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Approach to pediatric renal tumors: an imaging review

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Abstract

Renal tumors comprise 7% of all childhood cancers. A wide variety of renal tumors can affect the pediatric kidneys, which can be broadly classified as primary benign tumors, primary malignant tumors, and metastatic lesions. This article aims to enumerate usual benign and malignant renal tumors that can occur in childhood and emphasizes the characteristic imaging appearances which aid in their differential diagnosis. Additionally, the leading role of the Radiologist in primary diagnosis of renal infiltration by hematological malignancies and contiguous invasion by neuroblastoma is also introduced and unraveled. Imaging protocol comprises initial Ultrasound evaluation with subsequent computed tomography (CT) and/or Magnetic resonance imaging (MRI), all of which are invaluable in confirming the diagnosis, documenting the organ of origin, describing extent of local and distant spread. The complimentary role of nuclear medicine studies in delineating differential renal function, post-operative complications, and metastasis is also highlighted.

Key words: Benign tumors—Imaging appearances—Malignant tumors—Metastatic lesions—Padiatric renal tumors

Renal tumors comprise 7% of all childhood cancers and can be classified as primary benign tumors, primary malignant tumors, and metastatic lesions [1, 2]. It has been reported by most investigators that in neonates most tumors are benign and in older children they are more often malignant [1]. Primary benign tumors are mesoblastic nephroma, angiomyolipoma (AML), multilocular cystic nephroma, ossifying renal tumor of infancy, and metanephric adenoma. Primary malignant tumors are Wilms tumor, nephroblastomatosis, rhabdoid tumor, and some other rare entities are renal medullary carcinoma, renal cell carcinoma, and clear cell sarcoma [2–4]. Metastatic lesions are lymphoma and leukemia. Occasionally, a neuroblastoma may contiguously invade the kidney or rarely even originate from it [4–6]. Most Radiology literature highlights only Wilms tumor and therefore other pediatric renal tumors remain relatively unknown. This article aims to enumerate other benign and malignant renal tumors that can occur in childhood and emphasizes the characteristic imaging appearances which may aid in their differential diagnosis. Non-tumorous lesions are not included in this review. Additionally, the leading role of the Radiologist in primary diagnosis of renal infiltration by hematological malignancies and contiguous invasion by neuroblastoma is also introduced and unraveled.

The currently available imaging modalities for evaluation of renal tumors are sonography, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear medicine scans. The initial imaging evaluation is by ultrasound and is followed by cross-sectional imaging (CT and/or MRI). Ultrasound helps not only document the organ of origin but also classify the tumor as solid or cystic. However, for accurate characterisation and determining the perinephric and distant spread of the disease, locoregional and distant lymphadenopathy, cross-sectional imaging is imperative. Although MRI may be preferred for local staging as it is radiation free and can be used in patients with deranged renal function,

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CT has the advantage of documenting distant metastasis in the same setting. Furthermore, the disadvantage of MRI is prolonged examination time and necessity for sedation/short anesthesia in children. These modalities provide valuable information for confirming the diagnosis, staging a tumor, monitoring treatment response, and evaluating recurrence. The role of nuclear medicine studies is not only for documenting differential renal function and post-operative complications but also for assessing the locoregional and distant spread of disease, which is invaluable in long-term follow-up [7].

Primary benign tumors

Mesoblastic nephroma

Overview

It is the most common solid renal tumor in neonates and infants. Originally thought to represent congenital Wilms tumor, mesoblastic nephroma has been recognized as a distinct entity and is often referred to as fetal renal hamartoma or leiomyomatous hamartoma. With recent advances in prenatal imaging, mesoblastic nephromas are often diagnosed on routine antenatal ultrasound or MRI studies. It is more common in male infants and most often presents as a palpable flank mass [5, 8].

Imaging

Ultrasound demonstrates a solid renal mass with propensity to involve the renal sinus. It is typically unencapsulated, but may exhibit a pseudocapsule from compression of the surrounding residual renal tissue. Occasionally, it may contain cystic, hemorrhagic, and necrotic regions. Local infiltration of the perinephric tissues is common [5]. The underlying vascularity of a mesoblastic nephroma can be normal to increased. For perinephric extension, both CT and MRI perform equally. CT shows a solid intrarenal mass with ill-defined margins and no capsule. The enhancement pattern is variable. Mesoblastic nephromas show intermediate to low signal intensity on T1-weighted images and are hyperintense on T2-weighted images [8] (Figure 1).

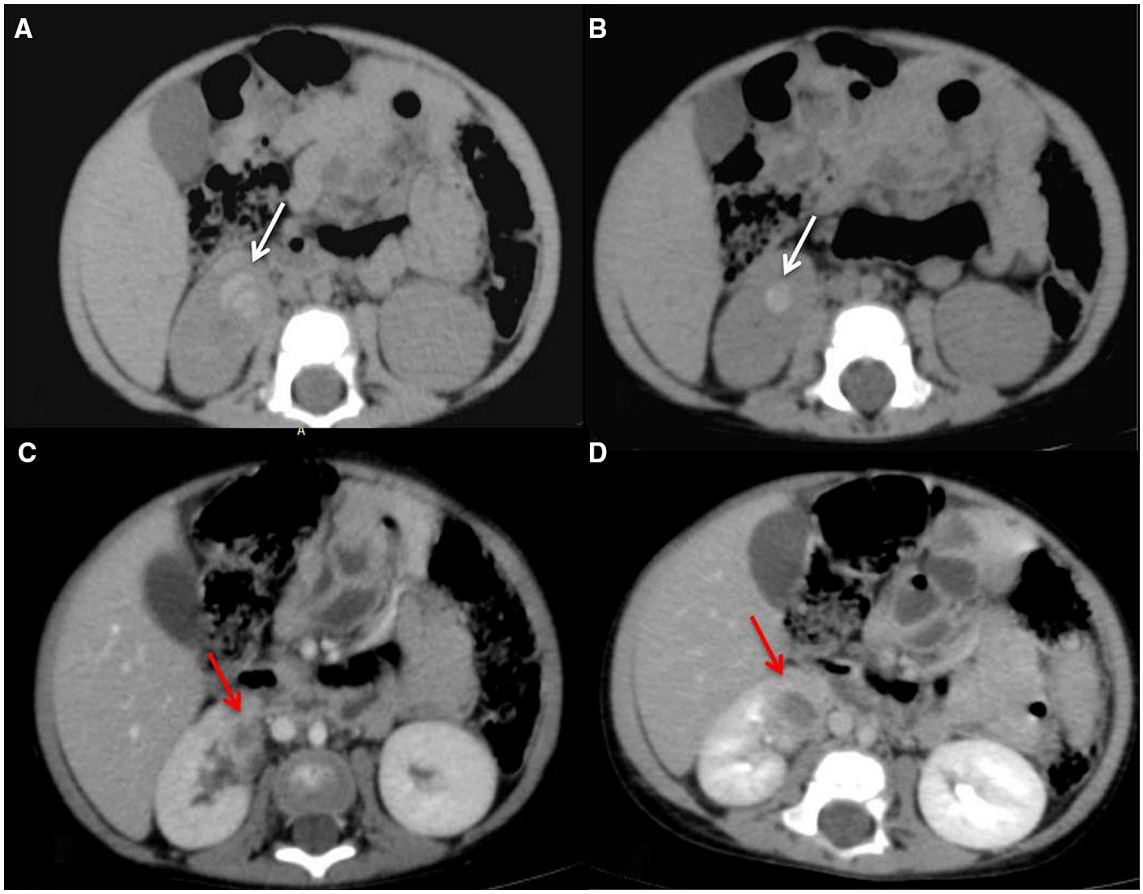


Fig. 1. **A**–**D** CT study in a male infant of 8 months with a palpable mass in the right lumbar region. NCCT study **A**, **B** shows a mass lesion in the lower pole of right kidney with few hyperdense foci (white arrows) due to hemorrhage. The contrast CT **C**, **D** shows a heterogeneously hypodense tumor (red arrows) extending from the renal sinus into the lower pole of the right kidney. The lesion has unsharp margins, indicating absence of a capsule. Imaging features were suggestive of a mesoblastic nephroma which was confirmed after partial nephrectomy and histopathology.

It is typically a benign tumor but can show rapid growth. However, the prognosis is excellent because surgery is usually curative [8]. The treatment of choice is nephrectomy with wide surgical margins due to its infiltrating nature. Overall survival is above 90% but 5–10% develops local recurrence or metastases to distant organs. Almost all recurrence develops within 1 year of the initial presentation, thus close follow-up by serial Ultrasound evaluation usually suffices [9].

Differential diagnosis

Mesoblastic nephroma should be differentiated from Rhabdoid tumor and Wilms tumor. Rhabdoid tumor is a rare, highly aggressive malignancy of early childhood (peak age is 6–12 months), shows synchronous and metachronous primary intracranial masses or brain metastasis [5, 8].

Teaching points

1. Mesoblastic nephroma is the most common intrarenal tumor in the neonate and infants and mostly presents within 6 months of age.
2. It should be considered as the first differential diagnosis in an infant with a solid poorly encapsulated renal mass arising centrally from the renal sinus.

Angiomyolipoma

Overview

Angiomyolipoma (AML) is a benign solid tumor, which in children usually occurs only with underlying Tuberous Sclerosis (TS) and presents by 10 years of age [4]. It is composed of varying amounts of three elements: dysmorphic blood vessels, smooth muscle, and fatty elements. Majority of AML (80%) are sporadic, while remaining 20% are seen in association with TS. The tumors in the latter group are more often bilateral, multifocal, and larger in size [5, 10].

Most of the tumors are asymptomatic and discovered during the work up for TS. The larger ones are symptomatic and discovered due to flank pain, fullness, and some due to hematuria. The dysmorphic blood vessels of the tumor are elastin poor and lead to the formation of aneurysms which may bleed and sometimes result in life-threatening hemorrhage. Occasionally, severe retroperitoneal hemorrhage occurring in such setting has been termed Wunderlich syndrome. Rarely, AML may become locally aggressive and invade neighboring structures. Extension into the inferior vena cava and regional lymph nodes has also been described [5].

Imaging

Imaging plays an important role in not just detection of such tumors, but also surveillance in patients with tuberous sclerosis, and follow-up of known cases that are kept on conservative management. [8] Radiologically, AML may be classified as 'Fat rich,' 'Fat poor,' or 'Fat invisible.' Ultrasound demonstrates highly echogenic non-shadowing foci (more echogenic than the renal sinus fat), which correlate with the fatty elements. Those which are 'fat poor' and 'fat invisible' will have variable echogenicity, may be iso-echoic to the renal parenchyma and hence can be missed on ultrasound [11]. Sometimes, abnormal vessels can be detected on color Doppler evaluation with pseudoaneurysms showing the characteristic ''yin-yang flow.'' CT scans and MR images are superior and more sensitive and specific than Ultrasound in the detection of fat. MRI with capability of chemical shift imaging scores over CT, for detection of microscopic fat in 'fat poor' AML. Diagnosis is confirmed by characteristic imaging features and biopsy is contraindicated in view of the risk of life-threatening hemorrhage [5, 11]. (Figure 2)

Catheter embolization is the main stay of treatment for the bleeding aneurysms which are believed to occur more frequently in tumors larger than 4 cm in size [5, 10]. Partial nephrectomy is considered in a few cases where embolization fails. Regular ultrasound surveillance is recommended for all patients, post-intervention and also for all patients with tuberous sclerosis for early detection of AML [5, 10].

Differential diagnosis

Fat poor variety of angiomyolipomas, which has paucity of fat, resembles Wilms tumor and renal cell carcinoma on imaging, thus a closely guarded image-guided percutaneous biopsy may be considered, despite the risk of hemorrhage [10].

Teaching points

1. Angiomyolipomas are rare in children unless they have underlying tuberous sclerosis. CT screening of both kidneys and brain should therefore be done in the same sitting to confirm the syndromic association.
2. The detection of mixed tissue elements, that is, fat, abnormal blood vessels, and smooth muscle component on ultrasound, CT, and MRI is characteristic for the diagnosis of AML.
3. In view of dysmorphic blood vessels, biopsy confirmation is usually contraindicated in fat invisible and fat poor variety of AML.

Multilocular cystic renal tumors

Overview

Multilocular cystic renal tumors is an umbrella term that comprises of benign tumors, namely, cystic nephroma and cystic partially differentiated nephroblastoma (CPDN) and a malignant tumor, namely, cystic Wilms [2].

The two benign tumors have been reported to have different age groups of presentation. CPDN presents in children aged 3 months to 4 years with male predominance. Cystic nephromas have also been reported in children, although it is believed that these tumors are more common in adult females. Patients frequently present with a painless abdominal mass, and systemic symptoms are rare. These two entities cannot be distinguished on imaging alone and can only be differentiated on histopathology. Microscopically, cystic nephroma is a purely cystic lesion lined by epithelium and fibrous septa with mature tubules. On the contrary, in CPDN, the septa contain foci of blastemal cells [5, 9].

Imaging

On ultrasound, the tumor typically appears as a mass containing cystic components of variable size and showing thin septa. Infrequently, parts of the lesion may appear solid since these multiple tiny cysts are below the resolution of ultrasound. On CT, multilocular cystic renal tumor appears as a well-circumscribed cystic mass containing multiple thin minimally enhancing septations. Occasionally, septal or wall calcifications can be seen. On MRI, septations and the surrounding capsule are hypointense on all pulse sequences, apparently due to the fibrous tissue within them. The cysts are hyperintense on T2-weighted images but can vary in signal intensity on T1-weighted images depending on the protein content and hemorrhage [5]. Hemorrhage is rare in multilocular cystic renal tumors and usually occurs only when the tumor herniates into the renal pelvis or the ureter causing disruption of the transitional epithelium [8]. (Figures 3, 4)

Multilocular cystic renal tumors are treated by surgical resection alone. Nephron-conserving surgery is preferred, given their benign nature, however, CPDN are closely followed up as it carries more aggressive behavior. As these tumors are benign in nature, a clinical examination and Ultrasound should be adequate for long-term follow-up [6].

Differential diagnosis

Benign multilocular cystic renal tumors apparently do not need differentiation between cystic nephroma and CPDN as both have identical treatment strategy. However, it is critical to differentiate these two from the malignant, cystic variety of Wilms tumor. On imaging, the only key to differentiate between cystic Wilms tumor and CPDN/cystic nephroma tumors is to look for the presence of solid-enhancing nodule within the cystic mass, which indicates a Wilms tumor [5].

Fig. 2. **A**–**F** Color Doppler study **A**, **B** of a 14-year-old girl with history of painless hematuria. The right kidney **A** shows abnormal aneurysmal vessels, with "yin-yang flow." The CT scans **C**–**E** show bilateral nephromegaly, caused by multiple tumorous foci comprising an admixture of fat, blood, and abnormal aneurysmal tortuous vessels (**D**, **E**; red arrows). Imaging features were characteristic of bilateral angiomyolipomas. Figure **F** is CT brain study showing coexisting sub-ependymal nodules (white arrow), confirming the diagnosis of tuberous sclerosis. The patient was managed by endovascular coiling of the aneurysmal vessels of both kidneys and advised regular clinical and radiological follow-up.

Teaching points

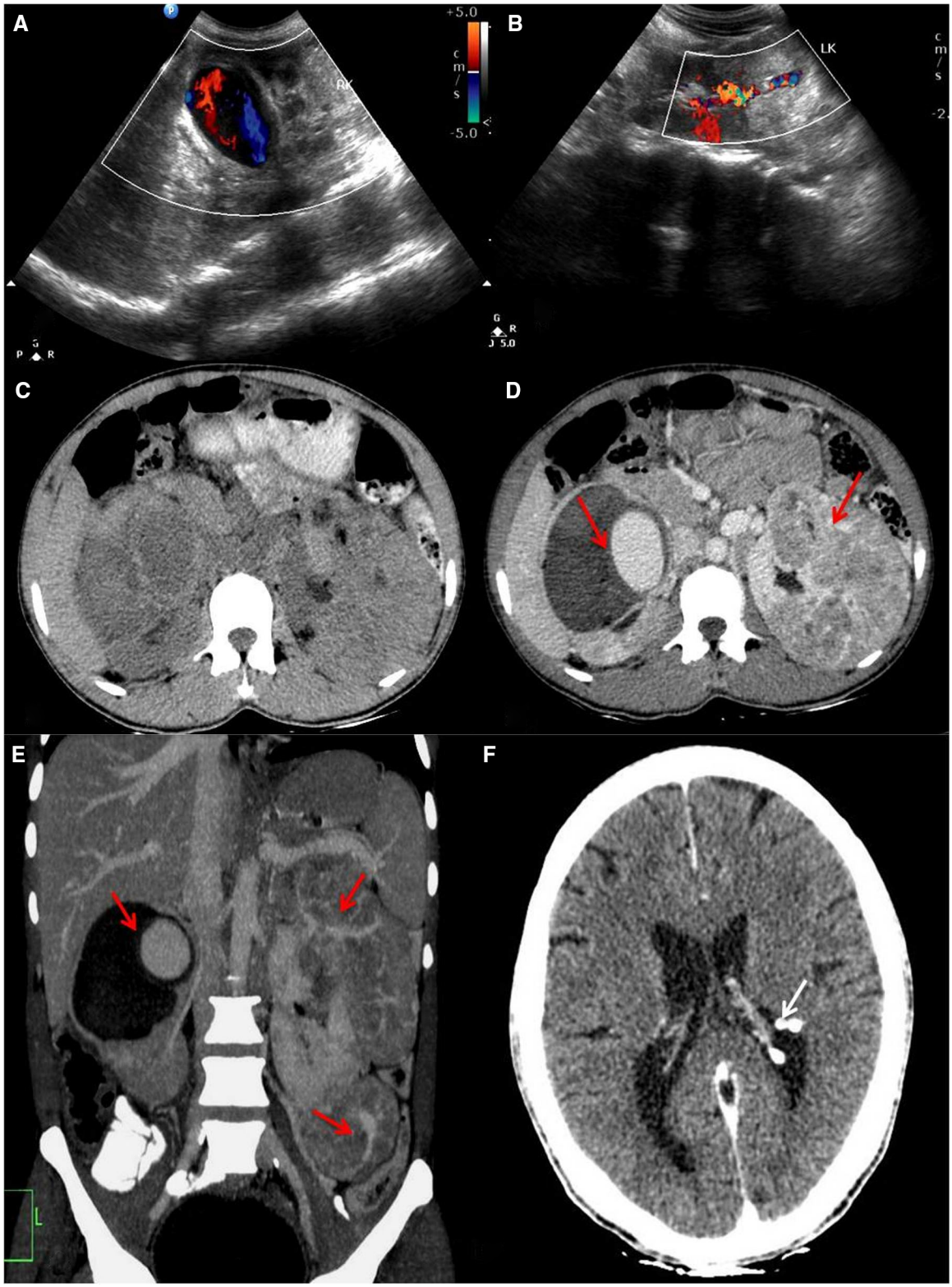
1. The three most important entities to be considered in multilocular cystic tumors in a padiatric patient are cystic nephroma, CPDN, and cystic variety of Wilms tumor.
2. Although the differential diagnosis of cystic renal tumors may be difficult on imaging alone and enhancing septae may be present in all these entities, the presence of solid-enhancing nodules favors the diagnosis of cystic variety of Wilms tumor.

Ossifying renal tumor of infancy

Ossifying renal tumor of infancy is an extremely rare benign tumor, which usually presents characteristically as an abdominal mass with gross hematuria. Hematuria results owing to the bulging of the tumor into the renal pelvis. Males are more commonly affected than females and the mass is believed to arise from the papillary region of renal pyramids and shows osteoid-core, osteoblast-like cells, and spindle cells on pathology. On ultrasound, it appears as a heterogeneously echogenic intrarenal mass with posterior acoustic shadowing due to the presence of osteoid component. CT reveals a poorly enhancing calcified soft tissue intrarenal mass associated with hydronephrosis. The tumor closely mimics staghorn renal calculi on imaging studies [5, 8, 12].

Metanephric adenoma

Also known as nephrogenic adenofibroma or embryonal adenoma. Rare benign tumor of renal cortex is seen to occur at any age ranging from 15 months to 83 years. Females are more commonly affected as compared to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males. Symptomatic patients present with flank pain, hypertension, hematuria, dysuria, hypercalcemia, and polycythemia. On US, it appears as well-defined solid mass lesion of variable echotexture. It can be hypoechoic or hyperechoic or cystic lesion with mural nodule. CT shows a hypoenhancing mass lesion with enhancement less than that of normal parenchyma. Small calcifications may also be seen. The lesion mimics imaging appearances of Renal cell carcinoma (RCC) and Wilms tumor (WT). Nephron-sparing surgery or partial nephrectomy is recommended in most cases, as histological evaluation is essential to differentiate it from RCC and WT [5, 12].

Primary malignant tumors

Wilms tumor

Overview

Wilms tumor or nephroblastoma accounts for at least 90% of padiatric renal tumors [5, 6]. The peak incidence is at 3–4 years of age and it is rare in neonates. The tumor is frequently sporadic in occurrence but is also known to be associated with few syndromes, namely, WAGR syndrome, Denys–Drash syndrome, and Beckwith Wiedemann syndrome, in which WT gene mutations on chromosome 11 are known to be present. Familial occurrence of the disease contributes to only 1% of the cases. The most common clinical presentation is a palpable abdominal mass; hematuria and pain are infrequent [5].

Wilms tumor arises from the metanephros and is occasionally found to arise in the extrarenal retroperitoneum, presumably within mesonephric remnants. Wilms tumor is a solid intrarenal mass with a pseudocapsule which causes distortion of the renal parenchyma and collecting system. It spreads by direct extension into adjoining structures and also more frequently displaces them [5, 6, 12]. Metastases are most commonly found in the lungs (85% of cases), liver, and regional lymph nodes [5, 6].

Imaging

Imaging contributes in the confirmation of the diagnosis and to a large extent, in staging the disease. On ultrasound, the solid mass has a heterogeneous echotexture due to areas of hemorrhage, fat, necrosis, or calcification. Particular attention to the renal vein and IVC with

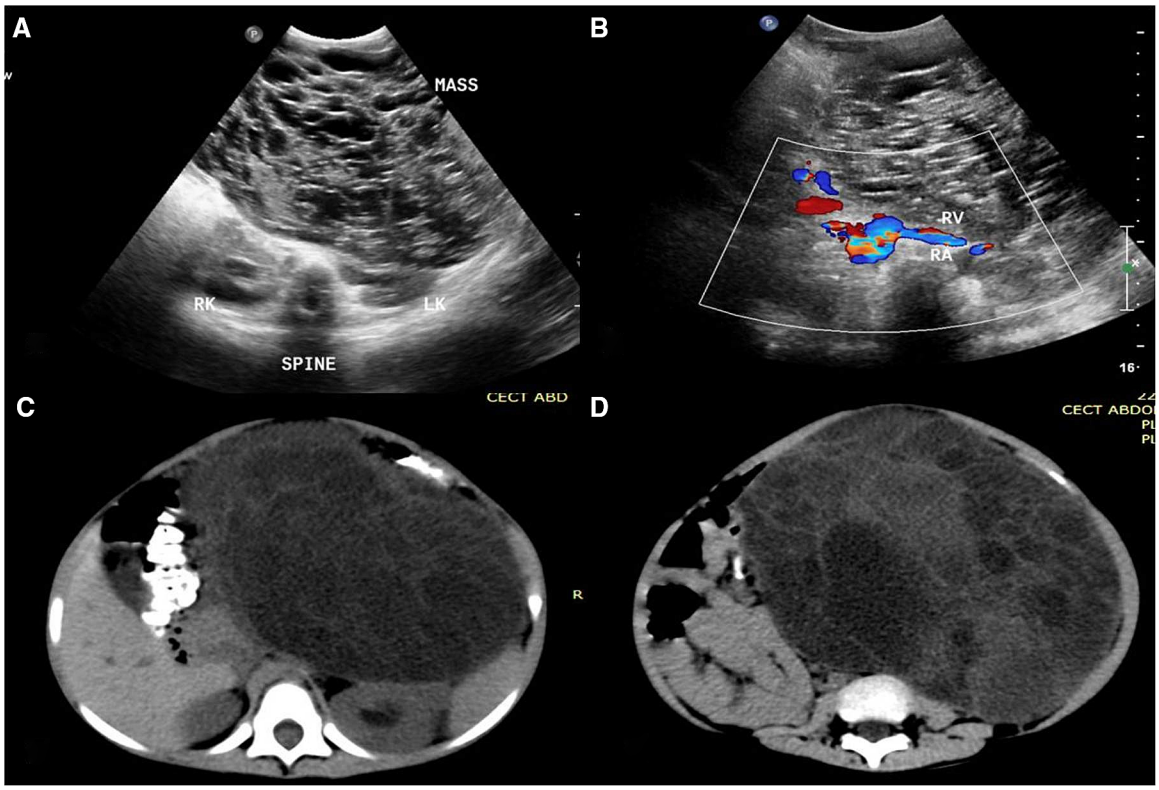
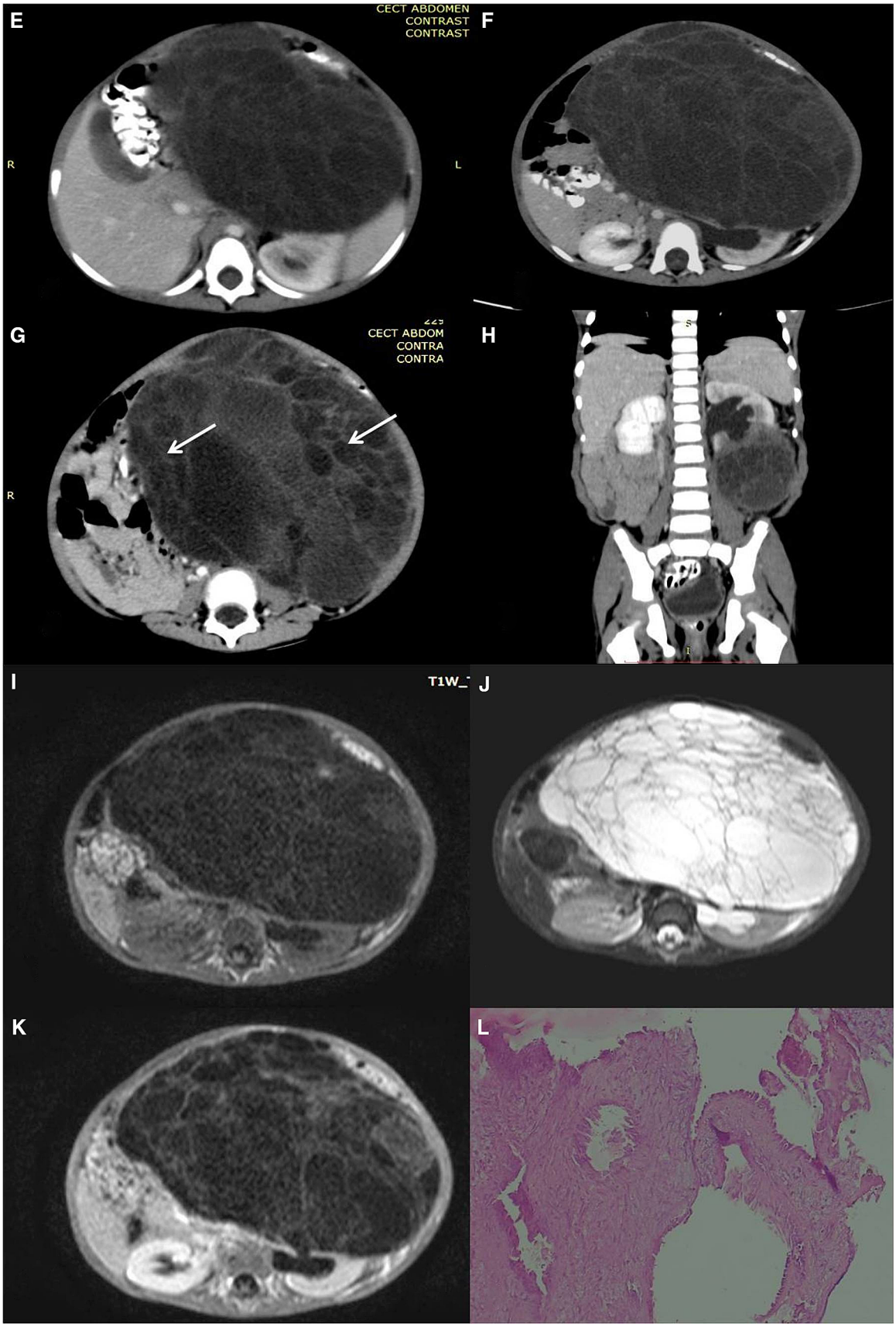


Fig. 3. **A**–**L** Imaging studies in a 4-year-old boy, with palpable left renal mass. The ultrasound (**A**, **B**) and CT study (**C**–**H**) show a large multilocular cystic tumor arising from lower pole of left kidney. The claw sign is seen in **F**. There is absence of solid component; however, faint enhancement of septa is seen (**G**; white arrows). The MRI appearances (**I**–**L**) replicate those of CT. Imaging features are characteristic of CPDN. The H&E-stained photomicrograph (**L**) shows multiple cystic spaces lined by hobnail cells, against a background of fibrous stroma consistent with diagnosis of cystic nephroma.



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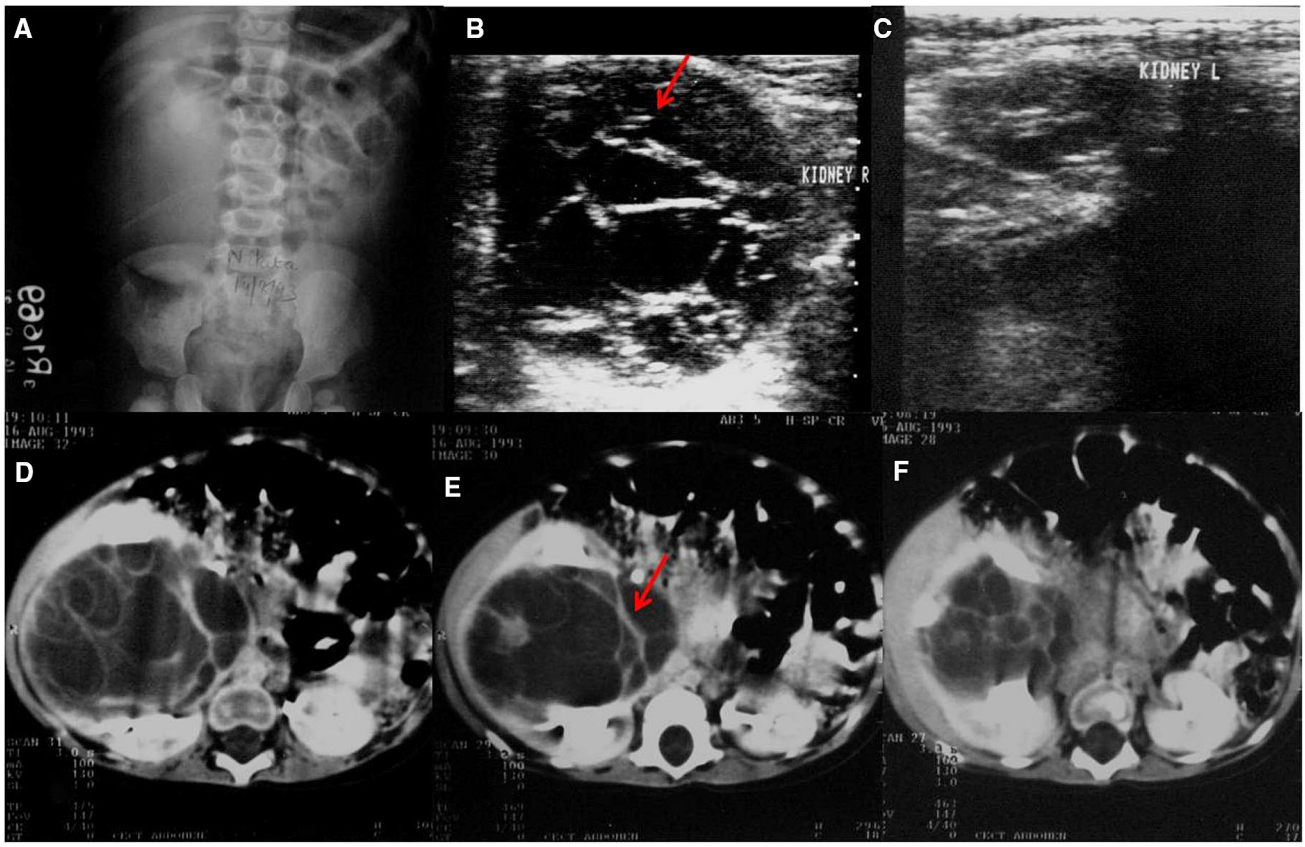


Fig. 4. **A–F** A girl of 8 months was brought with a palpable mass in the right renal angle. Radiograph of abdomen (**A**) showed a large right-sided retroperitoneal mass. Ultrasound right kidney (**B**) revealed a large multiloculated cystic mass with multiple septa (red arrow) replacing almost the entire mid and lower pole. The left kidney (**C**) was normal. CT study (**D–F**) illustrates a well-encapsulated multilocular cystic tumor with multiple enhancing septa (**E**; red arrow) and the claw sign is exquisitely demonstrated in (**D**, **e**). Diagnosis of cystic nephroma was confirmed following nephrectomy.

Table 1. Staging of Wilms tumor developed by National Wilms Tumor Study Group (NWTS)

Tumor stage	Description
I	Limited to the kidney and completely resectable with renal capsule intact; renal sinus may be infiltrated but not beyond hilum
II	Tumor infiltrates beyond kidney, completely resected; includes tumor with local spillage confined to flank
III	Residual tumor confined to abdomen, non-hematogenous; includes (a) positive abdominal nodes, (b) diffuse peritoneal contamination by direct growth, implants, or spillage, (c) positive margins, or (d) residual non-resected tumor
IV	Hematogenous disease (added: lungs, lymph nodes, liver)
V	Bilateral disease; each side should be staged separately, since prognosis is dependent on the individual stage

Doppler evaluation can help eliminate tumor extension or thrombosis into these veins. CT shows a heterogeneous mass with areas of calcification, hemorrhage, and necrosis with enhancement lower than that of the surrounding normal renal parenchyma. CT scores over ultrasound evaluation in the detection of pericapsular spread, nodal and hepatic metastases, associated nephrogenic rests, and contralateral synchronous tumor. (Figures 5, 7) MRI is considered superior to CT in detection of the latter two. The primary tumor shows low signal intensity on T1 and high signal intensity on T2-weighted images and heterogeneous mild–moderate enhancement on contrast studies [5, 8]. Occasionally, Wilms tumor may present as a predominantly cystic mass and in such cases, presence of enhancing solid nodule within it, differentiates it from other benign multilocular cystic tumors like cystic nephroma and cystic partially differentiated nephroblastoma [5].

Although the staging of Wilms developed by the National Wilms Tumor Study group (NWTS) [Table 1] is a post-operative staging system, imaging helps to pre-operatively determine the locoregional and distant spread of the tumor, with high accuracy [2]. The CT documentation of tumor rupture categorizes the tumor in stage III. CT signs of rupture described are ascites beyond the cul-de-sac, fat stranding around the tumor,

and extracapsular retroperitoneal fluid [13]. Dynamic nuclear medicine studies are vital in evaluating the functional status of each kidney both pre- and post-operatively and post-operative complications, if any. Additionally, FDG-PET scans can delineate the extent of disease both local and distant spread, evaluate residual or recurrent disease in early or delayed phase [7]. (Figures 5, 6, 7, 8)

Complete nephrectomy is the mainstay treatment of unilateral Wilms tumor followed by adjuvant chemotherapy and sometimes radiotherapy. Presurgical chemotherapy can also be used to promote tumor shrinkage and reduce the risk of hemorrhage and rupture [4, 9]. In children with bilateral Wilms tumor or tumor involving solitary kidney or horseshoe kidney, partial nephrectomy is considered the ideal treatment to preserve renal function. Cure rates and recurrence largely depend on the histological grade. Early recurrence occurs within 2 years in 15% of tumors which have a favorable histology versus 50% recurrence in those with anaplastic histology [5, 6].

The importance of thoracic evaluation in the same sitting is highlighted in patient shown in Fig. 6 who has lung metastasis and patient shown in Fig. 7 who has bilateral basal sub-segmental lung collapse. All these observations are important to the surgical and the anesthesia teams, not only in prognosis prediction and planning the surgical treatment but also for the intra-operative and post- operative respiratory care.

Differential diagnosis

The diagnostic dilemma is usually with neuroblastoma, from which Wilms tumor is distinguished by the presence of "claw sign," a characteristic feature of intrarenal origin of the tumor. Therefore other rare malignant intrarenal tumors such as renal rhabdoid tumor, clear cell sarcomas, and intrarenal neuroblastoma may also simulate a Wilms tumor. Wilms tumor has a propensity for venous thrombotic spread versus the tendency of neuroblastoma to both encase and displace the aorta and IVC. Neuroblastoma has a tendency to metastasise to the bone and bone marrow and also invade the spinal canal. Wilms tumor on the other hand, more frequently metastases to the lungs and does not invade the spinal canal.

Teaching points

1. In the presence of a solid, heterogeneous intrarenal mass with a "claw sign" in a child 1–11 years of is

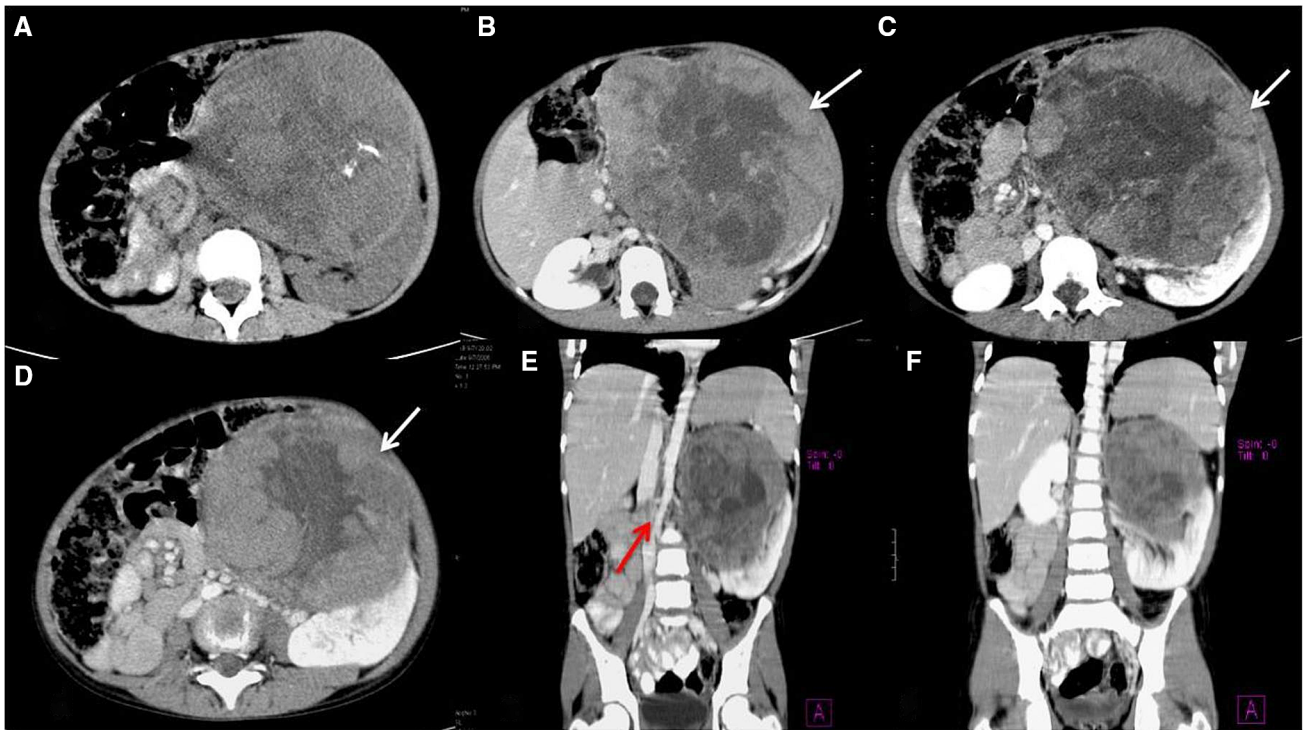


Fig. 5. **A**–**F** CT examination in a 4-year-old girl shows a left-sided Wilms tumor with evidence of calcification on non-contrast scan (**A**). The tumor shows pericapsular invasion along anterior abdominal wall (**B**, **C**, **D**; white arrow). There is evidence of para-aortic and para-caval lymphadenopathy (**B**, **C**). A large tumor thrombus is seen in the IVC (**E**; red arrow). The persistent parenchymal opacification of the normal right kidney (**F**) indicates thrombotic insult compromising its functional status.

most likely a Wilms tumor. Diagnosis of IVC and renal vein thrombus is a significant contribution of the radiologist.

2. Diligent assessment of contralateral kidney is imperative for two important aspects:

   a. Thrombotic insult to the contralateral kidney due to tumor thrombi in the IVC
   b. To rule out bilateral tumors.

3. CT of the thorax should be performed in the same sitting

   a. To rule out lung metastasis.
   b. To exclude secondary passive collapse and consolidation at lung bases in exceptionally large tumors.

4. Possibility of contiguous organ invasion into pancreas and/or diaphragm should not be underestimated as it affects the pre-operative staging and surgical planning.

Fig. 7. **A–M** Imaging studies in a 9-year-old girl with left-sided Wilms tumor: Ultrasound scan **A–D** shows a large solid mass arising from left kidney (**A**). The mass has necrotic foci within it and shows increased vascularity on color Doppler (**B**). Right kidney is normal (**C**). However, moderate ascites is present in the hepato renal pouch (**C**) and in the pelvis (**D**). NC & CECT abdomen **E–H** reveals a left renal tumor arising from lower pole. There is pancreatic invasion (**G**; red arrow) and capsular rupture (**H**; white arrow) on the anterior aspect of the tumor. The latter is substantiated by the presence of hyperattenuating ascites of 43 HU (**F**). CT thorax **I**, **J** shows bilateral sub-segmental collapse at the lung bases. MRI study (**K–M**), T1W sequence (**K**) reveals a hypointense tumor arising from the lower pole of left kidney. T1W Postcontrast scans **L** show mild contrast enhancement. T2W (**M**) sequence shows capsular rupture (red arrows) on the anterior aspect of the tumor. The H&E stain photomicrograph (**n**), shows sheets and clusters of tumor cells with scant cytoplasm with few of these cells showing rosette formation (**N**; black arrows). On immunohistochemistry, these cells were positive for WT1, confirming the diagnosis of Wilms tumor.

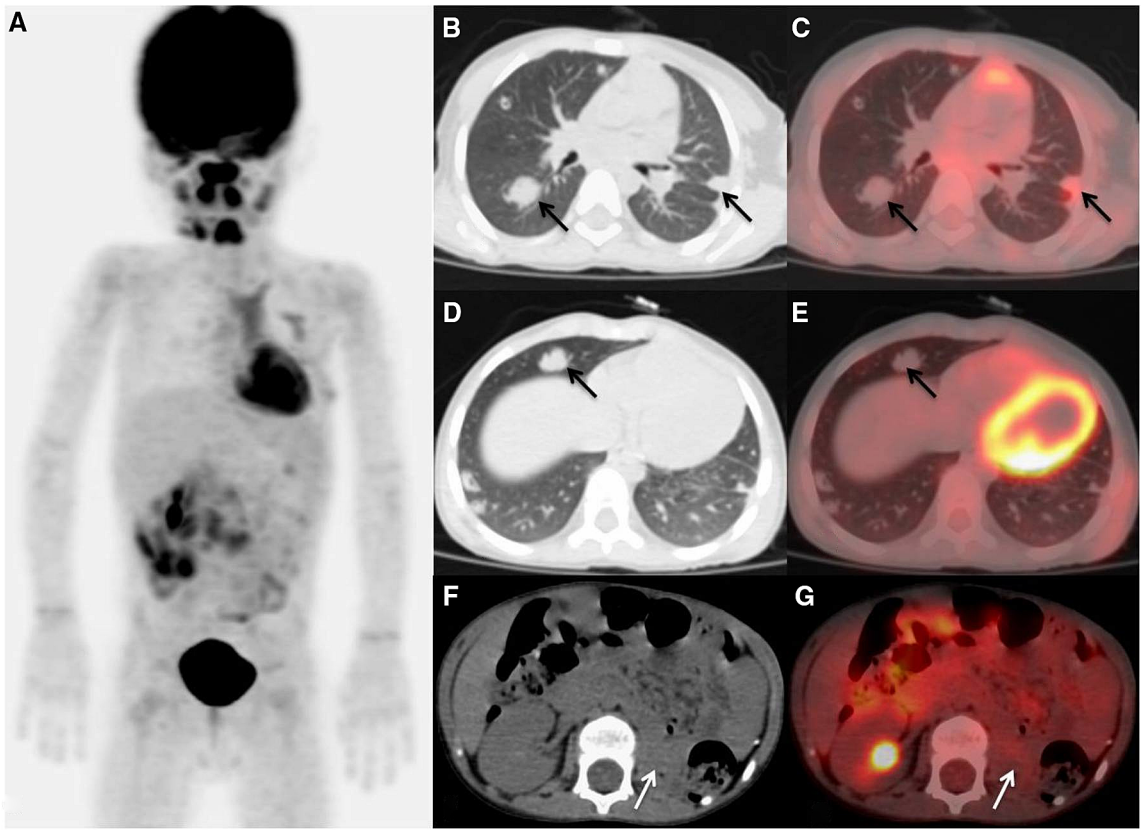
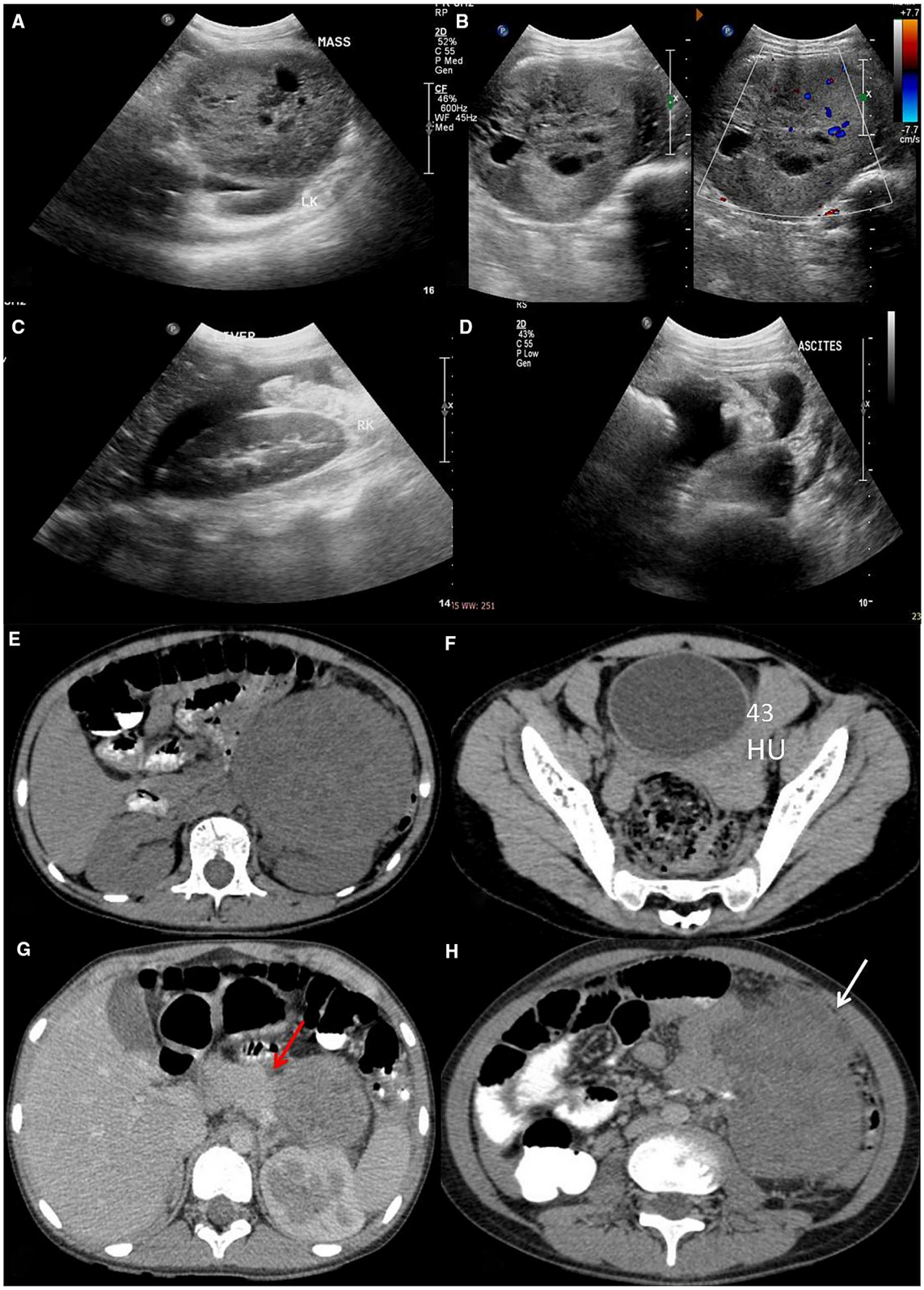


Fig. 6. **A–G** Whole body F-18 FDG-PET/CT in a 4-year-old boy at 18 months post left nephrectomy, for Wilms tumor: Projection image **A** shows physiological uptake in brain, neck lymphoid tissue, heart, right kidney, and urinary bladder. Axial CT and PET/CT of thorax **B–E** show multiple pulmonary nodules (black arrows) in both lungs which exhibit mild FDG uptake. Abdomen scans (**F**, **G**) show absence of left kidney (white arrows). The appearances are consistent with bilateral pulmonary metastases during late follow-up period.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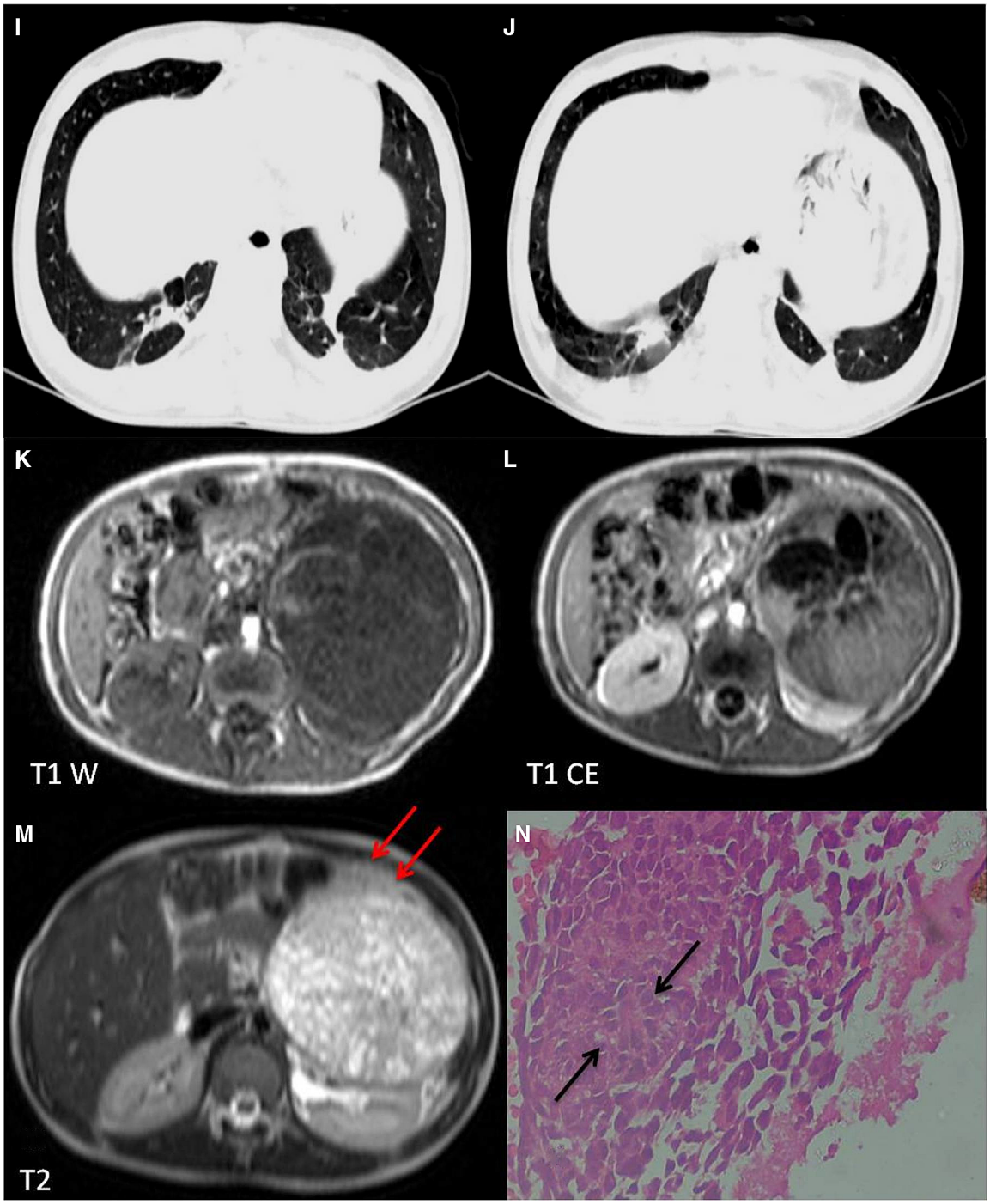


Fig. 7. continued.

Nephroblastomatosis

Diffuse or multifocal reniform involvement by persistent of embryonic nephrogenic rests is termed as nephroblastomatosis. This condition predisposes to Wilms tumor and multiple syndromes like Beckwith–Wiedemann, Perlman, and trisomy 18, mandating screening in these patients. On CT, it appears as multiple hypodense hypoenhancing peripheral nodules, which on MR imaging show hypointense T1- and T2-weighted signals and is probably better than CT for detecting the multiple foci [4, 5, 8]. The tumor closely mimics imaging appearance of lymphoma. Presence of generalized lymphadenopathy favors a diagnosis of lymphoma [4, 5].

Rhabdoid tumor

Rhabdoid tumor is a highly aggressive malignant tumor accounting for less than two percent of all pediatric renal masses. Majority of patients are less than 2 years of age with peak incidence at 11 months and has slight male predominance. Patient presents with fever and hematuria. On imaging, rhabdoid tumor appears as an enhancing soft tissue mass with typical subcapsular fluid collections, linear calcifications, hemorrhage, and necrosis. Distinct lung metastasis and associated synchronous and metachronous primary intracranial neoplasm are known to occur. Management includes surgical resection with adjuvant chemotherapy [5, 8].

Renal cell carcinoma

Renal cell carcinoma is an extremely rare tumor in young children. It usually occurs in adolescents with an average age of 10–11 years. Bilateral RCC in young children warrants thorough investigation for search of von Hippel–Lindau syndrome. Patients present with classical clinical features which include gross, painless hematuria, flank pain, and presence of palpable abdominal mass. Imaging findings are similar to the Wilms tumor, thus requiring histologic examination for further differentiation [5, 8].

Clear cell sarcoma

It occurs in children from 1 to 4 years of age, presenting as abdominal mass, pain, or hematuria. On ultrasound and CT, it appears as well-circumscribed solid renal mass. It cannot be differentiated from Wilms tumor on imaging alone; however, vascular invasion is less common in clear cell sarcoma [8].

Renal medullary carcinoma

It is a rare aggressive renal malignancy, having strong association with sickle cell trait. On imaging, there is a centrally located soft tissue mass with heterogeneous enhancement, ill-defined infiltrative margins. Associated lymphadenopathy and vascular invasion is common. The reniform shape is however preserved [8].

Metastatic lesions

Lymphoma

Overview

Primary lymphoma in the kidney is unlikely as the renal parenchyma does not contain lymphatic vessels. However, secondary involvement of the kidneys by hematogenous spread is more common and it is reported that these are the most frequently involved structures outside the lymphoreticular system. A less frequent occurrence is renal involvement by direct retroperitoneal infiltration from diseased lymph nodes [14]. Non-Hodgkin lymphoma, especially Burkitt's lymphoma, is more likely to involve the kidney. Clinically, renal involvement by lymphoma remains occult, as the symptomatology of the primary disease is profound.

Detection of renal involvement is important as extensive lymphomatous infiltration of the renal parenchyma and compression of the normal tubules can lead to acute renal failure. Furthermore, recurrence in the kidney is associated with an increased mortality rate [14]. Lymphoma is sensitive to chemotherapy, although surgical debulking and radiation therapy may also be needed [2].

Imaging

Ultrasound is recommended in all children with leukemia/lymphoma prior to commencement of chemotherapy to exclude renal infiltration [15]. Lymphomatous involvement of the kidney may appear as solitary or multiple renal masses or nodules, diffuse infiltration, direct invasion from contiguous retroperitoneal extension, and least commonly as isolated perinephric disease. Diffuse infiltration of the kidney may result in reniform enlargement. Retroperitoneal disease occasionally leads to vascular and ureteral encasement [15].

Imaging findings are variable and may often be subtle. On ultrasound, the kidneys may appear diffusely enlarged or may show single or multiple hypoechoic nodules. On CT, the kidneys are usually enlarged and homogeneously hypoattenuated on non-enhanced with hypoenhancement on contrast-enhanced images [15]. Added advantage of CT over ultrasound is that it can reveal concomitant lymph nodes and involvement of other organs [8]. MR is reserved for patients in whom iodinated contrast agents are contraindicated due to renal impairment as otherwise its accuracy is similar to that of contrast-enhanced CT [12]. FDG-PET scores over CT/MRI for initial staging of the disease, predicting response both during and after chemotherapy and for identifying residual and recurrent disease [7]. (Figures 9, 10)

Differential diagnosis

Renal infiltration by lymphoma resembles leukemia, the two cannot be differentiated on imaging alone and therefore need correlation with hematological profile for final diagnosis. Occasionally, nephroblastomatosis needs

differentiation from renal infiltration by leukemia and lymphomas as these may have similar imaging findings of bilateral nodular lesions and diffuse nephromegaly. The clinical setting of known hematological malignancies and that of associated syndromes of nephroblastomatosis is important in arriving at the diagnosis of each, respectively [5].

Teaching points

1. Renal involvement should always be excluded by the radiologist when a patient of lymphoma is referred for radiological evaluation.
2. The presence of renal involvement in lymphoma is of clinical significance as the possibility of acute renal failure increases with renal involvement. Furthermore, increased mortality is known in patients with renal recurrence.

Leukemia

Overview

Leukemic infiltration of kidneys occurs most often from acute lymphoblastic leukemia (ALL) which is the most common malignancy in children. Although leukemic infiltration occurs frequently in bone marrow, spleen, lymph nodes, and liver, renal involvement can also occur, in the form of renal enlargement with renal failure. The latter is usually not detected at the time of diagnosis of leukemia. Leukemic infiltration of the kidneys is more common in the late stage of ALL, and is reported to occur in 7–42% of childhood leukemia cases [16].

Acute renal failure can occur due to leukemic infiltration of the kidneys. However, therapy-related side effects, metabolic changes arising from chemotherapy, nephrotoxic drugs, and septicaemias may also cause acute kidney injury in leukemia patients [16].

Imaging

The imaging appearances of renal involvement in leukemia, are not very specific. Both ultrasound and CT show diffuse bilateral nephromegaly with loss of corticomedullary differentiation. Presence of focal renal mass is unusual [5]. Although bilateral involvement is the rule, isolated cases with unilateral nephromegaly have also been reported [17]. (Figure 11)

Differential diagnosis

Leukemic infiltration of kidneys cannot be differentiated from that of lymphoma on imaging alone, although nodular foci are reportedly more frequent in lymphoma.

Fig. 8. **A–C** Serial renal dynamic studies obtained using Tc99 m-Ethylene cystine in a patient with left Wilms tumor who underwent partial nephrectomy. **A** is pre-operative scan which shows normal perfusion in right kidney and absent perfusion in left kidney (upper two rows). Serial images (lower two rows) show normal uptake, drainage, and function (87.8%) in the right kidney, which is reflected in the renogram (green) curve. The left kidney shows small area of radiotracer uptake with poor function (12.2%) due the presence of Wilms tumor, which is reflected in the renogram (red) curve. **B** is early post-operative scan which shows normal perfusion in right kidney and restored but poor perfusion in left kidney (upper two rows). Lower two rows show normal uptake, drainage, and function (75%) in right kidney, also seen in renogram (green) curve. Residual lower pole of left kidney shows restored but poor function (24.5%) demonstrated by fair radiotracer uptake, also seen in renogram (red) curve. However, there is leak from the operated site, shown by gradual accumulation of radiotracer over a period of time (red arrows). **C** is delayed post-operative scan done at 8 weeks, shows normal perfusion in right kidney and restored but poor perfusion in residual lower pole of left kidney (upper two rows). Lower two rows show normal uptake, drainage, and function (74.7%) in the right kidney, also seen in the renogram (green) curve. Residual lower pole of left kidney shows fair radiotracer uptake with restored function (25.3%), also seen in the renogram (red) curve. The urine leak which was seen the early post-operative study (**B**), now shows complete resolution.

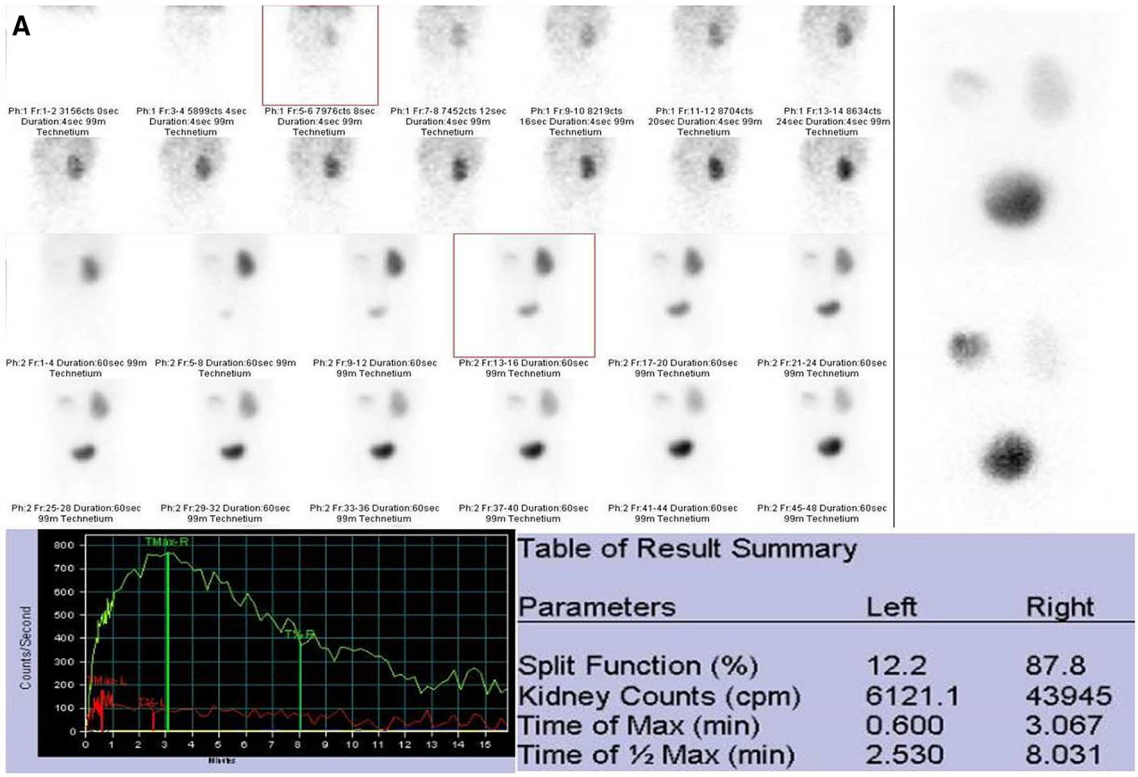
Teaching points

1. The radiologist may be the first one to alert the clinician of the possibility of leukemia in a child under evaluation for pyrexia of unknown origin associated with anemia.
2. Clinical significance of detecting leukemic infiltration of kidneys in known leukemia is to rule it out as a cause of renal impairment in leukemia patients.

Contiguous invasion by malignant disease

Neuroblastoma invading kidney

Renal invasion by neuroblastoma has been reported in about 20% cases of abdominal neuroblastoma [18]. Sometimes, an adrenal neuroblastoma invading the kidney may appear like an intrarenal mass. Adrenal neuroblastoma should be differentiated from Wilms tumor which is a primary intrarenal mass and forms a typical claw sign with the kidney. Wilms tumor has propensity for venous thrombotic spread versus the tendency of neuroblastoma to both encase and displace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Counts/Second
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Kidney Counts (cpm) 6121.1 43945
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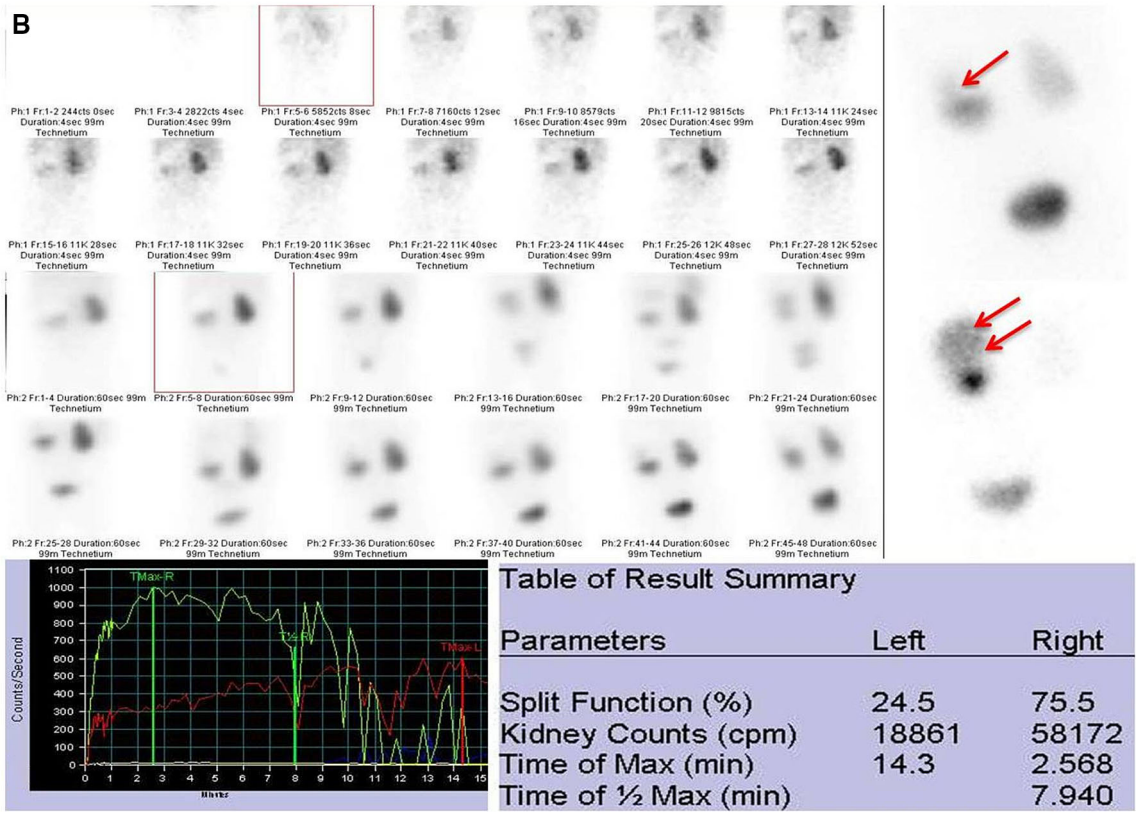
Time of ½ Max (min) 2.530 8.031


B
Counts/Second
TMax-R
TMax-L
Table of Result Summary
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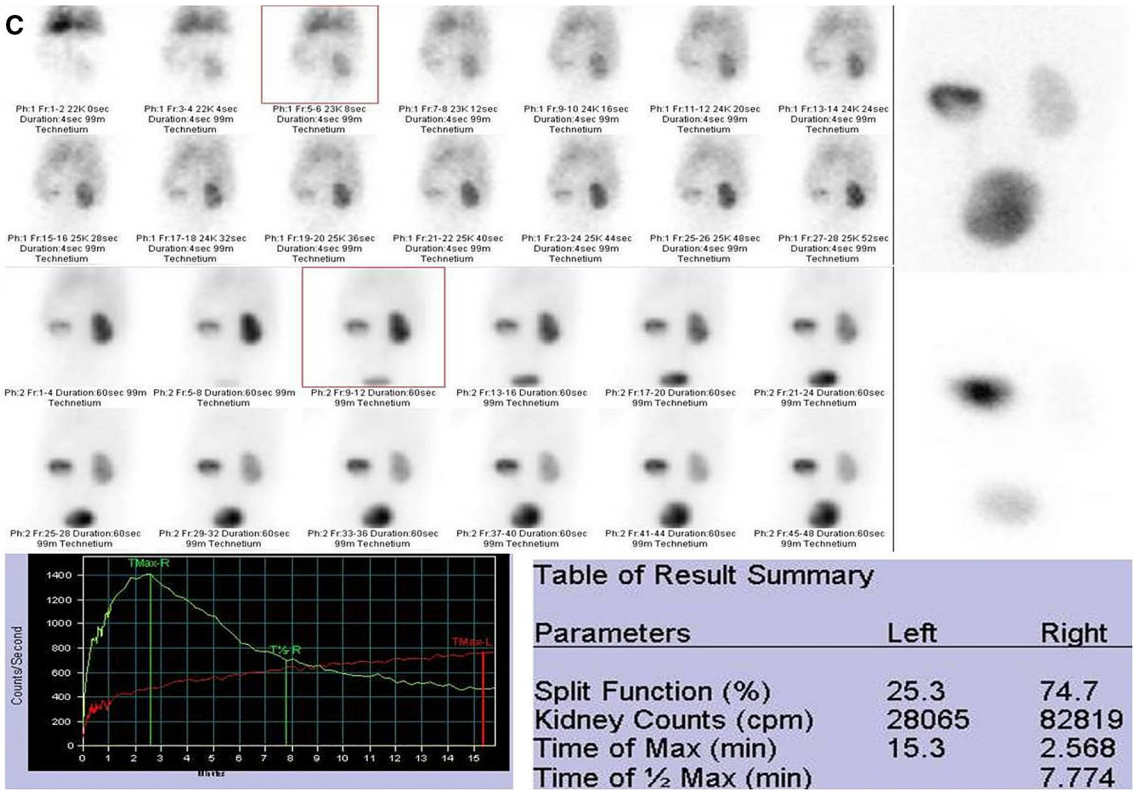
Kidney Counts (cpm) 18861 58172
Time of Max (min) 14.3 2.568
Time of ½ Max (min) 7.940



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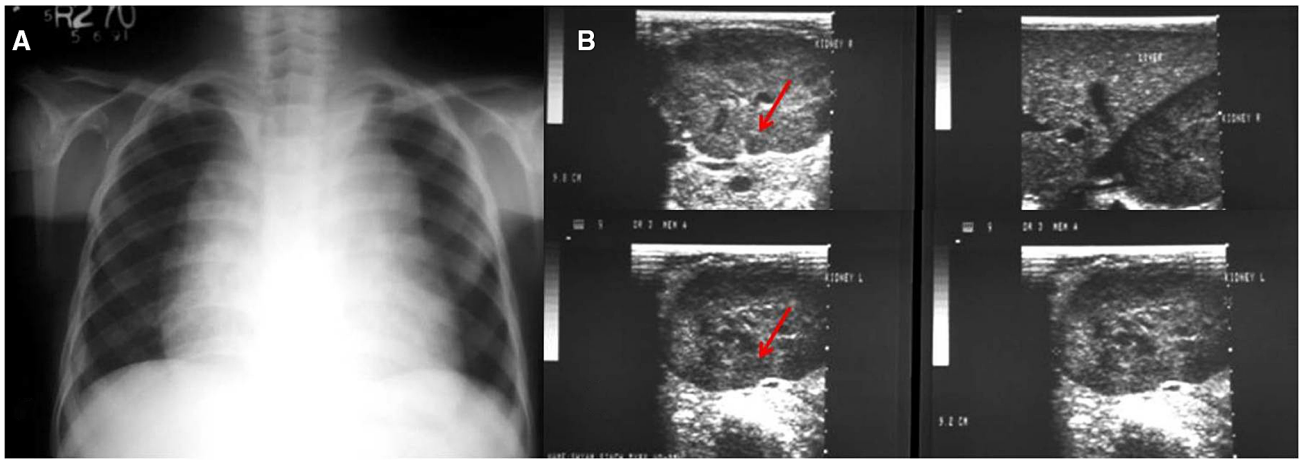


Fig. 9. **A**, **B** Chest radiograph (**A**) and the ultrasound examination of the abdomen (**B**) in a boy of 5 years who is a known case of lymphoma, shows mediastinal lymphadenopathy (**A**) and that both kidneys are enlarged (**B**). There is a mild diffuse increase in echogenicity in both kidneys with multiple hypoechoic nodules (**B**; red arrows) seen bilaterally.

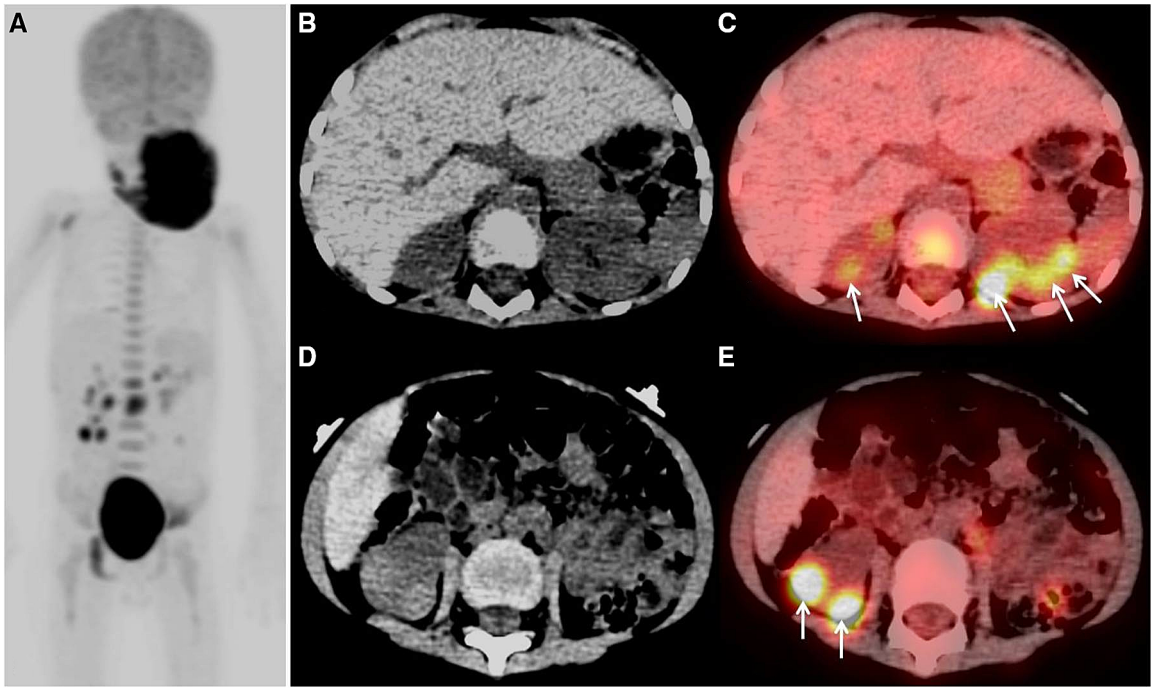


Fig. 10. **A**–**E** Whole body Fluorine 18 Fluorodeoxyglucose (F-18 FDG) Positron emission tomography/computed tomography (PET/CT) scan of a 2-year-old child with Burkitt's Lymphoma; whole body projection image **A** shows uptake in the nodal mass in the neck along with physiological uptake in both kidneys and urinary bladder. Axial section of CT and PET/CT of abdomen **B**–**E** shows multiple lymphomatous infiltration of both kidneys (white arrows).

the aorta and IVC. Neuroblastoma has a tendency to metastasise to the bone and bone marrow and also invade the spinal canal. Wilms tumor on the other hand, more frequently metastases to the lungs and does not invade the spinal canal [19]. (Figure 12)

Conclusion

Besides Wilms tumor, a wide variety of renal tumors can affect the pediatric kidneys, which can be primary benign tumors, primary malignant tumors, metastatic lesions, and also contiguous invasion by malignant disease. The characteristic imaging appearances which accurately confirm the diagnosis have been enumerated for a majority of these entities. The leading role of the Radiologist in primary and accurate diagnosis of malignant renal infiltration by hematological malignancies and in contiguous invasion by neuroblastoma has been unveiled. As the mainstay of treatment for the primary benign and primary malignant tumors is surgical, the vital contribution of Radiologist in assessing the pul-

Fig. 12. **A**–**H** A 5-year-old girl with abdominal heaviness and pain. NCCT scan **A** shows a large ill-defined mass in the region of left adrenal gland with multiple foci of calcification (yellow arrow). Contrast CT studies **B**–**D** show an ill-defined, poorly enhancing retroperitoneal mass lesion, which crosses the midline, encases the aorta (**H**; white arrow), and displaces it anteriorly. The more caudal scans **E**–**H** show tumor. ▶

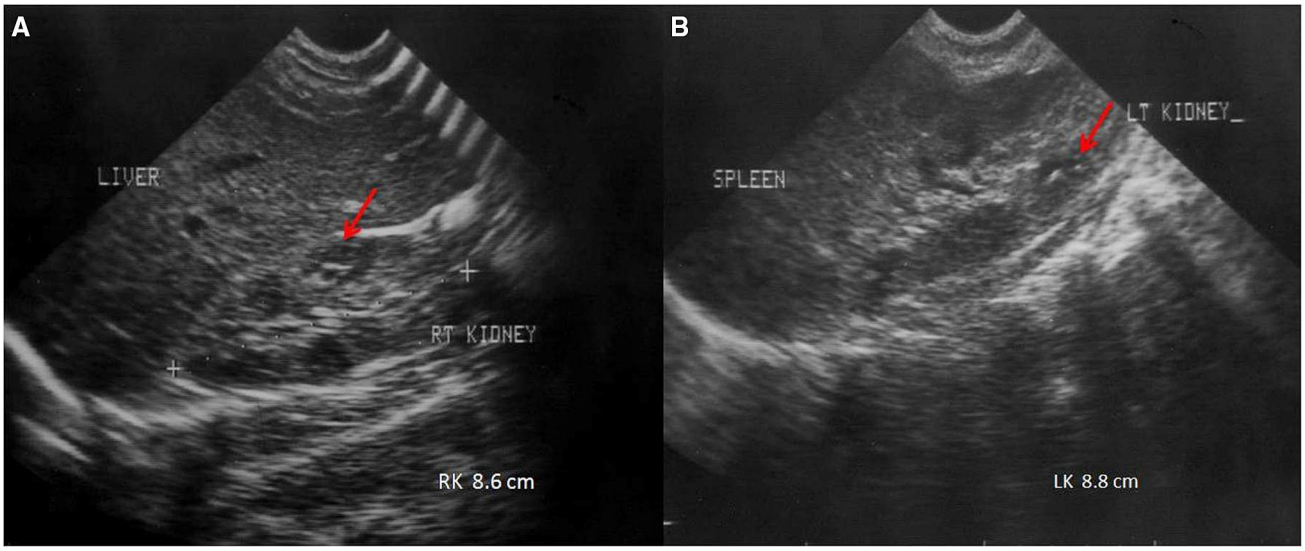
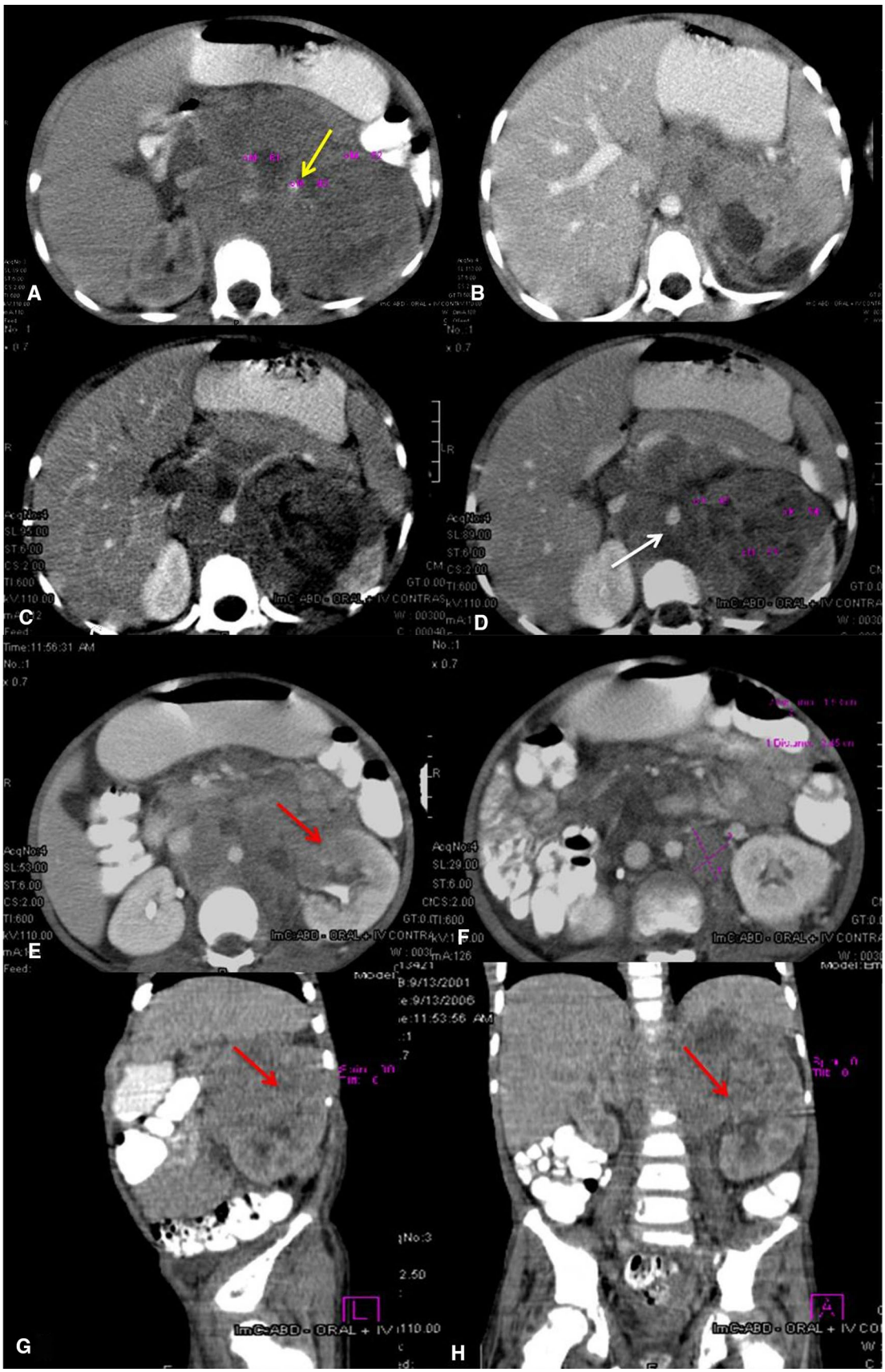


Fig. 11. **A**, **B** Ultrasound examination of the abdomen in a boy of 6 years, who is known case of acute lymphoblastic leukemia, shows both kidneys are enlarged attaining adult size, which is 8.6 cm on the right (**A**) and 8.8 cm on the left side (**B**). There is mild diffuse increased echogenicity in both kidneys, with multiple hypoechoic nodules seen bilaterally (red arrows). The spleen is also enlarged.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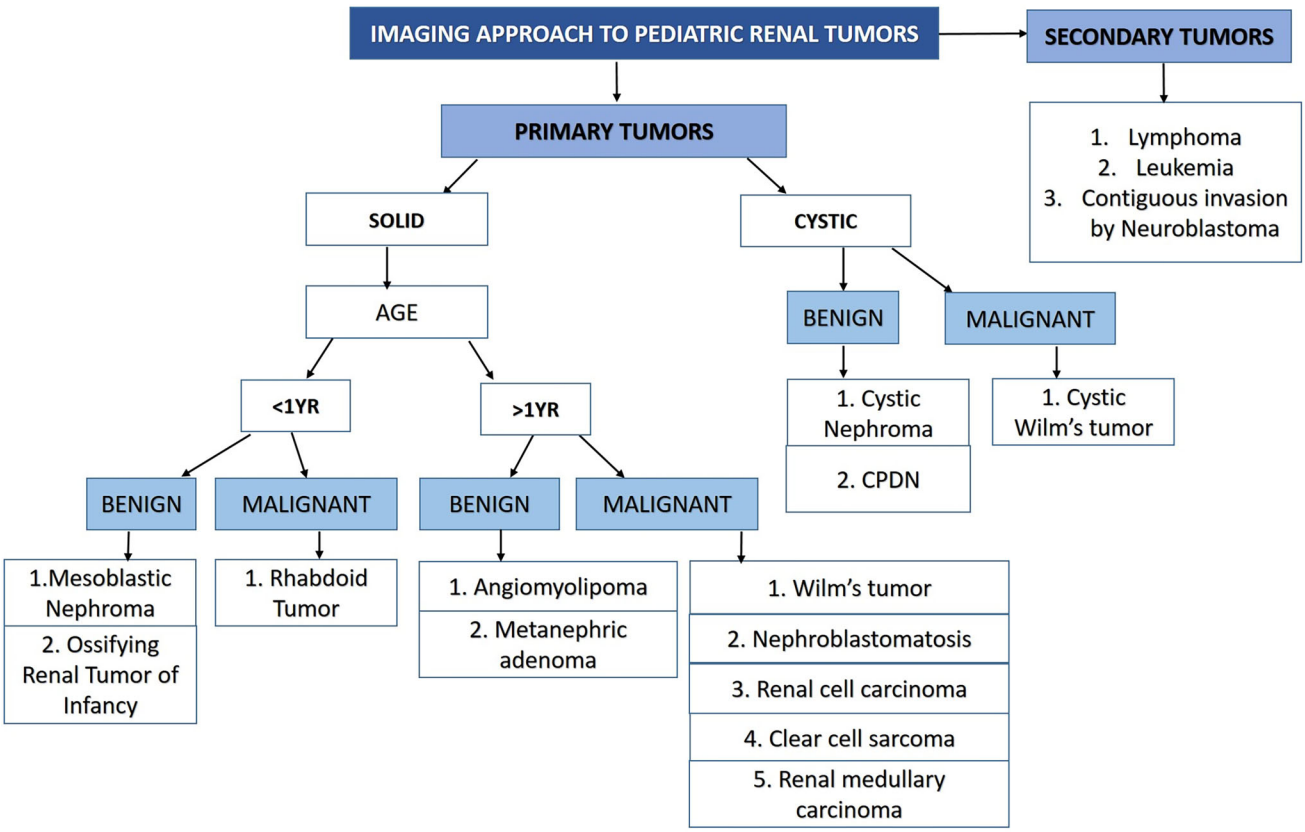

Fig. 13. Imaging approach to pediatric renal tumors.

Table 2. Imaging approach to pediatric renal masses

Renal tumor	Age	Single/multifocal	Laterality	Location	Calcification
Mesoblastic nephroma	Infants < 3 months	Single	Unilateral	Renal sinus is commonly involved. Perinephric extension may be seen	Uncommon
Ossifying renal tumor of infancy	Infants	Single	Unilateral	Arises from renal medulla	Ossified matrix
Rhabdoid tumor	< 2 years	Single	Unilateral	Arises from renal medulla	Curvilinear, outlining tumor lobules
Angiomyolipoma	In children with TSC	Multiple Bilateral if associated with TSC	Bilateral Common in TSC patients	–	Absent
Metanephric adenoma	Children and adults	Single	Unilateral	Cortex	±
Wilms tumor	1–11 years (peak 3–4 years)	Single or multiple (in patients with nephroblastomatosis or syndromic associations)	Bilateral in 4–13% (in patients with nephroblastomatosis or syndromic associations)	–	Present in 9%–15%
Nephroblastomatosis	12–15 months	Multiple	Often bilateral	Cortex	Absent
Renal cell carcinoma	6 months–60 years	Single; Multiple if associated with VHL	Bilateral if associated with VHL	–	Present in 25%
Clear cell sarcoma	1–4 years	Single	Unilateral	Medulla	Not common
Renal medullary carcinoma	10–39 years	Single	Unilateral	Renal pelvis	Not common
Cystic Nephroma	3 months to 4 years	Single or multiple (in patients with nephroblastomatosis or syndromic associations)	Bilateral in patients with nephroblastomatosis or syndromic associations	–	Wall or septal calcification may be present
CPDN	Young females, but can occur in children also	Single	Unilateral	–	Wall or septal calcification may be present
Cystic Wilms tumor	1–11 years (peak 3–4 years)	–	–	–	±
Leukemia	Any age	Multiple	bilateral ≫ unilateral	–	Absent
Lymphoma	Any age	Multiple ≫ solitary	Bilateral > unilateral	–	Absent
Contiguous invasion by Neuroblastoma	< 7 years Peak 16 months	Single	Unilateral	Suprarenal region with invasion of the upper pole of the ipsilateral kidney	Common 80–90%

Table 2. continued

Renal tumor	Echotexture solid/cystic	Doppler	CT	MR (additional advantage)	Associated features
Mesoblastic nephroma	Solid	No invasion of renal vein	Ill-defined margins with variable enhancement	–	–
Ossifying renal tumor of infancy	Solid	No invasion of renal vein	Hypoenhancing ossified renal mass	–	–
Rhabdoid tumor	Solid	IVC and renal vein invasion may be seen	Lobulated, enhancing mass, with indistinct margins, containing hemorrhage, and necrosis Renal subcapsular hemorrhage. Lung, liver, skeletal mets	Evaluation of brain if patient is having neurological symptoms	Synchronous or metachronous primary intracranial malignancy or metastasis
Angiomyolipoma	Solid	Abnormal intratumoral vessels, pseudoaneurysm	Fat rich < -10 HU Fat poor and fat invisible types > -10 HU. Park [11] Presence of abnormal vessels Can be complicated with presence of retroperitoneal hemorrhage	Chemical shift imaging useful for identifying fat poor AML	Systemic features of TSC
Metanephric adenoma	Solid Rarely cystic with mural nodule	No invasion of IVC or renal vein	Well-defined hypoenhancing mass	–	–
Wilms tumor	Solid Rarely cystic (refer below)	Invasion of IVC and renal vein common	Heterogeneously enhancing infiltrative mass with areas of hemorrhage, necrosis, fat, calcification (9%) Lung metastasis	More sensitive for caval patency, locoregional invasion, and multifocality	–
Nephroblastomatosis	Solid	No invasion of IVC **or** renal vein	Multiple peripherally arranged hypoenhancing nodules	Tl and T2 hypointense, more sensitive for multifocality	Suspect Wilms if associated with regional lymphadenopathy
Renal cell carcinoma	Solid	Invasion of IVC and renal vein common	Heterogeneously enhancing infiltrative mass with areas of calcification (25%), hemorrhage, cystic degeneration. Metastasis to lymph nodes, lung, bone, liver, brain	–	–
Clear cell sarcoma	Solid	No invasion of IVC or renal vein	Well-defined solid intrarenal mass. Metastasis to bones, lymph nodes, brain, liver, and lungs	–	–
Renal medullary carcinoma	Solid	May invade IVC or renal vein	Centrally located heterogeneously enhancing infiltrative mass. Peripheral satellite nodules	–	Common in patients with Sickle cell trait
Cystic Nephroma	Cystic multiseptated	No invasion of IVC or renal vein	Multiloculated cystic tumor with minimally enhancing septae	Septae better delineated on MR Useful to exclude presence of solid components	–
CPDN	Cystic Multiseptated	No invasion of IVC or renal vein	Multiloculated cystic tumor with minimally enhancing septae	Septae better delineated on MR Useful to exclude presence of solid components	–
Cystic Wilms tumor	Cystic with solid component	May invade IVC or renal vein	Multiloculated cystic tumor with enhancing septae and solid mural nodule	Better delineation of septae and solid component	–

Table 2. continued

Renal tumor	Echotexture solid/cystic	Doppler	CT	MR (additional advantage)	Associated features
Leukemia	Nephromegaly with loss of corticomedullary differentiation; Less commonly multiple nodules	–	Diffuse bilateral nephromegaly with loss of corticomedullary differentiation. Presence of focal renal mass is unusual	–	–
Lymphoma	Diffuse enlargement or multiple iso to hypoechoic nodules or contiguous invasion from RP lymphadenopathy	–	Kidneys are usually enlarged and homogeneously hypoattenuated with hypoenhancement on contrast-enhanced images or multiple hypoenhancing nodules. Useful for staging the disease	–	Lymphadenopathy and associated hepatosplenomegaly
Contiguous invasion by Neuroblastoma	Solid	Encasement of vessels and uplifting of aorta	Poorly marginated heterogeneously enhancing mass with areas of calcification within. Absence of claw sign with the kidney	Spinal canal and bone marrow involvement better depicted on MRI	–

monary status for intra-operative and post-operative patient prognosis has been emphasized. The Synergistic role of nuclear medicine studies both in pre-treatment and early post-treatment prognosis and in the late follow-up has also been adequately highlighted. The imaging algorithm suggested by us is summarized in Fig. 13 and Table 2.

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