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Primary Intra-Renal Neuroblastoma – A Diagnostic Dilemma: A Case Report

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Abstract ***Background:*** Primary intra-renal neuroblastoma is a rare tumour of the kidney in children. We report a case that mimicked Wilms' tumour. ***Method:*** A 15-month-old boy was referred to our hospital with incidental finding of a 10 cm left abdominal mass. Computerised tomography scan showed a left kidney tumour resembling Wilms' tumour. Metaiodobenzylguanidine scan showed no abnormal update of the sympathetic-nervous-system. Bone marrow aspiration was negative for malignant cells. In view of the clinical diagnosis of Wilms' tumour of the left kidney, exploratory laparotomy was performed and revealed a normal left adrenal gland with large tumour arising from the left kidney. Radical left nephrectomy with para-aortic lymph node dissection was performed. ***Results*:** The pathological report showed intra-renal neuroblastoma of the left kidney. Molecular genetic studies confirmed N-myc amplification. The result for the 24-hour urine, collected pre-operatively, showed elevated catecholamines level. The diagnosis of a primary intra-renal neuroblastoma was confirmed and adjuvant therapy was started. ***Conclusions:*** Primary intra-renal neuroblastoma may pose as a diagnostic challenge pre-operatively as it may clinically and radiographically resemble Wilms' tumour. With our literature search, this is the first case report on a primary intra-renal neuroblastoma in a Chinese child. Clinical, radiological and pathological correlation is essential in the management of primary intra-renal neuroblastoma.

Key words Diagnosis; Intra-renal neuroblastoma; Wilms' tumour

Introduction

Primary intra-renal neuroblastoma is a rare tumour of childhood. It can mimic Wilms' tumour in its clinical presentation.[1] We report a case of a 15-month-old boy presenting with this uncommon tumour and suggest diagnostic protocol to avoid the potential clinical dilemma.

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Method and Findings

A 15-month-old boy with good past health was presented to us with incidental finding of an abdominal mass. Physical examination showed a 10 cm non-tender solid mass in the left upper quadrant; blood test results showed normal haemoglobin level and electrolytes; liver and renal function tests were unremarkable. However, he was found to have hypertension with an average blood pressure of 190/80 mmHg, requiring early paediatric intensive care unit admission for close monitoring and blood pressure control with intravenous labetalol. Computerised tomography (CT) scan of the abdomen and thorax showed a 10 x 9 x 9 cm left renal mass encasing left renal artery and infrarenal aorta, with no liver or lung mass detected (Figure 1). In order to further delineate the status of the surrounding vessels, and to look for other possible causes of hypertension, Doppler ultrasound of the left renal vessels were performed.

It showed patent left renal artery with encasement, and no evidence of renal artery stenosis. As neuroblastoma and Wilms' tumour are our top two differential diagnoses at this stage, we decided to perform a 131 - Metaiodobenzylguanidine (MIBG) scan, and the left upper quadrant mass was found to be not MIBG – avid. Whole body bone scintiscan also did not show any suspicious active bone lesions. Bone marrow aspiration and trephine were carried out and both failed to detect any malignancy. Spot urine for vanillylmandelic acid (VMA) was collected, however, the initial result was inconclusive as there was only a marginally increase in urine VMA and the patient had been given beta blocker for hypertension control, which can potentially give rise to a false positive findings.[2] Therefore, repeated urine samples were collected after the medication was withheld.

In our patient, given the lack of metastatic disease at presentation and the negative finding in the MIBG scan, the diagnosis of stage 3 Wilms' tumour of the left kidney was made and surgical exploration was decided. Total left nephrectomy and para-aortic lymph node dissection was carried out, intra-op findings showed thrombus-free inferior vena cava (IVC) and tumour encasing aorta from celiac trunk, inferior mesenteric artery and IVC. Right kidney, spleen and liver were normal (Figures 2a & 2b). The patient has uneventful post-operative recovery and was discharged ten days after the operation.

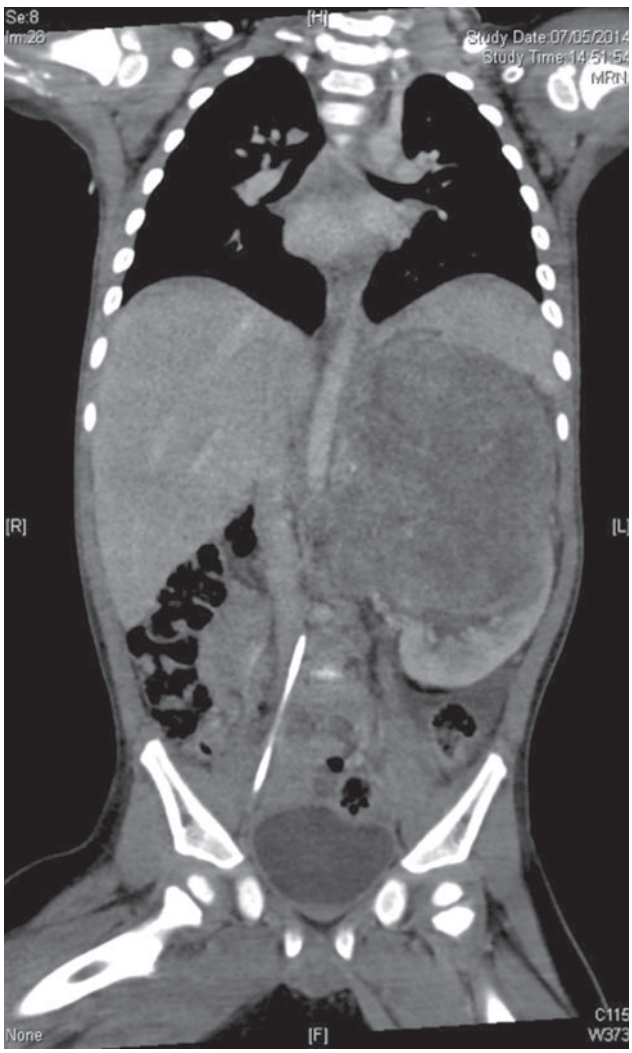

Figure 1 CT scan showing the left renal mass.

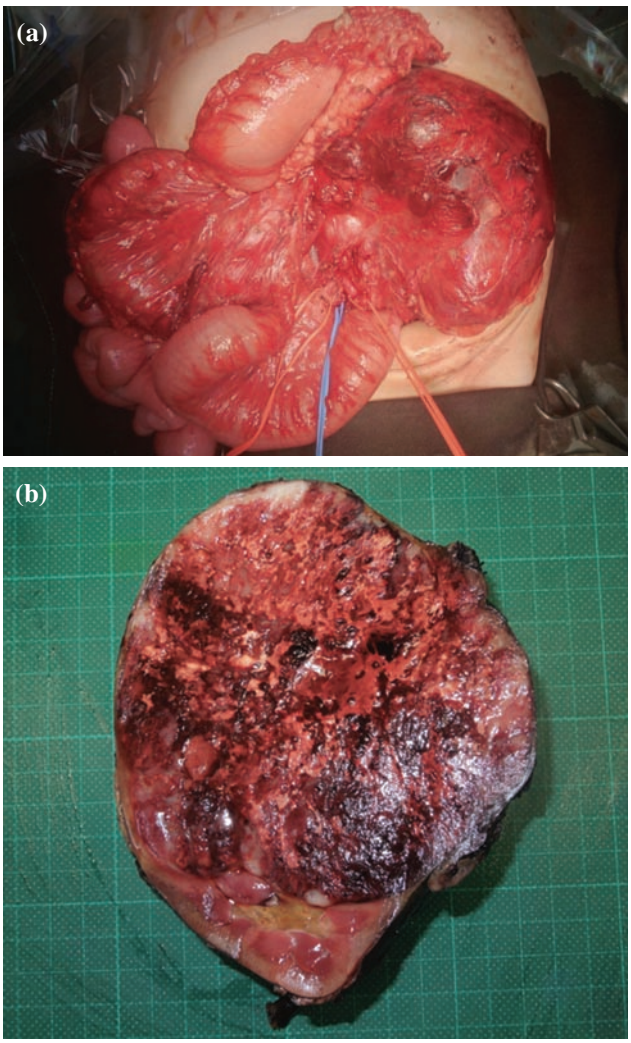

Figure 2 (a) Intra-op photo showing the left renal mass; (b) the cross section of the resected specimen.

The pathology report of the left kidney specimen came back to be N-myc gene amplification positive, stroma-poor intra-renal neuroblastoma with a mitosis-karyorrhexis index >200. Lymph nodes biopsy along the left iliac vessel, right iliac vessel, gastro-epiploic vessel and para-aortic region all came back to be positive for metastatic neuroblastoma. The diagnosis of a primary intra-renal neuroblastoma with metastasis was confirmed and aggressive adjuvant therapy including auto-bone marrow transplant was started.

Discussion

Intra-renal neuroblastoma is a very rare primary renal malignancy. The incidence of renal neuroblastoma was reported to be 1-2% in a series of 868 neuroblastoma cases in a 10-year span by Shamberger et al.[3] It was hypothesised that these tumours originate from adrenal rests within the renal parenchyma or from intra-renal sympathetic ganglia.[4] About 66-100% of intra-renal neuroblastoma was reported to be associated with hypertension at presentation compared with 27% of extra-renal neuroblastoma.[4] The cause is thought to be tumour secretion of catecholamines and/or tumour compression of renal vessels and subsequently activation of the renin-angiotensin-aldosterone system[5] However, hypertension also occurs in 20% of patients with Wilms' tumour,[6] especially when the Wilms' tumour is sufficiently large and strategically placed to stimulate the vascular event and activation of the renin-angiotensin system, or sometimes the Wilms' tumour may also secrete renin.[7] Therefore, urine catecholamine levels would become very useful to distinguish intra-renal neuroblastoma from Wilms' tumour.

While the diagnostic value of tumour marker such as urine VMA in the patients with neuroblastoma has been reported to have a sensitivity of 66-100% and a specificity of >99%,[8] the standard practice for the measurement of VMA requires 24-hour urine collections, which can be difficult to obtain in paediatric patients. Recently, spot urines were demonstrated to have similar diagnostic sensitivity as 24-hour urine.[9] And the VMA/Cr ratio is often used to correlate the VMA daily excretion. However, as creatinine excretion increases in proportion with growing muscle mass, it is recommended that a reference intervals related to the patients' population should be established in each local laboratory, stratified for key covariates including age, gender and ethnicity.[8] Moreover, the use of beta-blocker such as labetalol would also give rise to false positive elevation of urinary catecholamines.[2] In our patient, a second spot urine sample was collected five days after labetalol was stopped, however the results was again invalid because the urine was not adequately acidified. A third sample of the spot urine was finally collected and the results came back to be elevated (22.9 umol/mmol Cr), which is diagnostic of neuroblastoma.

Neuroblastoma is the most common extra-cranial solid tumour of childhood. Approximately 60-75% of patients would already have metastastic disease at presentation. MIBG scan was quoted to have a sensitivity of 88-93% and a specificity of 83-92%.[10] Kessler et al had previously discussed the difficulty in distinguishing intra-renal neuroblastoma from Wilms' tumour clinically and radiologically.[4] MIBG scintigraphy takes advantage of the neural crest origin of neuroblastoma, using the type 1 catecholamine re-uptake system for transport into tumour cells. Normal physiological uptake of MIBG can be seen in salivary glands, nasal mucosa, myocardium, liver and bowel. MIBG is excreted into the urine, therefore physiologic activity can also be seen in kidneys and bladder. Less than 10% of neuroblastoma demonstrates no MIBG uptake.[10] However, blocking agents such as pseudo-ephedrine, tricyclic antidepressants and labetalol would alter MIBG uptake. And this can potentially leads to confusion clinically when trying to detect neuroblastoma using this functional scanning, such as in our patient.

The distinction of intra-renal neuroblastoma from Wilms' tumour is important as both tumours have different prognostic and therapeutic responses.[3] A high proportion of intra-renal neuroblastoma are of unfavourable histology as defined by the International Neuroblastoma Pathology Classification and have a higher incidence of anaplasia when compared to Wilms' tumour. In our patient, given the tumour encasement to the infrarenal aorta on CT, if it had been known that it was indeed neuroblastoma, it would be classified as a stage 3 tumour according to the International Neuroblastoma Staging System. Neo-adjuvant therapy for high risk neuroblastoma such as combination chemotherapy and stem cell rescue might be considered prior to laparotomy. However, as stage 3 neuroblastoma is a hetergenous group of tumours with significant variability in outcome, it would be difficult to predict the long term outcome of our patient if the correct diagnosis had been made prior to surgery.

With this in mind, we hope to have highlighted some potential pitfalls when facing with the clinical dilemma in

distinguishing intra-renal neuroblastoma from Wilms' tumour, and to suggest a clinical protocol in avoiding the confusion. This will include:

(i) early multidisciplinary involvement of paediatrician, paediatric radiologist, paediatric oncologist, paediatric surgeon and chemical pathologist when dealing with uncommon paediatric renal tumour;
(ii) to have high index of suspicion and clinical awareness for less common tumour such as intra-renal neuroblastoma;
(iii) review medications that can potentially give rise to false positively elevated urinary catecholamines level;
(iv) review medications that can alter the interpretation of MIBG scanning;
(v) collaborate with the chemical pathologist to establish a local reference range for the appropriate VMA/Cr ratios for different age group and gender for the diagnosis of neuroblastoma in the local population;
(vi) education to frontline healthcare workers to acidify the urine to pH 4.0 immediately after collection and protection the sample from light to facilitate the accurate analysis of urinary catecholamines level.

Declaration of Interest

None

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