-one years later, this patient came to our attention complaining of LUTS, haematuria and intermittent fever. At DRE, the prostate was tender and mildly aching. Despite treatment with wide-spectrum antibiotics, the symptoms persisted and the patient experienced an episode of acute urinary retention, needing a bladder catheter. A CT scan was performed revealing a necrotic mass of 34 mm in diameter in contact with the prostate and the right seminal vesicle (Figure 1). A subsequent MRI could not clarify the nature of the mass, prompting a transrectal biopsy. The biopsy revealed the presence of necrotic blastemic cells and a pathological pattern which suggested a correlation with the previous WT. A laparoscopic resection of the mass was planned. Unfortunately, the mass was not cleavable from the right prostatic lobe, a fact that required a radical prostatectomy, left sparing on the left side. The postoperative course was uneventful. The pathological diagnosis of the mass, which measured 35 mm × 30 mm (Figure 2), was really challenging. Microscopically, the tumour was composed of undifferentiated intermediate size cells with a very high mitotic index (>50/10 HPFs) (Figure 3(a)). An extraprostatic extension and vascular embolism were also observed (Figure 3(b) and (c)). Immunohistochemical staining was negative for CKAE1-AE3, CK7, CK20, PS100, ERG, chromogranine A and caldesmon. The CD56 was positive but not specific, while focal positivity was shown for CD34 and P63 (indicating persistence of basal cells in the gland). An initial pathological diagnosis defined the mass as a malignant tumour, but did not suggest a link to the earlier WT diagnosis made during patient's childhood. A second, more complete pathological examination of the sample, classified the mass as a prostatic embryonal rhabdomyosarcoma (immunohystochemical stains positive for desmin and myogenin). No PAX3-FKHR translocations were found, ruling out the possibility of an alveolar rhabdomyosarcoma. Completed the diagnosis, the patient underwent a second CT scan to re-evaluate the evolution of the disease. Unfortunately, exceedingly fast progression was revealed, with metastases affecting lungs, liver, bone, peritoneum and both the ischiorectal fossae. After multidisciplinary consultation, given the patient's age and good performance status, a doxorubicin, dacarbazin, ifosfamide and vincristin chemotherapy regimen was started. After 2 years the patient died for progression of the disease.

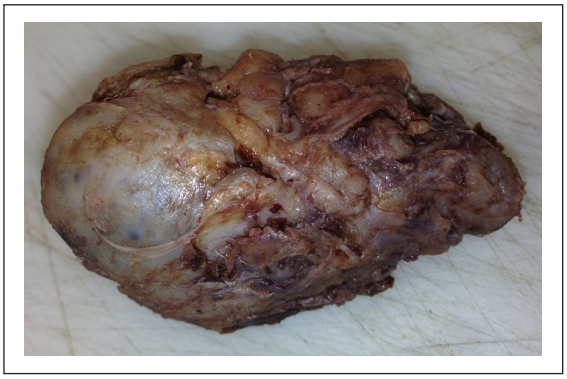

Figure 2. Macroscopic features of the mass.

Conclusion

At present, the improvement in chemo- and radiotherapy regimens have led to 85%–90% overall cure rate in low stage WT at 5 years.[2] The relapse rate has decreased to 15% and 50% in patients with favourable and unfavourable histology, respectively.[3,4] Although approximately 90% of recurrences occur in the first 2 years after diagnosis and the remainder in the next 2 years, several cases of late WT recurrence have been described, up to 25 years after initial treatment.[2] However, even relapsed tumours can be salvaged: among patients with favourable histology WT, 3-years survival rates are significantly lower after recurrence in the abdomen (28.7%) than after relapse confined to the lung (44.5%).[3,4] The pathogenesis

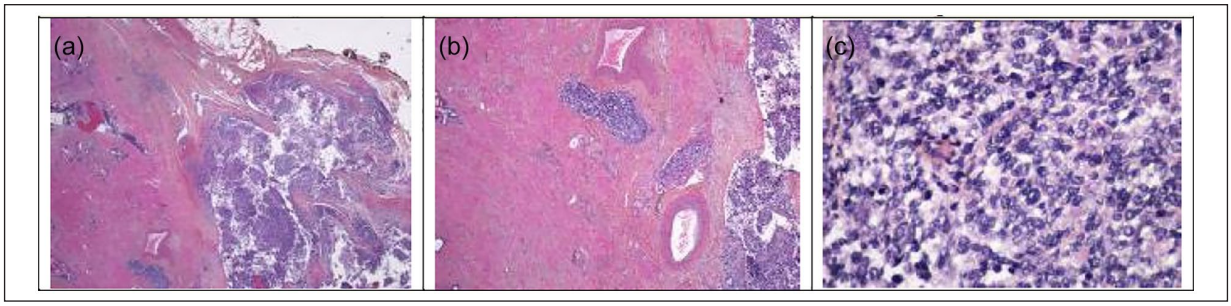

Figure 3. (a–c) Histological features of the blastemic cells with high mitotic index with extraprostatic extension and vascular embolism.

of these rare recurrences is poorly understood, although several hypotheses have been formulated, including escape from immune surveillance or presence of nephrogenic rest.[1] Aggressive, blastematous WT can be resistant to treatments; on the other hand, chemotherapy may induce differentiation along the epithelial or mesenchymal lines in WT (skeletal, muscle, cartilage, or adipose tissue).[3] Previous radio-therapy may also play a role in the pathogenesis of late WT recurrences, causing a delay in the biological activity of the cells, which escape from the host's immunological surveillance system.[4] Given the presence of necrotic blastemic cells in the mass discovered in our patient, we were leaded to treat it as a late WT recurrence, induced by the previous radio-chemotherapy regimen. The intra-operative decision to perform a radical prostatectomy, due to the absence of a cleavage plane between the mass and the prostate, was a difficult one to make, given the patient's young age, but it became necessary to achieve a radical resection of the tumour. The final pathological diagnosis was unexpected. Previous experiences have highlighted cases of late WT recurrences with rabdomyosarcomatous differentiation, a fact that seems to indicate that treatment of the primary WT, designed to eradicate blastemic cells, could induce maturation of cancer cells along the epithelial and mesenchymal lines.[5] Anderson et al.[6] found rhabdomyomatous differentiation after chemotherapy in 61% of surgical specimens in bilateral WT suggesting that chemotherapy may play a role in promoting myogenic differentiation of immature Wilms tumour components. Our pathological diagnosis, however, pointed to a prostatic embryonal rhabdomyosarcoma (PER), not correlated with the WT. Therefore seems not to be correlated with the previous WT, but rahter a real 'de novo' growth. However, the etiopathogenesis of this second tumour could be linked to the radiation treatment the patient had undergone for the WT: post-radiation sarcomas are possible, as well as chemotherapy-linked sarcomas are a well known phenomenon.[7]

PER is almost anecdotal in adults and has a very aggressive behaviour: it is usually characterized by extensive locoregional spread, with symptoms of urinary obstruction and a tendency to metastasize by blood stream and regional lymphatics and to give early lung and bone involvement.[8]

The histogenesis of PER is not clear: cancer cells have a tendency to grow from undifferentiated mesenchymal cells, which in the distal urogenital tract surround the mesonephric duct and become incorporated into the bladder and prostate during embryogenesis.[9] These cells, which have the capacity for rhabdomyoblastic differentiation, can persist in a dormant state for years, and this may explain the growth in adults of second tumours.

Our patient experienced the same clinical presentation and natural history described in the literature for PER, showing fast progression of the disease. Could the delayed diagnosis have negatively affected treatment choices in our patient? According to the literature, in the case of a localized PER[9]: radical surgical removal of the tumour mass should be performed, as it was in our case. Even if locally treated, however, PER unfortunately shows a poor prognosis, despite radical treatment. A multimodal approach, with a combination of surgery, radiotherapy and chemotherapy, has been suggested to improve the outcomes, even if treatment guidelines are lacking due to the rarity of this disease.[8] The multidisciplinary approach seems to be the best in management of PER; in our case it helped to define the best adjuvant treatment strategy suitable for the patient, in the intent of improving his survival. This case report represents a rare case of co-existence of two different and rare oncological diseases: a WT during childhood and a PER in the same patient as an adult. In this case the two conditions were not correlated, although this could have been possible in principle. The possibility of a primary prostatic sarcoma in a patient with a prostatic mass with blastemic cells, should never be overlooked, even in cases of patients with a history of WT. A multidisciplinary approach, the availability of a skilled pathologist, associated to the novel EU-supported Network ERN eURO-GEN, a multidisciplinary international platform to discuss in the near future such complex and rare cases as the one reported in this paper,[10] are key for correct management of this challenging and rare clinical condition.

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