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Extrarenal Wilms' Tumour of the Ovary

A case report

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Abstract

Wilms' tumour (nephroblastoma) is the most common abdominal malignancy in children. Extrarenal Wilms' tumour (ERWT) is rare, with limited reports in the literature. Hereby, we report a case of unilateral ovarian Wilms' tumour, which was diagnosed initially by closed biopsy and confirmed later by histopathology study of the excised tumour. We are discussing the unusual location and presentation of Wilms' tumour and showing the medical challenges in both the initial clinical impression and the pathological diagnosis. Demonstrating therapeutic plans and showing the good outcome achieved by using the classic renal Wilms' tumour therapy protocols.

Keywords: Extrarenal tumour; Wilms' tumour; nephroblastoma; Ovary; paediatric tumour.

Introduction

Wilms' tumour (nephroblastoma), is the most frequently occurring abdominal malignancy of childhood: comprising more than two-thirds of paediatric renal masses in the first 5 years of life.[1] Extrarenal Wilms' tumour (ERWT) is rare with occasional reports.[1, 2, 3] The estimated incident rate of Extrarenal Wilms' tumour is almost 0.5 to

1% of all cases of Wilms' tumour. [2,3,4] Common reported location of Wilms' tumour outside the kidney included: retroperitoneum, inguinal canal, scrotum, and vagina. [4] Misdiagnosis for other common retroperitoneal masses of that region is not uncommon. [1]

Case Report

A two-year-old girl was admitted for evaluation of abdominal mass with a history of two months of poor appetite, night sweat, fever, and undocumented weight loss . The initial abdominal and chest CT revealed a large well-defined heterogeneous soft tissue mass occupying most of the abdominal cavity. The mass measured 13.5x10.5 cm with few specks of calcification. It encased most of intra-abdominal vessels, including the upper abdominal aorta and renal arteries; the anterior wall of the inferior vena cava is not well demarcated, likely obstructed by the mass. The Kidneys were displaced posteriorly with moderate obstructive hydronephrosis with reduced enhancement. The bowel loops were displaced laterally. There was moderate right pleural effusion and small effusion on the left without pulmonary metastasis or nodules (Fig.1).

The child was admitted to Pediatric Intensive Care Unit (PICU) with severe respiratory distress and highly suspected bacterial ascites. The child was treated with broad-spectrum antimicrobials. Ultrasound-guided emergent stents were inserted bilaterally in the lower pole of each kidney and core biopsy was taken from the periphery of the mass. Basic Laboratory screening tests showed hypercalcemia (serum calcium 3.8 mmol/L); so intravenous furosemide and maximum hydration therapy were delivered.

Tissue Histopathology showed a malignant blue round cell tumour with the positive immunohistochemical stains to WT1 and CD99, focally positive for AE1/AE3. The tumour cells were negative for LCA, CD3, CD20, TDT, BCL-2, NB84, Synaptophysin, Chromogranin, NSE, MYOD1, and desmin. Slides were sent abroad for a more expert opinion (Fig 2).

Based on radiological findings and histopathology reports, our initial clinical impression was a peripheral neuroectodermal tumour (PNET) or desmoplastic small round cell tumour (DSRCT) with less likely Wilms' tumour. As the child's condition

was critical, without any delay in waiting for histopathology expert opinion, the first cycle of chemotherapy based on Ewing /PNET (VDC/IE)- COG AEWS 1031 protocol-regimen A was started.

After one cycle of chemotherapy, the final expert histopathology report came as poorly differentiated malignant neoplasm consists mainly of the rounded cells with limited amounts of amphophilic cytoplasm and irregular vesicular nuclei. The neoplastic cells show diffuse nuclear positivity for WT-1 as well as multifocal striking positivity CD-99. The appearance would fit well with Wilms' tumour, blastemal – predominant.

In light of the final histopathology report, the medical decision was to change the treatment protocol to High-Risk Wilms' tumour AREN0321-UFH. Basically, the child received 13 cycles of chemotherapy as per the protocol. The treatment was interrupted for some time due to prolonged neutropenia for a total of one month but at different time points.

Post week 13 of chemotherapy, abdomen, and chest CT assessment showed interval resolution of pleural effusion. There was a regression of lower abdominal mass, measuring 5x4.5x3.4cm with specks of calcification. The abdomen mass was anterior to iliac vessels, and the bowel displaced away from the tumour, with no vascular or bowel encasement. The small extension around the left renal hilum also regressed in size. This lesion abuts the renal vessels but no encasement or invasion. The kidneys were normal with no focal lesions, with mild residual dilation of collecting systems as before (Fig 3). After this scan, she underwent debulking surgery. Findings during surgery, the tumour originates from the left ovary as a continuation of the left fallopian tube adherent but looks like a minimal invasion to the sigmoid colon and the dome of the bladder wall. Also, the right ovary looks pathological. The left ovary was excised with salpingectomy and appendectomy and biopsies from the right ovary and the tissue around the tumour was taken. Abdomen CT assessment post-surgery showed interval resection of the lower abdominal mass and no apparent tumour residual.

Tumour and tissue biopsies' histopathology of left ovary and fallopian tube revealed

residual of small round blue cell tumour constituting around 7% of the examined sample, in a background of chemotherapy-related changes. These residual tumour cells were positive for WT1, CD99, and focally for EMA. The immunophenotypical features were consistent with extrarenal (ovarian) Wilms' tumour, mixed type (pre-treated, intermediate risk). There was no evidence of anaplasia in the residual tumour. The percentage of necrosis was 93% of the whole examined tissue. Few defects were seen in the ovarian capsule; these show chemotherapy-related changes but no viable residual tumour. All resection margins were free of viable tumour. There was no evidence of vascular invasion. No teratomatous elements were present. The right ovary had chemotherapy-related changes and negative for tumour.

Eventually, the child completed the chemotherapy plan and received whole abdomen radiotherapy (12 Gy in 8 fractions) as per the protocol. The end of the treatment assessment showed a normal chest appearance with no evidence of tumour residual or disease recurrence.

Currently, the child is on regular follow- up for tumour surveillance on her second-year post-therapy follow-up, doing well without any concern.

The patient's parent informed consent for publication of this report was obtained.

Discussion

Extrarenal Wilms' tumour (ERWT) (nephroblastoma) is defined when the tumour meets two criteria: histologically confirmed nephroblastoma and extrarenal location. ERWT is rare in adults and children, with scarcely reported cases. [5]

ERWT develops in the retroperitoneum in males, and in the inguinal area in females. In reference to the literature, there is no specific manifestation of extra-renal Wilms' tumor. [5] In a discussion of 34 cases of extra-renal Wilm's tumor, Coopes et al**. (1991)** highlight that stage I contributed to 30%, II to 10%, III to 57%, and IV to 3% of all cases.[6] In our case, the tumour was located in the unilateral ovary, which is not a commonly observed location for ERWT. Besides, it presented in the advanced stage with the presentation of the ascites and pleural effusion. There are so far 11 reported cases with unilateral ovarian extrarenal Wilms tumour. [7]

In Turashvili et. al, (2020) review of the reported cases of primary ovarian Wilms tumour showed that the mean age was 22 (range 1-56). Moreover, the most frequent clinical symptom at presentation was abdominal pain (n=8 patients). The median tumour size was 13 cm (range 2.5-18), and all tumours were unilateral. Only four out of eleven reported cases of ovarian Wilms' tumour were treated with chemotherapy. No recurrences have been reported in any of the eleven patients. [7] Our reported case fall within the reported age range (2-years old) and tumour size range (13.5 cm). Our reported case presented with abdominal pain and unilateral ovarian mass. She was treated with high-risk Wilms' tumour chemotherapy protocol and is currently on her second year of follow- up.

The exact embryonic origin of extrarenal Wilms' tumor is uncertain.[1, 4] It is conflicting with reasonable hypothesis including origin from ectopic metanephric blastema or from primitive mesodermal tissue.[1] The popular theory was based on the Connheim's cell rest theory, which explained that persistent embryonal cells are likely to undergo malignant transformation at any point in time.[4]

It is well known that extrarenal Wilms tumour does not show characteristic radiological features. [5] This was the case in our patient; hereby we would like to stress not to rely solely on radiological reports when deciding the treatment plan for obscure abdominal mass in children. The histopathology diagnosis is encouraged at least with ultrasound-guided biopsy. Accurate diagnosis and then appropriate therapy are based on histology report after tumour removal. It is important to emphasize the significance of having a second opinion with other experts if there is any doubt in the histopathological findings, so the most effective and appropriate therapy can be applied. The Therapy should not be initiated without proper histopathology report, with exceptions when there are clinical emergencies. In our case, we used the most related therapy based on the provisional report until the final and accurate histopathology report was received.

According to Shojaeian et al. (2016), out of 87 reported childhood ERWT cases, favorable histology was observed in most cases. This made the prognosis better in ERWT compered to the classic Wilms' tumour with the same stage and histology.[2] In

our case, the predominant component was the blastemal type, which has a poor prognosis and puts the patient at high-risk protocol.

Molecular studies were not done due to cost limitations and the unavailability of specialized laboratories providing such services. The Immunohistochemical studies helped us to reach for the diagnosis. ETV4 was negative in this case making CIC-related sarcoma unlikely. PHOX2b, which is very specific for neuroblastoma, was negative in our case. Importantly, our case was negative for desmin and EMA, and that eliminates the likelihood of desmoplastic tumour. CD99 is a very non-specific marker with lots of antigen cross-reactivity, and in Ewing sarcoma we expect it to be strong and diffuse unlike the weak patchy positivity in this case. Hence, the absence of other markers and positive findings for WT1 confirms the diagnosis of Wilms' tumour.

Moving to the treatment plan; it depends on the renal Wilms' tumour protocol by using chemotherapy and radical surgery plus radiotherapy if indicated. [2,5,6] The therapeutic steps following the surgical excision depends on both the tumour stage and the histological finding. [2] In this presented case, total excision of the ovary invaded by the tumour, full inspection to any suspected tissue and removal of any enlarged lymph nodes were performed. This step was being conditioned by the Children Oncology Group (COG) chemotherapy plan, followed by adjuvant chemotherapy and focal radiotherapy to the abdomen. The lastly mentioned treatment approach was adopted duo to the previous history of ascites, the closed biopsy at the diagnosis phase, and the blastemal type of histological component.

The chemotherapy- radiotherapy modality of treatment may cause injury to the hypothalamic-pituitary (HPT) gonadal axis and impair gonadal function especially if used for abdominal radiation[8]. However, the radiation risk is dependent on treatment volume, total dose, fractionation schedule, and age at treatment. It was found that higher than 18 Gy radiation does result in effects ranging from altered pubertal timing to complete ovarian failure [8]. Our case required as per COG protocol, 12 Gy focal abdominal radiations. Permanent ovarian failure occurs mainly in childhood cancer patients who are treated with radiation doses > 20 Gy. What was found to be useful is an ovarian transposition to a region that is lateral or medial to the planned radiation

volume as this may preserve ovarian function in young girls. [8]

For therapy outcome, the two-year event-free survival of the reported ERWT cases was almost 85% and the mortality rate was 5%, which are approximately similar to renal Wilms' tumour outcome. [2] About our patient, she has completed her first year of regular follow-up with a good outcome and no active issue or any consequences to be reported so far.

Conclusion

Though extrarenal Wilms' tumour can be difficult to diagnose preoperatively, it should be considered in the differential diagnosis list approaching any asymptomatic abdominal mass. Furthermore, as there is neither typical clinical presentation nor specific radiological findings, the diagnosis is based on a pathology report from the excised tumour.. The recommended therapy plan for ERWT is similar to that of renal Wilms ' tumour therapy plan..

Authors' Contribution

KAA, AS and NM drafted the manuscript. SS provided the radiological images and handled the radiological part of the manuscript. ZIA provided the histopathology images and handled the histopathological part in the manuscript. KH reviewed the manuscript and provided critical feedback. NM revised and edited the manuscript. All authors approved the final version of the manuscript.

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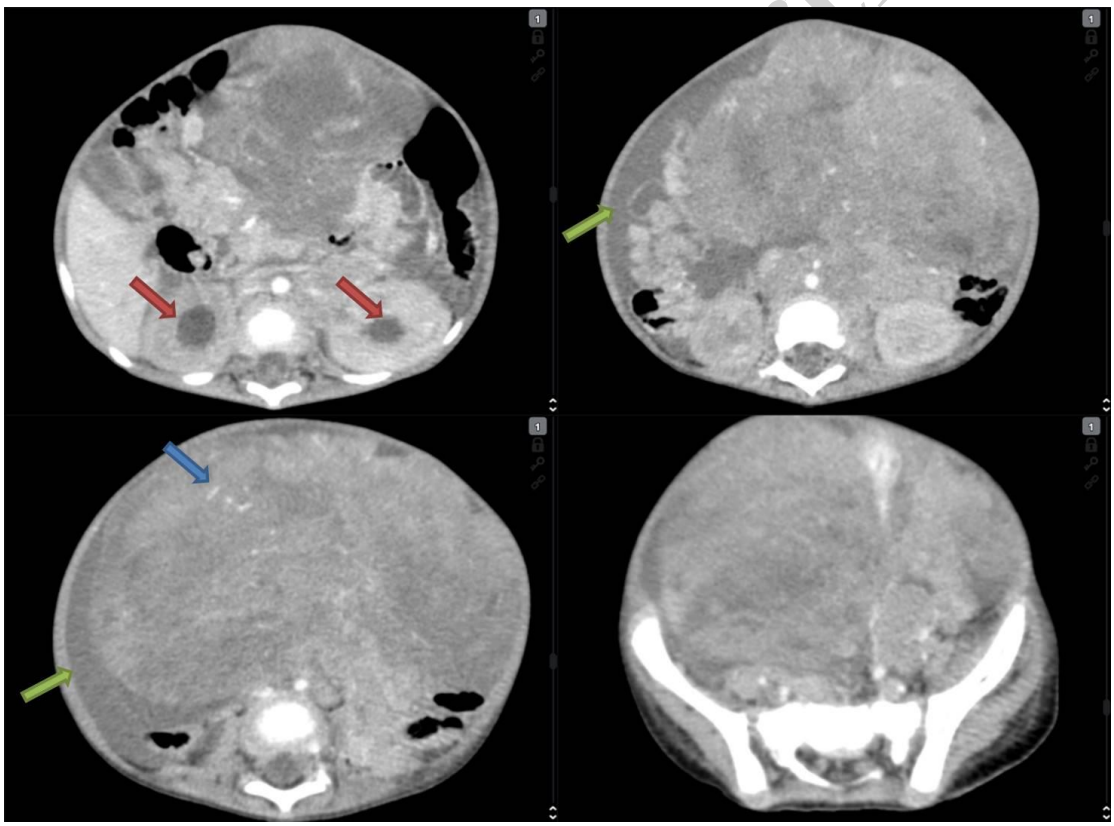

Figure 1: Axial images of contrast enhanced CT abdomen show large intra-abdominal soft tissue mass with heterogenous enhancement and intra-lesional enlarged blood vessels (Blue arrow). It surrounds major abdominal vessels. There is secondary obstructive bilateral hydronephrosis (Red arrows) with reduced renal parenchymal enhancement (Images A and B) denoting long-standing obstruction nephropathy. Ascites is also present (Green arrow).

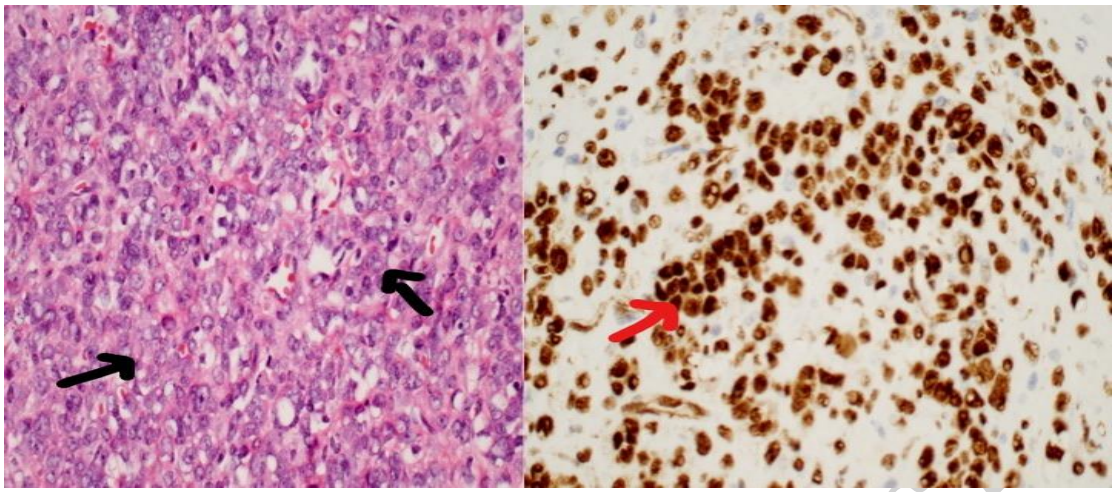

Figure 2: Sheets of small to medium-sized undifferentiated cells with hyperchromatic nuclei and scant eosinophilic cytoplasm (Black arrows). The tumour cells show diffuse nuclear positivity for WT1 (Red arrow, brown staining).

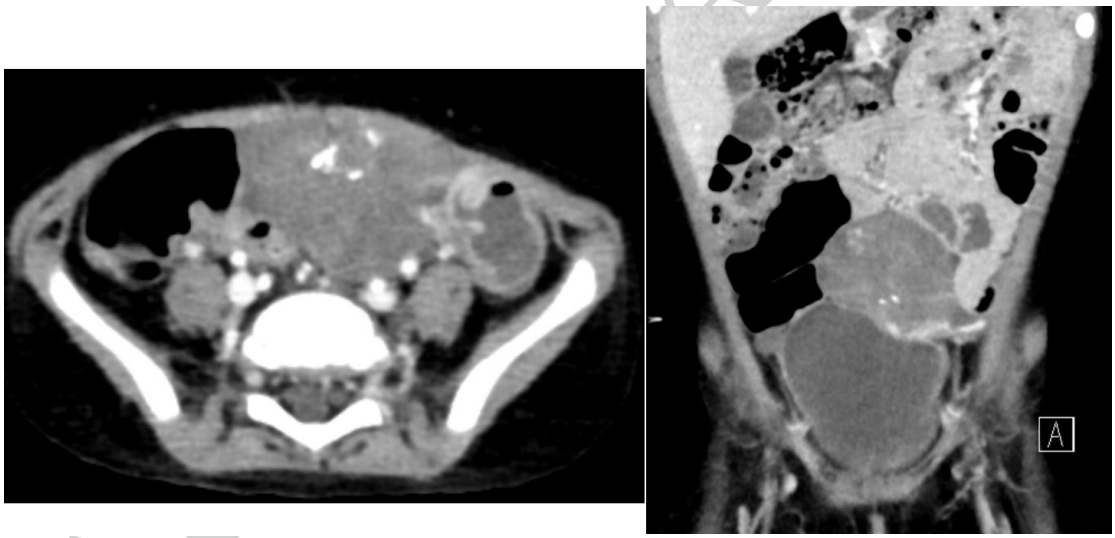

Figure 3: Follow up abdomen CT showed significant response manifested as reduction in size and consequent mass effect on kidneys.