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Adult Wilms tumour: A case report

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Abstract

The Wilms tumour is the fourth most common paediatric malignancy. On the contrary, it is extremely rare in adults as it accounts for less than 1% of all renal malignancies. This scarcity of cases placed a significant challenge in generating evidence-based treatment. Hence, treatment of adult Wilms considerably varies between centres. Standardised guidelines based on international expert consensus for adults have been introduced to help steer management. However, reporting patient outcomes remains limited. In this article, a case study will be presented. This includes modalities of treatment, side effects, tolerability, and outcome. A 40-year-old gentleman with histology consistent with the Wilms tumour received adjuvant chemotherapy according to the UMBRELLA SIOP2016 adult guidelines. Such guidelines were originally adapted from the International Society of Paediatric Oncology protocol. The patient underwent eight cycles of vincristine, actinomycin-D, and doxorubicin and concurrent radiation therapy. Use of the UMBRELLA SIOP2016 adult guideline was shown effective at treating the Wilms tumour in this adult case with minimal severe toxicity. Ongoing follow-up is still needed to determine the long-term effects and prognosis of the patient.

Keywords

Oncology, nephrology, the Wilms tumour, adult

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Introduction

The Wilms tumour is a rare form of renal malignancy that occurs in less than 1% of all renal malignancies in the adult population.[1,2] Conversely, in the paediatric population, the Wilms tumour represents 95% of all renal malignancies in the United States alone, and approximately 85% of all paediatric renal tumours worldwide.[2,3] Due to the rarity of this condition in the adult population, there are no high-quality studies and very limited documented cases in the literature.[1,2,4] Within the documented cases, the clinical management varies.[4] Recently, an updated guideline has been published by the International Society of Paediatric Oncology (SIOP) for the treatment and management of the Wilms tumour in adults.[2] These guidelines were developed through international expert consensus and through adaptation of the original paediatric protocol (UMBRELLA SIOP2016 Protocol).[2] Adaptation of this paediatric protocol has shown an improvement in survival rate in adults of up to 82%–90%.[5] However, due to the rarity of this condition in adults, the reported number of cases and the outcomes of being treated by this multimodal guideline remains low.[1,2,4] This article provides a case report of the Wilms tumour in an adult with the aim to provide additional information regarding the use of a standardised treatment protocol in this patient group to further increase understanding, improve patient outcomes, and better manage toxicity. A written patient/client case study consent form was signed and provided to authorise the publication of this case by the patient.

Case report

A 40-year-old male with no family history of cancers or personal comorbidities presented initially with persistent high blood pressure. An abdominal and pelvic computed tomography (CT) scan revealed a peripheral calcified 4 cm mass arising from the right kidney and a 19-cm heterogeneous mass within the right upper abdomen which may be in continuity with the first mass described. In the context of the patient's age, the differentials were adrenal carcinoma, renal carcinoma, and pheochromocytoma. Magnetic resonance

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imaging (MRI) was conducted for further characterisation of the lesion. It showed a large right adrenal mass with areas of haemorrhage suggestive of pheochromocytoma. No metastatic or avid nodal disease was seen in the 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET). Right nephrectomy was performed in July 2019. No lymph nodal sampling was conducted during the operation. Histology was consistent with the Wilms tumour. The predominant tumour pattern was that of a sheet-like growth of pleomorphic basaloid cells with enlarged moderately pleomorphic nuclei, and small amounts of surrounding granular cytoplasm. Cells within these areas showed tubule formation and occasional apoptotic cells. At the peripheral advancing of these areas, the architecture of the tumour showed more regular tubule formation and a reticular pattern. There was a relatively abrupt transition to a second tumour architecture which showed papillary and irregular glandular like formations with mucinous-like material. The tumour was limited by a uniform fibrotic and hyalinised capsule. Immunohistochemistry was positive for CK (AE1/AE3) and negative for nuclear staining of WT1 within tumour cells. 90% showed epithelial differentiation and 10% stromal component. In spite of the nuclear changes concerning for anaplasia which included hyperchromatic large nuclei, the lack of multipolar mitotic figures made the diagnosis of anaplasia unlikely. Tumour was 255 mm in maximal dimension surrounding with non-neoplastic kidney; some areas of necrosis were present but 90% was viable. The tissue was referred for secondary expert opinion and the diagnosis of triphasic Wilms tumour was retained. Such findings are consistent with intermediate-risk Wilms tumour according to the revised SIOP histologic classification. Staging was incomplete due to the lack of lymph node sampling.

In multidisciplinary meetings with the involvement of paediatric medical oncology, the consensus was to follow the adult UMBRELLA SIOP-RTSG 2016 (the UMBRELLA protocol). Such protocol was dependent on cancer staging; the decision was to treat as presumed positive lymph nodes which classify as Stage III. The updated treatment included vincristine 2 mg (1.5 mg/m^2 intravenous (IV), max dose 2 mg), actinomycin-D 2 mg (1.5 mg/m^2 IV, max dose 2 mg), and doxorubicin 60 mg (30 mg/m^2 IV, no dose cap) every 3 weeks for eight cycles with additional vincristine being given on day 1 of weeks 2, 5, and 8. Along with adjuvant chemotherapy, the patient was also planned to undergo concurrent radiation therapy as indicated in the adult guidelines.

The patient commenced chemotherapy 6 weeks after the surgery. According to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, the patient experienced Grade 1 nausea and fatigue after the first cycle. He also developed Grade 1 dysesthesia likely attributed to vincristine. To avoid the potential major radio-sensitising complications of actinomycin-D,[6,7] concurrent radiation was timed after 48 h of the chemotherapy and 2 weeks before the next cycle. This led to deferring the second cycle. The patient received 14.4 Gray in eight fractions to the right flank. After the first cycle, the patient developed Grade 1 neutropenia (1.6×10^9/L) which progressed to Grade 3 neutropenia (0.8×10^9/L) after the third cycle. In addition, Grade 2 lymphopenia (nadir 0.6×10^9/L) commenced about 6 weeks from starting chemotherapy. He also developed Grade 1 derangement of transaminases (aspartate transaminase 59 U/L and alanine aminotransferase 75 U/L) as well as an increase in creatinine after the first cycle to 118 µmol/L. After cycle 4, doxorubicin was decreased by 25% because of the Grade 1 hepatic impairment. A reduced dose of doxorubicin continued for one more cycle before it was re-escalated back to full dose as liver function was stable with no further derangement, and to reap the maximum benefits of adjuvant treatment. A total of eight cycles were administered. Other major drug-related events included lethargy, mucositis, and severe stomatitis. Other minor (but expected) side effects were taste changes, hyperaesthesia, and hair loss.

At 2-month follow-up, most symptoms subsided apart from Grade 1 peripheral neuropathy. Re-staging CT scans showed no evidence of relapse. Protracted neutropenia and lymphopenia persisted for 8 months after chemotherapy. Liver derangement in the form of transaminitis lasted for an average of 11 months before it normalised. Serum creatinine level remained stable (120 µmol/L). Patient's overall fitness continued to improve. One year after completion of chemotherapy, peripheral neuropathy has completely resolved. CT scans showed no evidence of relapse.

Discussion

The Wilms tumour in adults is a rare form of renal malignancy with most cases reported differing in treatment protocols.[4] It is also known to differ on clinical, histopathological, and biological levels. Adulthood malignancy, in general, is less rapidly growing and less responsive to chemotherapy.[8] Adults are assumed to have less favourable prognosis stage-by-stage compared to children.[5,9] Following a review of the 1982 National Wilms Tumour Study-1 (NWTS-1), it was found that adults had an overall 3-year survival rate of 24% compared to 74% in children at that point in time following treatment.[2,10] The first documented improvement in the prognosis of adults with the Wilms Tumour was in the second study conducted by the National Wilms Tumour Study Group (NWTSG) in 1990 after being treated with multimodal treatment protocols similar to that used in children.[2] This was then later confirmed by a third report by the NWTSG with patients being treated in a similar way to their paediatric equivalent with the NWTSG paediatric protocol which showed a 5-year survival rate of 83%.[1,4] Similar outcomes were also reported in a study of 27 patients treated with the SIOP paediatric protocol.[2]

Multimodal approach including surgery and chemotherapy is the mainstay of treatment. Radiation is also added if

the risk of recurrence is high. There are two main approaches in treating the Wilms tumour. The NWTSG protocol focuses on a detailed anatomical and histopathological assessment of the tumour which will eventually dictate treatment strategy. However, the SIOP protocol aims to reduce operative risk by starting with neoadjuvant chemotherapy. Consequently, the Children's Oncology Group (COG)/NWTSG cohort tends to prescribe more radiation than SIOP. In terms of chemotherapy, three-drug chemotherapy with vincristine, actinomycin-D in addition to doxorubicin is still the backbone of most regimens. For Stage III Wilms tumour, radiation to the abdomen or flank is to reduce risk of recurrence.[8]

Delays in starting adjuvant therapy post-nephrectomy are also shown to greatly affect the outcomes of treatment.[4] In the Italian group of 17 patients who were included in the NWTSG study, no identifiable factor other than a duration of more than 30 days to start chemotherapy post-nephrectomy could explain the worsening survival rates in their cohort. Patients who started adjuvant chemotherapy within 30 days of diagnosis showed a 5-year event-free survival rate of 60% (±15%) and overall survivability (OS) rate of 80% (±12%). This is compared to the 5-year event-free survival rate and OS of 14.3% (±13%) and 28.6% (±17%), respectively, in patients who started chemotherapy after 30 days.[2] These findings support the current recommendation in the SIOP adult guideline that treatment should begin within 30 days of nephrectomy.[2,11]

The development of the Wilms tumour in childhood is associated sometimes with a variety of syndromes and congenital abnormalities. Testing for genetic abnormalities and assessing the importance of such tests is an area that needs further research. In addition, biological prognostic factors in children served as a tool to guide treatment decisions in trials.[8]

Neurotoxicity and hepatotoxicity owing to vincristine and actinomycin-D, respectively, are also reported in the adult population.[2] In a small adult study, severe neurotoxicity was shown to occur at a much higher rate compared to children.[2] The incidence of severe hepatotoxicity after administration of actinomycin-D between children and adults could not be drawn though due to the lack of a large adult series study.[2] In this case, the patient experienced Grade 1 hepatitis which could be attributed to any three of the chemotherapy agents. The worsening liver function led to a temporary dose reduction of doxorubicin during the course of treatment. At the time of writing, the patient shows no residual side effects attributed to his chemotherapy regimen. Although some toxicity occurred during the treatment course, there were no delays or cessation of treatment.

The patient showed no relapse after chemotherapy and radiotherapy. However, ongoing follow-up is still needed to determine long-term side effects and prognosis of the patient.

In addition to managing toxicities in this patient, challenges were faced regarding coordinating the chemotherapy cycles with the radiotherapy treatment. The importance of separating actinomycin-D and radiotherapy is well established in the literature due to its radiosensitiser effects.[12] This case involved the coordination of two hospitals and the oversight of the oncology pharmacists to ensure that sufficient space was given between administration of actinomycin-D and radiotherapy.

In terms of long-term toxicity and survivorship, the Wilms tumour treatment in children is known to affect one in four of the treated patients 25 years after the diagnosis.[8] Given the latency of such side effects, it is expected to be less in the adult population. However, further research is required guided by what is known from treatment in paediatrics.

In addition to finding unifying treatment protocols, there are other challenges with the Wilms tumour in the adult population. The diagnosis cannot rely solely on imaging in contrast to paediatric population. This has its implication on management as SIOP protocol relies on giving neoadjuvant treatment relying on radiological diagnosis. It is also difficult to ascertain if paediatric prognostic criteria can be generalisable to the adult cohort. Such as the lack of anaplasia in children was associated with less adverse outcome.[8]

Conclusion

Due to the rarity of adult Wilms Tumour, it is important to report cases in order to further developing treatment guidelines, reducing toxicities experienced, and improving patient outcomes. Furthermore, most information about the Wilms tumour stems from research in paediatric cohort. This can be used as a guide and comparator for further research in the adult population. Also, consultation with paediatric medical oncologist is important as they are more familiar with diagnosis and treatment of this disease. This also applied to the pathology department. International registry of patients can facilitate revising guidelines of treatment and comparing toxicities.

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