Clinical Presentation

8

Parveen Kumar and Parthapratim Gupta

8.1 Clinical Presentation

The patients are usually asymptomatic during the early stages of development of Wilms' tumor (WT). An *asymptomatic abdominal mass* usually noted by a family member while bathing, dressing, or playing with the child is the commonest presentation (90%). The other symptoms may be due to the tumor itself, its mass effects/extensions, or metastasis. It may include abdominal pain, fever, hypertension, blood in urine, loss of appetite, unexplained weight loss, constipation, etc. Rarely, it may present with respiratory symptoms (cough, fast breathing, or distress) secondary to lung metastasis.

Hypertension occurs in 35–63% cases of WT, presenting with both raised systolic and diastolic pressure [1]. This is due to increased production of renin probably due to ischemic effects of the kidney by the expanding mass. The expanding mass (rapidly growing tumor or sudden hemorrhage into tumor) causes compression effect on kidney substance and its vasculature, leading to activation of renin angiotensin system and thus hypertension [2]. The hyperreninemia is mostly due to tumor secretion and possibly due to compression of the surrounding renal tissue. High renin levels induce aldosteronism causing electrolyte imbalances (hypokalemia), which in turn may cause polyuria and vasopressin resistance and polydipsia [3]. Hyperreninemia, hypertension, and secondary hyperaldosteronism has been associated with WT [4–6]. Hypertension may also be caused rarely by intrarenal arteriovenous fistula formation secondary to tumor [1]. It may not cause any symptoms at own, but very high blood pressure may cause headaches, vision, and consciousness issues.

Hematuria (microscopic and/or gross/macroscopic) occurs in 5–30% of patients [7]. Macroscopic hematuria is blood in urine as seen by naked eye. Microscopic hematuria is more common (20–30%) as compared to microscopic hematuria (5–18%). This may be due to extension of the tumor within the renal pelvis or rarely renal vein thrombosis. Tumor extension into ureter (2–4%) may present with hematuria, passage of clots/mass per urethra, or hydronephrosis [8]. Engel described three cases of gross hematuria with nonfunctioning kidney (NFK) on intravenous pyelography, which later proved to be WT [9]. Retrograde pyelography revealed collecting system mass causing nonfunctioning of kidney. In all the three patients, there was no invasion of venous drainage system, and the tumor was exclusively protruding into the collecting system rather than displacing the parenchyma itself.

Abdominal pain may be a presenting feature in 30–40% patients [8]. It occurs due to expand-

P. Kumar (✉)
Department of Pediatric Surgery, Chacha Nehru Bal Chikitsalaya, New Delhi, India

P. Gupta
Department of Pediatric Surgery, Institute of Child Health, Kolkata, India

Y. K. Sarin (ed.), *Wilms' Tumor*, https://doi.org/10.1007/978-981-19-3428-5_8

ing mass, subcapsular hemorrhage, mass effects of tumor, or liver metastases.

Constitutional symptoms like loss of appetite, unexplained weight loss, constipation, etc. are due to mass effects, or malignant potential of tumor, or metastases. Low-grade fever occurs due to high metabolism secondary to fast growth of tumor. Loss of 5% of weight over past 6 months is considered significant.

Any history of easy bruisibility should be noted. WT may also cause *coagulopathy*. Acquired von Willebrand disease has been reported in 4–8% of children with WT [10, 11]. The exact etiology remains unknown, but von Willebrand factor (vWF) inhibitors and rapid abnormal vWF clearance have been the proposed mechanisms. Though the bleeding is usually clinically insignificant, it may present with epistaxis, hematuria, or gingival bleed. *Anemia* may occur secondary to hemorrhage in tumor. Though rare, *polycythemia* has also been reported in children with WT, and it has been ascribed to elevated erythropoietin levels [12].

Ramsay et al. in 1977 described three cases of acute hemorrhage in WT, which caused rapidly developing abdominal mass, hypertension, anemia, and fever [2]. It has been usually described as *Ramsay's triad* and is associated with poor prognosis; some mention Ramsay's *tetrad*, incorporating the fourth feature of egg-shell calcification that may be seen on imaging in such cases. Peng et al. also emphasized the need of paying attention of complains of abdominal pain and anemia, so as not to miss malignancy (WT) in children [13].

Occlusion of the left renal vein by tumor extension may obstruct the drainage of left spermatic vein, resulting in *left side varicocele* and a dragging pain in left scrotum. Hence, it is prudent to examine the abdomen thoroughly while evaluating a patient presenting with varicocele on left side and vice versa.

In rare cases, more so in right-sided WT, *cardiac manifestations* including arrhythmias may be the presenting symptoms at the time of diagnosis, and the prognosis of these patients is poor. This is due to the tumor extension through the inferior vena cava to the right atrium [14]. Thrombus embolization to pulmonary artery may be lethal.

The patient may also rarely present to emergency room with an *acute abdominal crisis* (acute abdominal pain, anemia, and hypotension) that can happen due to rupture of tumor secondary to trivial abdominal trauma [15]. The quoted incidence of such an event in WT patients is ~2% [16]. There have been occasional patients with WT cases who have been managed conservatively with a misdiagnosis of renal trauma [17, 18].

The *metastases* in WT are usually to regional lymph nodes, lungs, and liver. The patient may present with cough, tachypnea, or respiratory distress as a result of metastases in the lung. It may be associated with chest retractions, indrawings, and use of accessory muscles of respiration. Lung metastasis has been reported to cause pneumothorax [19, 20]. Liver metastasis may cause right hypochondriac pain, vomiting, loss of appetite, generalized weakness, jaundice, ascites, edema, or coagulation disorders.

Rare sites of metastases include bone, spine, mediastinum, brain, gonads, pancreas, etc. [21–24] The postmortem examination of WT patients had cerebral metastasis in 12.9% cases, but these are rarely diagnosed before death [25]. The intracranial metastasis may present with cerebral bleeding and hydrocephalous [26]. Brain and/or spinal compression may present with signs of irritability, seizures, projectile vomiting, radicular pain, muscular weakness, paraplegia, or loss of bowel or bladder control [27–30]. Bone pains or pathological fracture may be presenting feature of bone metastasis [28].

Any history of similar complains in other siblings, family members, or first cousins should be inquired about. Any history of other congenital anomalies and cause of death for deceased family members if any should also be elicited.

8.2 Examination

A meticulous head-to-toe examination should be carried out.

1. Temperature: Low-grade fever because of high metabolism secondary to fast-growing tumor.

2. Blood pressure (surveillance to rule out hypertension). It should be recorded when child is calm and with proper arm cuff size to avoid false readings.
3. Eye examination to rule out of aniridia (partially formed or not at all formed) and pallor (anemia).
4. Face: Dysmorphic features/bulldog facies (large protruding jaw, widened nasal bridge, upturned nasal tip, broad nose, wide mouth, thick lips) and macroglossia to be looked for.
5. Spine needs to be examined to rule out any gross abnormalities and bone pain.
6. Any evidence of easy bruisibility (acquired vWF deficiency).
7. Nutritional status should be assessed. Height, weight, mid-arm circumference, skin fold thickness, etc. need to be recorded.
8. Genitalia examination: Look for hypospadias, undescended testis, any evidence of varicocele (especially on the left side).
9. Isolated hemihypertrophy to be ruled out.
10. Developmental milestones to be assessed (rule out mental retardation or intellectual disabilities).

The physical examination should characterize the location and extent of the abdominal mass. The abdominal mass should be carefully examined. The mass should not be palpated too vigorously as it could lead to the rupture of a large tumor into the peritoneal cavity. Any other organomegaly or ascites to be ruled out. Renal angle fullness and tenderness to be noted.

WT needs to be clinically differentiated from abdominal neuroblastoma (NB) and other non-Wilms' renal tumors (NWRT) based on history and examination. A child with WT is usually well preserved, while it's ill-looking child with NB; more than half of the patients with NB with have metastases and malnutrition at presentation. On palpation, the abdominal NB mass almost always crosses the midline, whereas this presentation is uncommon with WT and seen only in those patients that present very late. Most of the patients with malignant rhabdoid tumor of kidney also present with a fast-growing tumor and fever and look sick, similar to NB. Clear cell sarcoma kidney usually presents with bone and/or brain metastasis. Renal cell carcinoma starts showing up from pre-adolescence. Congenital mesoblastic nephroma is most common tumor kidney in first 6 months of life, while WT commonly occurs in children of 1–3 years of age. The signs and symptoms of NWRT are detailed in another chapter.

8.3 Associated Syndromes

As associated abnormalities or syndromes may be present in patients with WT, the examination should include assessment of urological abnormalities like maldescended testis or hypospadias. These associated syndromes have been detailed elsewhere in the book.

References

1. Sukarochana K, Tolentino W, Klesewetter WB. Wilms' tumor and hypertension. J Pediatr Surg. 1972;7:573–8. https://doi.org/10.1016/0022-3468(72)90215-1.
2. Ramsay NK, Dehner LP, Coccia PF, D'Angio GJ, Nesbit ME. Acute hemorrhage into Wilms tumor: a cause of rapidly developing abdominal mass with hypertension, anemia, and fever. J Pediatr. 1977;91:763–5. https://doi.org/10.1016/S0022-3476(77)81035-4.
3. Sheth KJ, Tang TT, Blaedel ME, Good TA. Polydipsia, polyuria, and hypertension associated with renin-secreting Wilms tumor. J Pediatr. 1978;92:921–4. https://doi.org/10.1016/S0022-3476(78)80361-8.
4. Corm JW, Cohen EL, Lucas CP, McDonald WJ, Mayor GH, Blough WM, et al. Primary reninism, hypertension, hyperreninemia, and secondary aldosteronism due to renin-producing juxtaglomerular cell tumors. Arch Intern Med. 1972;130:682–96. https://doi.org/10.1001/archinte.1972.03650050016004.
5. Schambelan M, Howes EL Jr, Stockgt JR, Noakes CA, Biglieri EG. Role of renin and aldosterone in hypertension due to a renin-secreting tumor. Am J Med. 1973;55:86. https://doi.org/10.1016/0002-9343(73)90153-8.
6. Brown JJ, Fraser R, Lever AF, Morton JJ, Robertson JIS, Tree M, et al. Hypertension and secondary hyperaldosteronism associated with a renin-secreting renal juxtaglomerular cell tumor. Lancet. 1973;302(7840):1228–32. https://doi.org/10.1016/S0140-6736(73)90972-0.
7. Fischbach BV, Trout KL, Lewis J, Luis CA, Sika M. WAGR syndrome: a clinical review of 54 cases. Pediatrics. 2005;116:984–8. https://doi.org/10.1542/peds.2004-0467.

8. Fernandez C, Geller JI, Ehrlich PF, Hill DA, Kalapurakal JA, Grundy PE, et al. In: Pizzo P, Poplack D, editors. Renal tumors: principles and practice of pediatric oncology. 6th ed. St. Louis: Lippincott Williams & Wilkins; 2011. p. 861.
9. Engel RM. Unusual presentation of Wilms' tumor. Urology. 1976;8:288–9. https://doi.org/10.1016/0090-4295(76)90390-3.
10. Fosbury E, Szychot E, Slater O, Mathias M, Sibson K. An 11-year experience of acquired von Willebrand syndrome in children diagnosed with Wilms tumour in a tertiary referral centre. Pediatr Blood Cancer. 2017;64:e26246. https://doi.org/10.1002/pbc.26246.
11. Coppes MJ, Zandvoort SW, Sparling CR, Poon AO, Weitzman S. Blanchette vs. acquired von Willebrand disease in Wilms' tumor patients. J Clin Oncol. 1992;10:422–7. https://doi.org/10.1200/JCO.1992.10.3.422.
12. Murphy GP, Allen JE, Staubitz WJ, Sinks LF, Mirand EA. Erythropoietin levels in patients with Wilms' tumor. Follow-up evaluation. N Y State J Med. 1972;72:487–9.
13. Peng JY, Wu HJ, Yong SB. A typical presentation of Wilms tumor, an 11-year-old girl with abdominal pain and anemia: a case report. Int J Clin Exp Med. 2019;12:9463–7.
14. Patel CC, Rees A, Bertolone SJ. Intracardiac extension of Wilms' tumor. Am J Pediatr Hematol Oncol. 1989;11:46–50. https://doi.org/10.1097/00043426-198921000-00012.
15. Brisse HJ, Schleiermacher G, Sarnacki S, Helfre S, Philippe-Chomette P, Boccon-Gibod L, et al. Preoperative Wilms tumor rupture: a retrospective study of 57 patients. Cancer. 2008;113:202–13. https://doi.org/10.1002/cncr.23535.
16. Adu J, Watson T. 107 Imaging features of preoperative Wilms tumour rupture on CT and MRI with histopathological confirmation. Arch Dis Child. 2018;103:A43. https://doi.org/10.1136/goshabs.107.
17. Levant B, Feldman BJ. Traumatic rupture of Wilms' tumor. J Urol. 1952;67:629–33. https://doi.org/10.1016/S0022-5347(17)68398-8.
18. Fraley EE, Halverstadt DB. Unsuspected Wilms tumor: dangers in the conservative therapy of renal trauma. N Engl J Med. 1966;275:373–4. https://doi.org/10.1056/NEJM196608182750707.
19. Siegel MJ, McAlister WH. Unusual intrathoracic complications in Wilms tumor. Am J Roentgenol. 1980;134:1231–4. https://doi.org/10.2214/ajr.134.6.1231.
20. Kassner EG, Goldman MD. Cavitating lung nodules and pneumothorax in children with metastatic Wilms' tumor. Am J Roentgenol. 1976;126:728–33. https://doi.org/10.2214/ajr.126.4.728.
21. Magill HL, Strang MS. Paraspinal metastasis of Wilms' tumor visualized on bone imaging. J Nucl Med. 1981;22:481–2.
22. Magill HL, Sackler JP, Parvey LS. Wilms' tumor metastatic to the mediastinum. Pediatr Radiol. 1982;12:62–4. https://doi.org/10.1007/BF00972432.
23. Pearson D, Duncan WB, Pointon RCS. Wilms' tumours. A review of 96 consecutive cases. Br J Radiol. 1964;37:154–60. https://doi.org/10.1259/0007-1285-37-434-154.
24. Dokmak S, Cabral C, Couvelard A, Aussilhou B, Belghiti J, Sauvanet A. Pancreatic metastasis from nephroblastoma: an unusual entity. JOP. 2009;10:396–9.
25. Vannucci RC, Baten M. Cerebral metastatic disease in childhood. Neurology. 1974;24:981–5. https://doi.org/10.1212/WNL.24.10.981.
26. Takamiya Y, Toya S, Otani M, Inoue H, Okui S, Takenaka N. Wilms' tumor with intracranial metastases presenting with intracranial hemorrhage. Childs Nerv Syst. 1985;1:291–4. https://doi.org/10.1007/BF00272029.
27. Ramdial PK, Hadley GP, Sing Y. Spinal cord compression in children with Wilms' tumour. Pediatr Surg Int. 2010;26:349–53. https://doi.org/10.1007/s00383-010-2563-z.
28. Watanabe R, Takahashi A, Suzuki M, Toki F, Kanazawa T, Hirato J, et al. Adolescent Wilms tumor with intraspinal and bone metastases. J Pediatr Hematol Oncol. 2009;31:45–8. https://doi.org/10.1097/MPH.0b013e318190d718.
29. Sikorski CW, Pytel P, Rubin CM, Yamini B. Intradural spinal Wilm's tumor metastasis: case report. Neurosurgery. 2006;59:942–3. https://doi.org/10.1227/01.NEU.0000232663.48673.A3.
30. Cohn SL, Hamre M, Kletzel M, Chou P, Radkowski MA. Intraspinal Wilm's tumor metastases. Cancer. 1994;73:2444–9. https://doi.org/10.1002/1097-0142(19940501)73:9<2444::AID-CNCR2820730930>3.0.CO;2-A.