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PEDIATRIC RADIOLOGY

PICTORIAL ESSAY

Imaging findings of primary adrenal tumors in pediatric patients

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ABSTRACT

Apart from neuroblastomas, adrenal tumors are rarely seen in children. The most common adrenal tumors are adrenocortical carcinoma and pheochromocytoma. Adrenocortical carcinoma is usually a large heterogeneous, well-marginated mass with solid/cystic areas and calcifications, with poor prognosis. Most of the pheochromocytomas are benign tumors and usually show intense contrast enhancement, the pattern of which may be diffuse, mottled, or peripheral on computed tomography and magnetic resonance imaging. The purpose of this article is to evaluate primary nonneurogenic adrenal tumors.

In children, neoplastic and non-neoplastic lesions might be seen in the adrenal region. Pediatric adrenal lesions may be found incidentally, can be suspected in children that suffer endocrine, metabolic, neurological problems or with an abdominal mass. In fetal life, adrenal glands are much larger than in adults because of the existence of a prominent fetal cortex. Their prominent fetal size is also seen in early neonatal life. Ultrasonography (US) is the initial imaging technique to examine the adrenal glands in newborns. In older children, due to the physiologic atrophy of the fetal adrenal cortex, adrenal limbs are thinner than the adjacent crura of the diaphragm. Consequently, they are much more difficult to specify with US, but can be easily identified on computed tomography (CT) or magnetic resonance imaging (MRI). US is the primary modality for imaging the pediatric abdomen. CT or MRI are used as a problem-solving tool for lesion characterization, to determine the relationship to adjacent tissues, and to differentiate benign from malignant masses after initial US evaluation (1). In older children MRI should be preferred rather than CT examination. In adults, abdominal CT examinations assess tumor washout of contrast material based upon multi-phase CT, which is necessary to characterize adrenocortical masses (especially adenomas). However, pediatric CT examinations should be done in single portal venous phase to comply with "Image Gently" and "as low as reasonably achievable" (ALARA) principles.

Primary adrenal tumors are classified according to their origin and function. They might originate from the medulla or cortex, and they are hyperfunctioning or nonfunctioning. Primary medullary tumors encompass a spectrum of sympathetic neuroectodermal tumors, which are neuroblastoma, ganglioneuroblastoma, ganglioneuroma, and pheochromocytoma, all of which stem from the neural crest and may take place anywhere along the sympathetic chain aside from the adrenal gland itself. Neoplasms arising from the adrenal cortex are adrenocortical carcinoma and adenoma.

In the literature, few studies have reported imaging findings of pediatric adrenal tumors, including all types of involvement (i.e., benign, malignant, and metastatic) (1–3). The aim of this article is to describe the imaging findings of primary nonneurogenic adrenal tumors.

Adrenal tumors

Adrenal neoplasms, apart from the neurogenic tumors, are rare in childhood, and they display different histological spectrum and better clinical outcomes compared to the adult patients. Much more has been reported from the clinical and surgical perspectives and less

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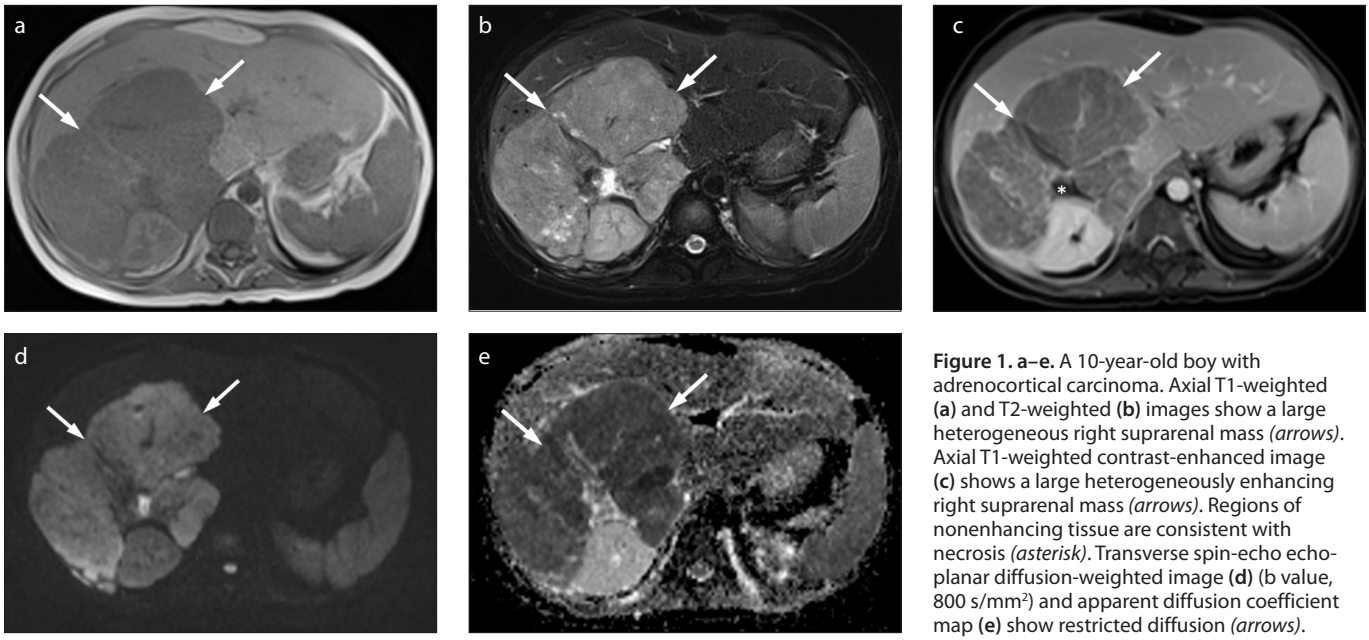

Figure 1. a–e. A 10-year-old boy with adrenocortical carcinoma. Axial T1-weighted **(a)** and T2-weighted **(b)** images show a large heterogeneous right suprarenal mass *(arrows)*. Axial T1-weighted contrast-enhanced image **(c)** shows a large heterogeneously enhancing right suprarenal mass *(arrows)*. Regions of nonenhancing tissue are consistent with necrosis *(asterisk)*. Transverse spin-echo echo-planar diffusion-weighted image **(d)** (b value, 800 s/mm^2) and apparent diffusion coefficient map **(e)** show restricted diffusion *(arrows)*.

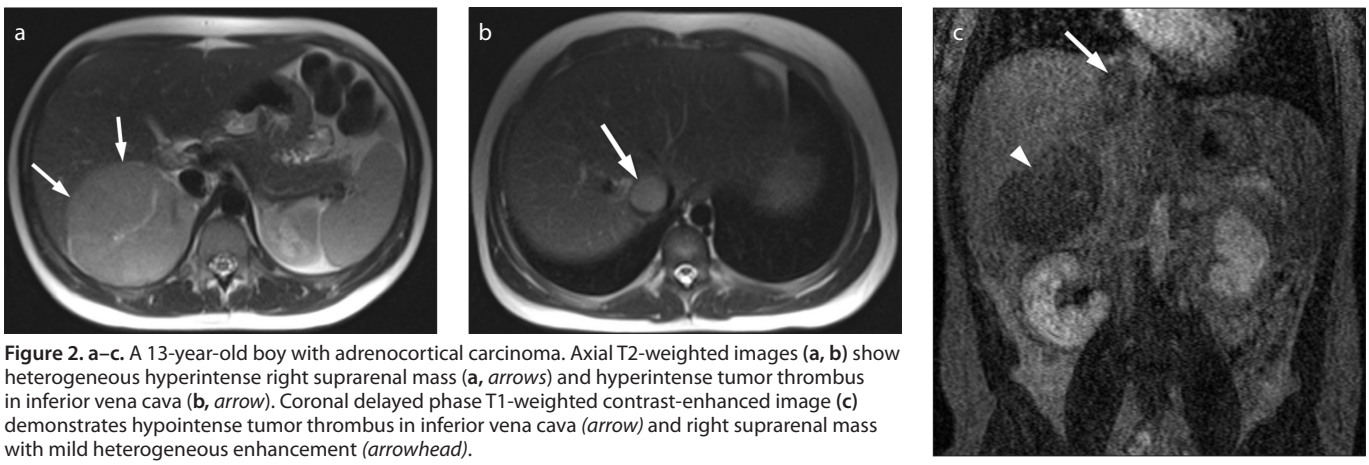

Figure 2. a–c. A 13-year-old boy with adrenocortical carcinoma. Axial T2-weighted images **(a, b)** show heterogeneous hyperintense right suprarenal mass (**a,** *arrows*) and hyperintense tumor thrombus in inferior vena cava (**b,** *arrow*). Coronal delayed phase T1-weighted contrast-enhanced image **(c)** demonstrates hypointense tumor thrombus in inferior vena cava *(arrow)* and right suprarenal mass with mild heterogeneous enhancement *(arrowhead)*.

about imaging findings (4–6). The most frequently detected pediatric primary adrenal tumors are adrenocortical carcinoma and pheochromocytoma.

Adrenocortical carcinoma

Adrenocortical carcinoma constitutes less than 1% of malignancies in the childhood (7). Patients with adrenocortical carcinoma can manifest with findings linked to hormonal overproduction (typically virilization in girls), and pseudoprecocious puberty in boys with or without Cushing syndrome. Rarely, patients can present with abdominal pain or a palpable mass. Adrenocortical carcinoma incidence has been estimated at 0.3 per million children annually with two peaks, i.e., below the age of 5 and above the age of 10 years, whereby girls are more frequently involved than boys (8). In our country, Turkish Pediatric Cancer Registry shows that 0.18% of childhood cancers are adrenocortical carcinoma (9). Children with adrenocortical carcinoma can be found in association with two genetic syndromes: Beckwith-Wiedemann and Li-Fraumeni (10). Generally, 5-year survival of adrenocortical carcinoma is better in children than in adults, at almost 50% (8). Favorable prognostic factors are younger age (<4 years), low stage at diagnosis, tumor volume <200 cm^3, and virilization alone (11). Radiological findings that suggest the diagnosis of adrenocortical carcinoma are size of tumor >8.5 cm, volume of tumor >212.5 mL, heterogeneous structure, and typically heterogeneous contrast enhancement corresponding to hemorrhage, necrosis, intratumoral calcifications, local invasion, and distant metastasis (Figs. 1 and 2) (12). However, the shortage of these findings does not rule out carcinoma in the differential diagnosis (2). On MRI, diffusion-weighted images (DWI) have been used with increasing frequency in the abdomen. Miller et al. (13) reported that benign adrenal lesions can not be distinguished from malignant lesions using DWI because of considerable overlap in apparent diffusion coefficient values.

Main points

- Adrenocortical carcinoma is a heterogeneous tumor with necrosis and calcifications.
- MRI cannot accurately distinguish the benignity of adrenocortical tumors in pediatric patients.
- It is important to differentiate neurogenic tumors from other types of adrenal tumors.

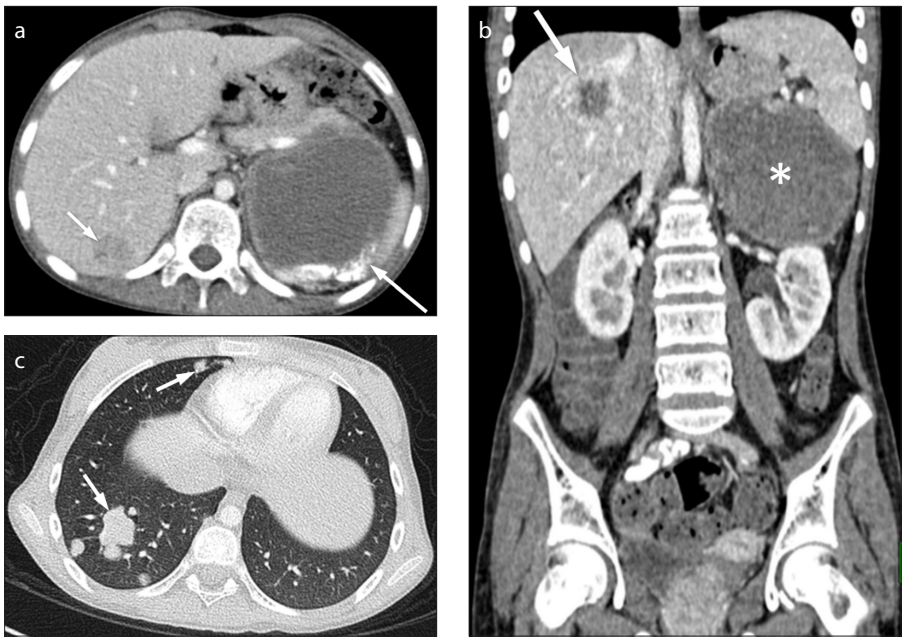

Figure 3. a–c. A 12-year-old girl with adrenocortical carcinoma. Axial contrast-enhanced CT image **(a)** shows heterogeneous left suprarenal mass with calcification *(long arrow)*. Note the liver metastasis *(short arrow)*. Coronal reformatted contrast-enhanced CT image **(b)** shows heterogeneous left suprarenal mass *(asterisk)* with liver metastasis *(arrow)*. Axial CT image of the lung **(c)** demonstrates multiple small metastatic lesions in right lung *(arrows)*.

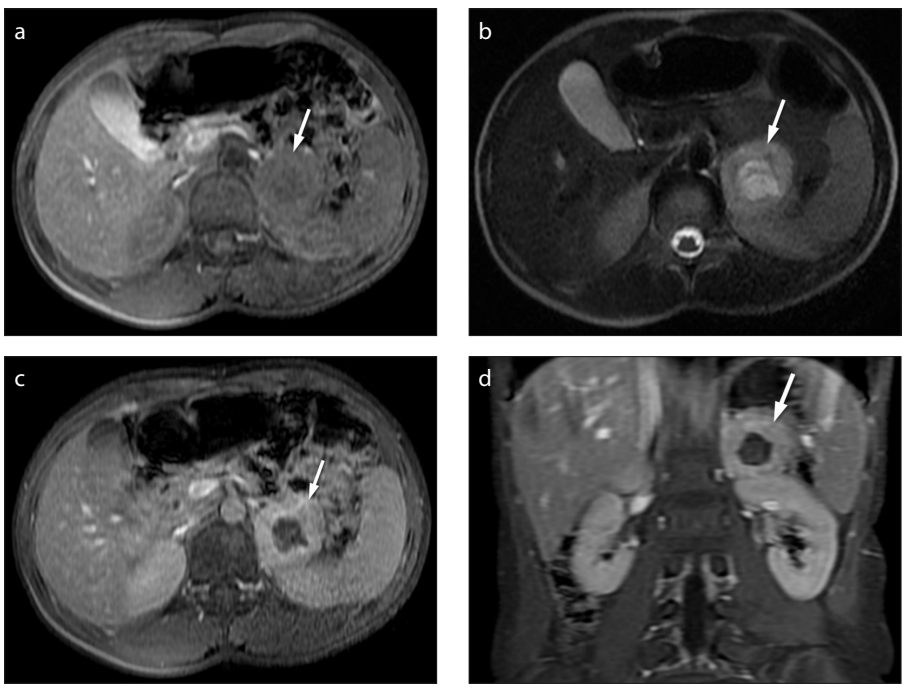

Figure 4. a–d. A 10-year-old girl with pheochromocytoma. Axial T1-weighted **(a)** and T2-weighted **(b)** images show heterogeneous left suprarenal mass with necrosis *(arrows)*. Axial and coronal contrast-enhanced T1-weighted images **(c, d)** show peripheral contrast enhancement with necrotic central part *(arrows)*.

The most common sites for adrenocortical carcinoma metastases are lungs, liver, and lymph nodes (Fig. 3) (2). Metastatic disease during the diagnosis of adrenocortical carcinoma was reported as an independent prognostic factor (14). FDG-PET/CT is used to identify the malignant adrenal tumors, and it may also localize metastases.

Pheochromocytoma

Pheochromocytoma and paraganglioma are unusual neuroendocrine tumors that are derived from the neural crest (15). Pheochromocytoma refers to the tumor originating from chromaffin (neuroendocrine) cells in the adrenal gland/medulla; however, paraganglioma represents the tumor originating apart from the adrenal gland, from sympathetic or parasympathetic ganglia. In pediatric pheochromocytomas, nearly 80% of patients are related to a genetic syndrome, e.g., multiple endocrine neoplasia type 2 (MEN 2), neurofibromatosis type 1, von Hippel-Lindau disease, and familial paraganglioma syndromes (16). Hence, genetic counseling and testing ought to be applied in all patients. In children, 80% of pheochromocytomas occur in the adrenal gland. Bilateral adrenal involvement was seen in 20%–40% of the cases, and pheochromocytoma might appear at multiple locations in 30%–70% of cases (17). Less common extra-adrenal locations include the sympathetic chain in a cervical, thoracic, or pelvic location and rarely they may occur in the urinary bladder, spinal cord, and vagina. Malignant pheochromocytoma is less frequent than in adults, and is determined by imaging—presence of local invasion and/or metastasis—rather than histopathological analysis. The nuclear imaging is better for patients with familial syndromes and those with possible existence of a multifocal/metastatic disease. Evaluation of plasma and/or urine-free metanephrine and normetanephrine levels are the most sensitive diagnostic tests. These catecholamines are the reason of main tumor manifestations: hypertension, headache, arrhythmia, sweating, and weight loss. They can be seen as a soft-tissue mass in the suprarenal fossa, with various echogenicity on sonography with high vascularity on color Doppler US. On contrast-enhanced CT images, they have increased vascularity and strong enhancement, which is mostly homogeneous in small tumors; however, they might be heterogeneous in larger ones due to cystic, necrotic, and/or hemorrhagic parts. On MRI, they have diminished signal intensity on T1-weighted images, increased signal intensity on T2-weighted images and avid enhancement on post-contrast images (Fig. 4). However, up to 30% of them show heterogeneous or decreased signal intensity on T2-weighted images (18). ^{68}Ga-DOTATATE PET/CT is the nuclear imaging of choice

with its higher sensitivity and specificity to detect the lesions that could not be seen on CT and MRI (2).

Adenoma

Adenomas are exceptional pediatric tumors that originate from the adrenal cortex. Pediatric age group adenoma is histopathologically and clinically distinct from adult adenoma. Hallmarks, such as washout thresholds on CT examination and signal loss on out-of-phase MRI cannot reliably distinguish the benignity of these tumors in pediatric patients. Hence, the expression "adrenocortical tumor" rather than adenoma or carcinoma is generally used to define a primary tumor in the adrenal cortex in pediatric patients (12, 19). Although not a solid criterion, adrenocortical tumors are much smaller than adrenocortical carcinomas. Nevertheless, malignancy cannot be excluded according to the tumor size. On imaging, adenomas are well circumscribed and have mild homogeneous contrast enhancement (Fig. 5).

Small round cell tumor with neuroendocrine differentiation

Small round cell tumor with neuroendocrine differentiation is an uncommon, highly aggressive pediatric malignancy, which rarely occurs in the adrenal gland. On radiological examinations, they are large heterogeneous tumors indistinguishable from adrenocortical carcinoma (Fig. 6).

Leiomyosarcoma

Primary adrenal leiomyosarcoma is an uncommon tumor and it is thought to arise from the smooth muscle wall of the central adrenal vein and its branches (20). On imaging, they typically show lobulated mass with heterogeneous contrast enhancement (Fig. 7). Their radiological features are analogous with other adrenal tumors and therefore they should be considered in the differential diagnosis of a suprarenal mass with malignant characteristics.

Malignant rhabdoid tumor

Malignant rhabdoid tumor is an extremely malignant pediatric tumor with very poor prognosis. They are mainly present in the kidneys of children and extrarenal presentations are extremely rare. They are large infiltrative masses and the diagnosis depends on histopathology.

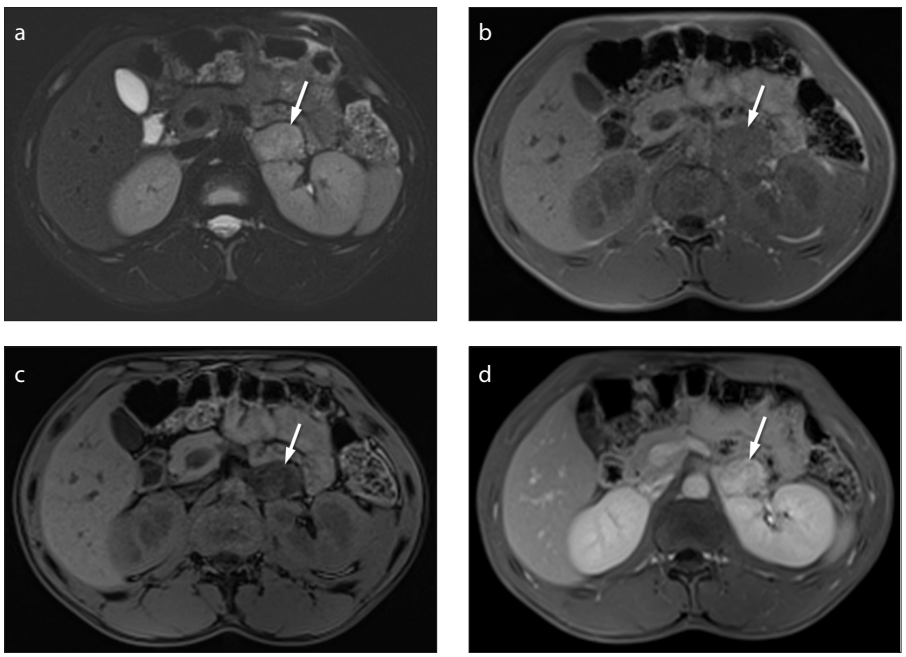

Figure 5. a–d. A 16-year-old boy with adrenal adenoma. Axial T2-weighted image **(a)** shows mild heterogeneous left suprarenal mass *(arrow)*. Chemical shift imaging demonstrates left-sided lesion that show signal loss between in-phase **(b)** and out-of-phase **(c)** images *(arrows)*. Axial T1-weighted contrast-enhanced image **(d)** shows mild heterogeneous enhancement of the left suprarenal mass *(arrow)*.

Conclusion

In conclusion, apart from neuroblastomas, adrenal tumors are exceedingly rare in the pediatric population. Adrenocortical carcinomas are typically heterogeneous tumors with necrosis and calcifications and can behave aggressively by encasement of localized vascular structures and widespread metastasis. Pheochromocytomas are usually benign tumors, and most of them have intense contrast enhancement on CT and MRI. Signal loss on out-of-phase MRI cannot accurately distinguish the benignity of adrenocortical tumors in pediatric patients. Radiological examinations have an important role in recognizing and differentiating malignant and benign adrenal neoplasms. However, radiologists need to err on the side of caution when differentiating

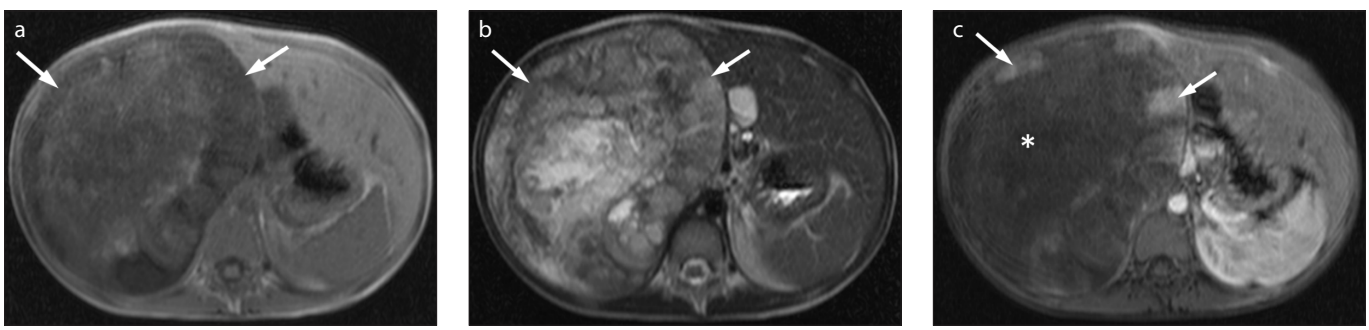

Figure 6. a–c. An 11-year-old girl with small round cell tumor with neuroendocrine differentiation. Axial T1-weighted image **(a)** shows heterogeneous right suprarenal mass *(arrows)*. Axial T2-weighted image **(b)** shows heterogeneous right suprarenal mass with necrosis *(arrows)*. Axial T1-weighted contrast-enhanced image **(c)** demonstrates heterogeneous enhancement of tumor *(arrows)*. Regions of nonenhancing tissue are consistent with necrosis *(asterisk)*.

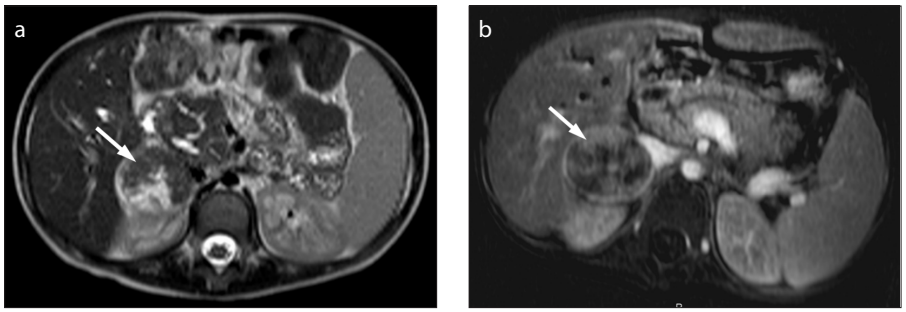

Figure 7. a, b. A 12-year-old girl with adrenal leiomyosarcoma. Axial T2-weighted image **(a)** shows heterogeneous right suprarenal mass *(arrow)*. Axial subtracted image **(b)** shows heterogeneous enhancement of the tumor *(arrow)*.

malignant adrenal tumors, by considering all imaging and clinical findings and laboratory tests.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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