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Atypical imaging features of adrenal gland lesions in children – report of three cases and review of literature

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Summary

Background:

The differential diagnosis of adrenal pathology depends on the child's age and imaging findings.

Case Report:

Three children without clinical symptoms of neoplasm, with an adrenal lesion discovered on diagnostic ultrasound imaging. Laboratory tests for neoplasm were negative. The final diagnosis was based on histopathological examinations after surgical resection.

Conclusions:

1. The value of diagnostic imaging and laboratory tests in differential diagnosis of adrenal gland lesions is limited. 2. Malignant tumors of adrenal glands should be taken into account in children. 3. Surgical resection should be considered in diagnostic algorithm of adrenal gland masses. 4. The final diagnosis is always based on histopathological examination.

Key words:

neuroblastoma • adrenal gland • children

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Background

We present three children diagnosed with adrenal gland pathologies and atypical clinical courses, presenting atypical pictures in diagnostic imaging and atypical results of laboratory tests.

Case Report

Patient 1

A three-week-old neonate was admitted to hospital due to regurgitation, abdominal distention, episode of fever and elevated inflammatory markers (leukocytes $26 \times 10^3/\mu\text{L}$, CRP 17 mg/dL; normal value <1 mg/dL). Pregnancy and delivery proceeded without complications.

Ultrasound examination showed a cystic, thick-walled lesion above the upper pole of the right kidney, measuring $48 \times 37 \times 35$ mm, filled with heterogeneous fluid (Figure 1).

In CT imaging there was an oval lesion in the right adrenal gland, $53 \times 43 \times 42$ mm in size and with density of 26

HU. The described lesion caused displacement and rotation of the right kidney. The lesion was not enhanced upon administration of a contrast medium. Only its capsule was enhanced from 50 HU to 150 HU. The remaining abdominal organs were unremarkable, visceral and retroperitoneal lymph nodes were not enlarged (Figures 2, 3).

Laboratory tests for markers for neuroblastoma were negative.

An inflammatory tumor was found on macroscopic examination performed during surgical procedure.

An adrenal abscess was diagnosed in histopathological examination.

Follow-up ultrasound examinations on the 6th and 12th day after surgery did not reveal any abnormalities. However, in the next study performed 40 days later we were not able to visualize the right kidney in the abdominal cavity. There was no accumulation of the radiotracer in the right kidney in scintigraphy performed after 2 months following the procedure; a follow-up CT carried out two months

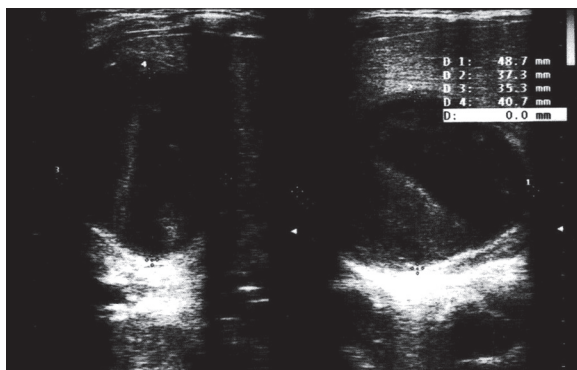


Figure 1. A 3-week-old male infant, abdominal US: in the upper pole of the right kidney a thick-walled cystic mass, with a fluid-fluid level inside.

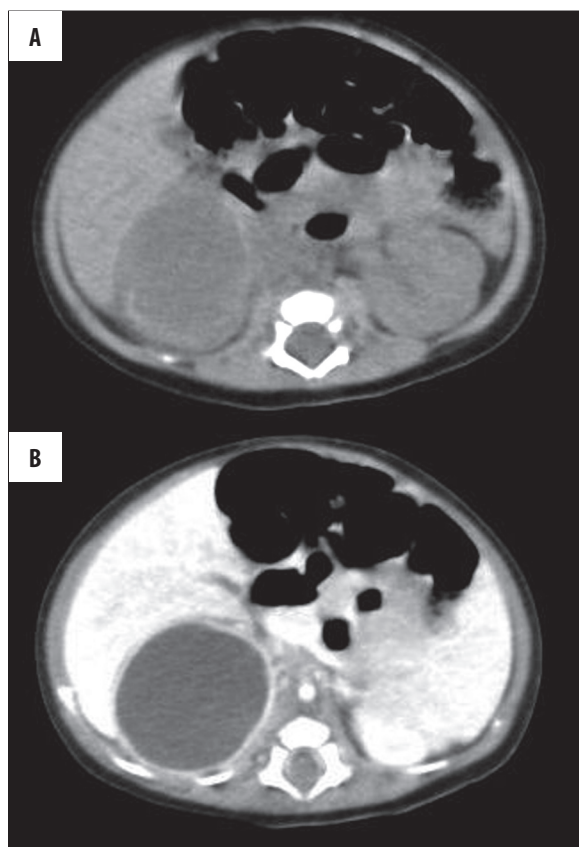


Figure 2. A 3-week-old male infant, an unenhanced (A) and enhanced (B) abdominal CT: in the right adrenal fossa an oval, well-demarcated, low-attenuation lesion with contrast-enhanced capsule. There were no calcifications.

afterwards showed a picture that could correspond to a small, cirrhotic kidney. Literature describes complications of an adrenal hematoma such as kidney compression or renal vein thrombosis [1], which could be the case in our patient, leading to renal atrophy.

Patient 2

A two-year-old healthy boy whose mother died of a lymphoma. Cervical lymph nodes enlarged for about 2 weeks were the reason for a visit to the doctor. Ultrasound

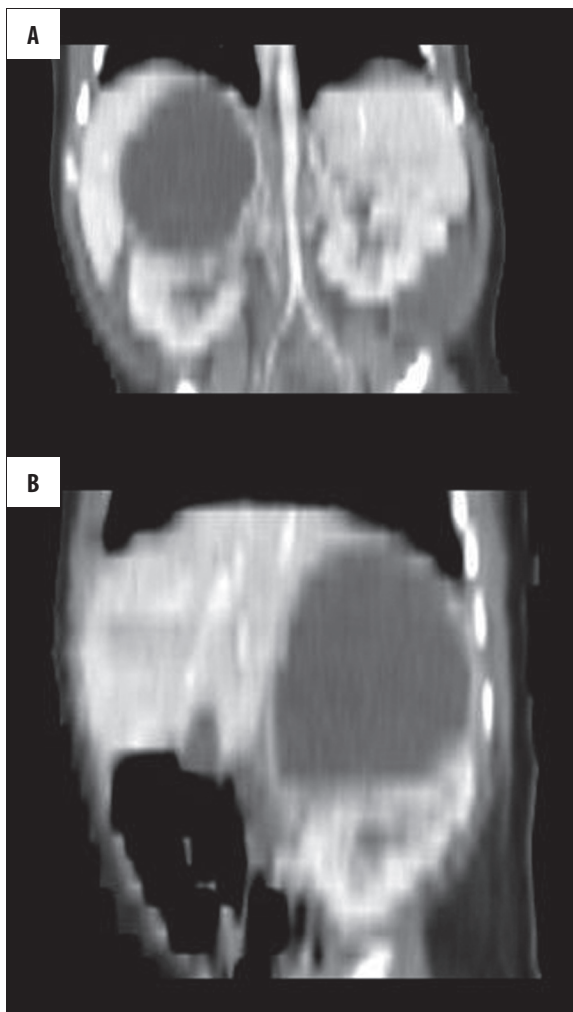


Figure 3. A 3-week-old male infant, coronal (A) and sagittal (B) contrast-enhanced reformatted abdominal CT: a lesion in the right adrenal fossa displaces and rotates the right kidney.

examination of the neck showed reactive lymph nodes measuring up to 15 mm in the long axis. Abdominal ultrasound revealed a fluid-filled cystic lesion with numerous septa above the upper pole of the right kidney. It measured 28×27×33 mm, showing a visible vascular flow in the thick walls of the septa. Biphase CT scan showed a picture of a cyst 30×30 mm in size, filled with fluid of 20–30 HU density located in the right adrenal gland. Septa within the cyst underwent pronounced contrast enhancement (Figures 4, 5). The remaining abdominal organs were unremarkable, visceral and retroperitoneal lymph nodes were not enlarged. Laboratory tests were negative for neuroblastoma and hydatid cyst. A follow-up ultrasound examination was carried out after one month, before an elective surgery. The image of the cyst changed: a lesion in the right adrenal gland measured 35×38×37 mm, had irregular margins, contained hyperechoic septa and an echoic content that could correspond to dense fluid or solid elements. Following surgical resection of the lesion, a hemorrhagic form of stage 1 neuroblastoma was diagnosed in histopathological examination. A two-year follow-up (to date) has not revealed signs of recurrence.

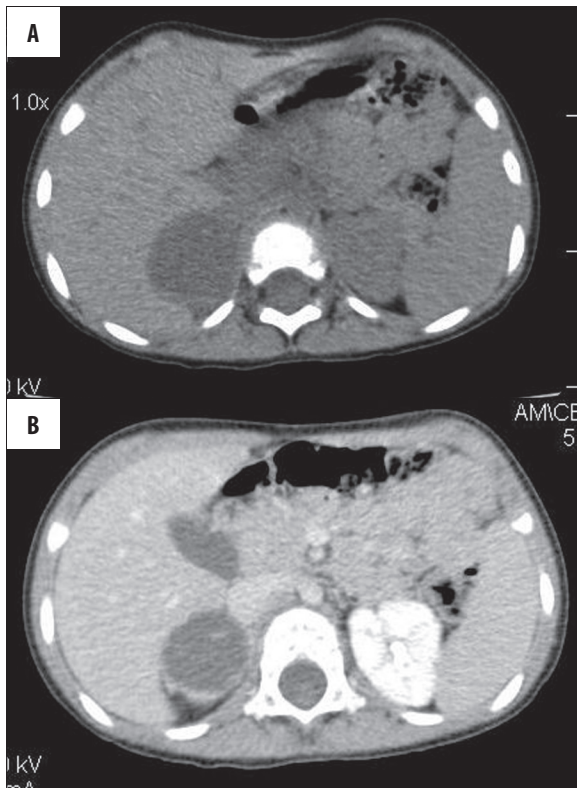


Figure 4. A 2-year-old boy, an unenhanced (A) and contrast-enhanced (B) abdominal CT: a well-defined, oval, low-attenuation lesion in the right adrenal gland with many contrast-enhancing septa. There were no calcifications.

Patient 3

A 10-year-old healthy boy with a solid mass discovered on ultrasound examination (performed for the first time in his life) in the left adrenal gland, 60×55×51 mm in size (Figure 6). A triphasic CT examination was performed revealing a left-sided epigastric tumor mass measuring 50×61×65 mm, enhanced upon application of contrast, without calcifications or areas of necrosis. Left adrenal gland was a likely point of origin. The tumor displaced the pancreas and the left kidney, touched the renal hilum and modeled renal vessels (Figure 7). There were no evident signs of infiltration of those structures. Pictures of the remaining abdominal organs were unremarkable. CT examinations of the chest and the head were unremarkable. In further diagnostic imaging there was an increased uptake of I-¹²³MIBG within the tumor. On the other hand, catecholamine levels in serum and concentrations of their metabolites in urine as well as the results of bone marrow examination were within normal limits.

During surgery we found a macroscopically large, solid tumor of the left adrenal gland penetrating the left kidney and renal hilum, which was removed in one block with the kidney (sparing procedure was not possible). Resection was subtotal due to infiltration of periaortic structures. Histopathological diagnosis of poorly differentiated neuroblastoma with N-myc gene amplification was made. Treatment continuation: chemotherapy according to the COJEC regimen.

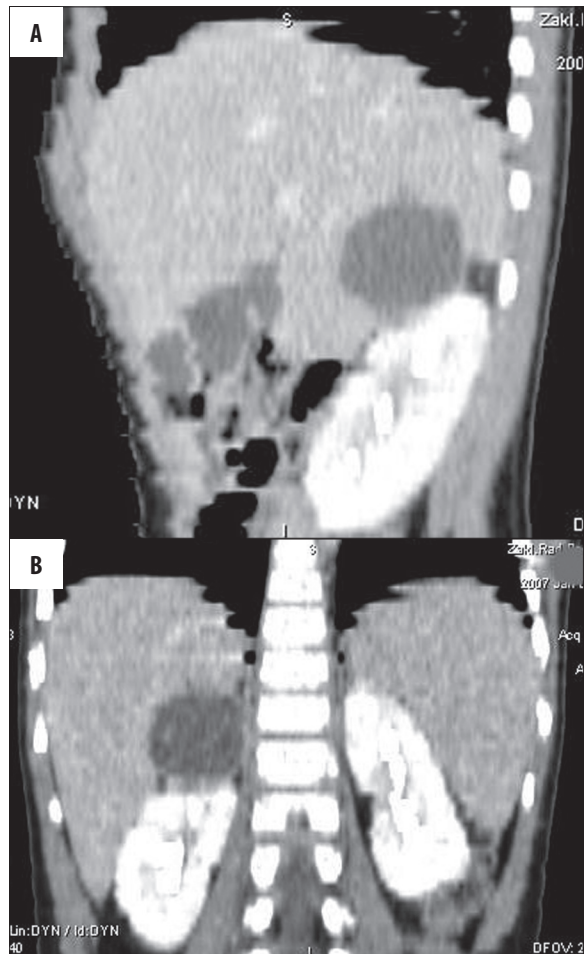


Figure 5. A 2-year-old boy, coronal (A) and sagittal (B) contrast-enhanced reformatted abdominal CT: a well-defined, adjacent to the right kidney, oval, low-attenuation lesion in the right adrenal gland with many contrast-enhancing septa.

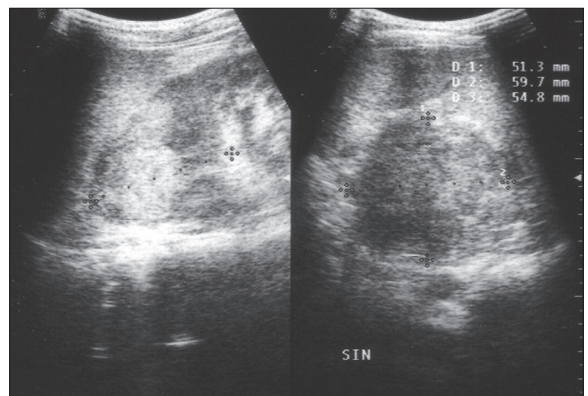


Figure 6. A 10-year-old boy, abdominal US: a solid, echogenic, homogeneous mass in the left adrenal gland.

Typical and atypical features of neuroblastoma in particular patients are presented in Table 1.

Discussion

Each disorder has a characteristic clinical course and morphology in diagnostic imaging. However, in a small

percentage of patients, the lesions may present with an atypical picture, run a different clinical course and be associated with atypical test results making the diagnosis more difficult – as it was in the case of our patients.

Incidentalomas of the adrenal glands are rarely found in children during diagnostic imaging but their incidence increases [2]. Such lesions may be solid or cystic, benign or malignant. Differential diagnoses of solid and cystic lesions originating from adrenal glands in children are presented in Table 2.

Neuroblastoma is the third most frequent, along with Wilms' tumor, malignancy in children with peak incidence between the 2nd and the 5th year of life (90% occur in patients under 5 years). At the same time it is the most frequent malignant tumor in infants [3–5]. In 25% it originates from adrenal glands [6].

Neuroblastoma may appear in any place where sympathetic ganglion cells are present. Most often, i.e. in about 60–80% of cases it is found in the abdominal cavity. About 35% of tumors in total originate from adrenal glands. In about 10% it may grow bilaterally. As much as 90% of neuroblastomas produce catecholamines leading to elevated concentrations of their metabolites (vanillylmandelic acid – VMA, and homovanillic acid – HVA) in urine and nonspecific enolase levels (NSE) in serum.

On the other hand, I-¹²³MIBG may be negative in as much as 30% of cases. On physical examination it usually presents as a painless tumor located in the abdominal cavity. In most cases (60–70%) it is diagnosed in a disseminated form with metastases to retroperitoneal lymph nodes, bones, bone marrow, liver, lungs or skin. It may also penetrate the spinal canal and infiltrate the spinal cord. The tumor infiltrates large vessels such as superior and inferior vena cava, aorta and its branches.

In diagnostic imaging studies neuroblastoma usually reveals features of a solid, round, poorly demarcated and well-vascularized tumor located in the retroperitoneal space, crossing the midline and extending toward the chest. Adrenal lesions typically displace the kidney inferiorly and posteriorly.

In classical X-rays, 55–60% of tumors contain calcifications, but in CT they are present in as much as 80–90% of subjects. Areas of necrosis and hematomas within the tumor give rise to a heterogeneous image of the lesion. A cystic neuroblastoma is rare, almost always located in adrenal glands [6–9] and occurs almost exclusively in neonates [8]. In comparison to the solid form, it is diagnosed earlier, with less frequent metastases and VMA and HVA levels are within normal limits [6,7]. Also, clinical course of the disease is not that severe [6].

In differential diagnosis of incidental adrenal cystic lesions one should take morphology of the lesion and child's age into consideration.

The most common cause for adrenal enlargement in newborns and neonates is bleeding into the organ. Image of a hematoma changes over time in a typical manner which, in

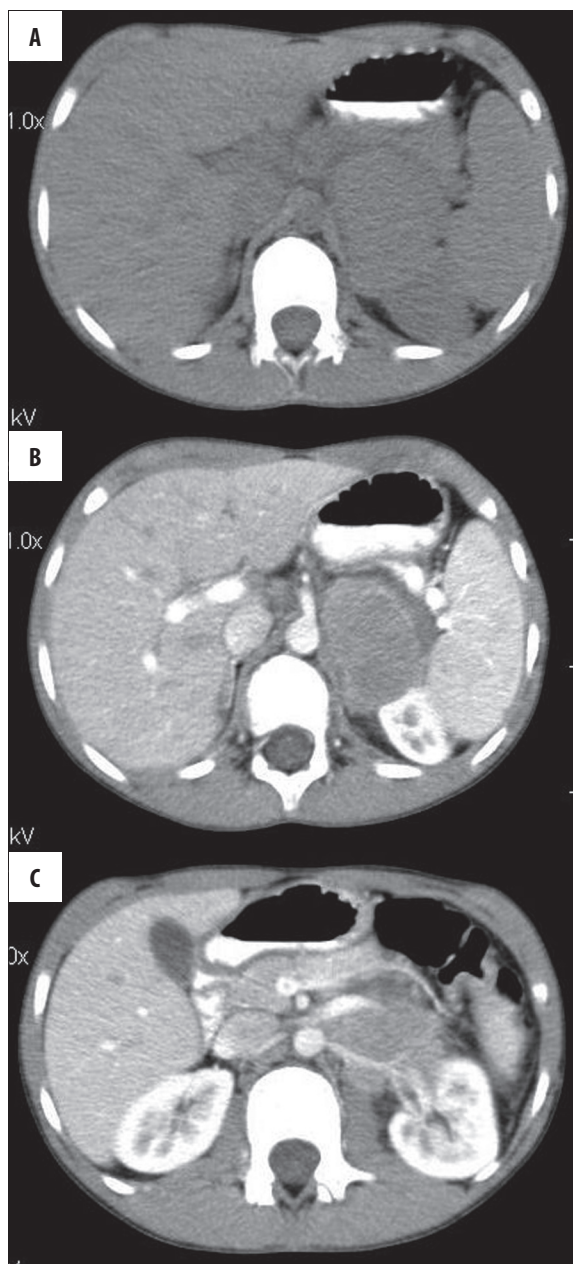


Figure 7. A 10-year-old boy, an axial unenhanced (A) and axial contrast-enhanced (B,C) abdominal CT. B the same level as A, C below A and B. In the left adrenal gland an oval mass undergoing homogeneous enhancement. The mass surrounds the vessels of the left kidney, displaces the pancreas and the left kidney, but does not infiltrate them (C). There were no calcifications or necrotic areas.

conjunction with history and clinical symptoms allows for stating a proper diagnosis. However, adrenal hemorrhage may be asymptomatic which, in case of a lack of previous imaging studies, is an indication for extending diagnostics [5] especially since calcifications may appear in an "old" hematoma or in a neuroblastoma. Bleeding into a neuroblastoma or a spontaneously "disappearing" tumor is difficult to differentiate from adrenal hematoma in imaging. Literature describes cases of adrenal hematomas that were diagnosed as neuroblastomas

Table 1. Typical and atypical features of neuroblastoma in individual patients.

| Patient | Final diagnosis | Typical features | Atypical features |
|--------------------|---|--|---|
| 3-week-old neonate | Adrenal abscess | <ul style="list-style-type: none"> • Age • Point of origin – adrenal gland | <ul style="list-style-type: none"> • Concentrations of catecholamines and their metabolites within normal limits • Fluid density in CT examination • Isolated enhancement of the capsule following application of contrast agent on CT • Lack of calcifications within the tumor • Elevated inflammatory markers |
| 2-year-old boy | Hemorrhagic form of neuroblastoma | <ul style="list-style-type: none"> • Age • Point of origin – adrenal gland | <ul style="list-style-type: none"> • Absence of clinical symptoms • Cystic lesion • Fluid density in CT examination • Concentrations of catecholamines and their metabolites within normal limits • Normal I-¹²³MIBG uptake • Lack of calcifications in the tumor |
| 10-year-old boy | Poorly differentiated neuroblastoma with N-myc gene amplification | <ul style="list-style-type: none"> • Solid lesion • Increased uptake of I-¹²³MIBG within the tumor • Point of origin – adrenal gland | <ul style="list-style-type: none"> • Age • Absence of clinical symptoms • Concentrations of catecholamines and their metabolites within normal limits • Lack of calcifications |

Table 2. Differential diagnosis of solid and cystic adrenal lesions in children.

| Cystic lesions | Solid lesions |
|---|--|
| <ul style="list-style-type: none"> • Adrenal hemorrhage • Adrenal hematoma or abscess • Simple cyst • Pseudocyst • Parasitic cyst • Lymphangioma • Teratoma • Hemorrhagic neuroblastoma • Cystic neuroblastoma | <ul style="list-style-type: none"> • Neuroblastoma • Adrenal hemorrhage • Congenital adrenal hyperplasia • Ganglioneuroblastoma • Ganglioneuroma • Pheochromocytoma • Adrenal adenoma and adrenal cancer • Wolman disease • Non-Hodgkin or Burkitt's lymphoma • Teratoma • Rhabdomyosarcoma |

in situ in histopathological examinations [7,9]. Therefore, every lesion arising from adrenal glands found in a neonate should be monitored with ultrasound examinations [10].

Another cause for a cystic adrenal lesion is adrenal abscess. Most commonly it develops within a hematoma, very rarely in a healthy adrenal gland [1]. It is accompanied by symptoms of infection and a characteristic picture in an ultrasound and CT – a cystic lesion, sometimes containing a fluid-fluid level and a thick wall enhanced upon administration of contrast medium.

Single, acquired adrenal cysts rarely occur in neonates.

An incidental cystic adrenal tumor in a child older than 1 year should be differentiated from a hematoma, an adrenal

abscess, lymphatic hemangioma, teratoma, simple cyst, pseudocyst, parasitic cyst and a hemorrhagic or cystic neuroblastoma.

Cysts and pseudocysts rarely occur in children.

Massive adrenal bleeding is also rare in children beyond the neonatal period and is often asymptomatic. In older children, adrenal bleeding occurs due to accidental or non-accidental traumas, meningococcal sepsis or anticoagulation treatment [1].

Lymphatic hemangioma is a rare congenital vascular malformation deriving from lymphatic ducts. It is most often seen in the cervical and axillary regions, less commonly within the abdominal cavity: omentum, mesentery and retroperitoneum. Clinical symptoms depend on the size and location of hemangioma. In ultrasound examination it appears as a well-demarcated, thin-walled cystic lesion containing septa. Likewise, CT examination shows a cyst or several cysts filled with fluid or fat and enhancing wall and septa [11].

Teratomas, neoplasms developing from pluripotential cells, most commonly develop in ovaries or testicles, less often in other locations including retroperitoneal space. Adrenal gland is a rare location but more typical for children. Teratomas contain tissues arising from all embryonic leaves composed in a chaotic manner. In imaging studies they may appear as solid, cystic or mixed lesions. They often contain fat, connective tissue, epithelium, skin adnexa, calcifications or teeth. Their mature forms are benign but may undergo malignant transformation. They are often found incidentally in an ultrasound examination [12].

Parasitic cysts of the Echinococcus family may be found in patients of all ages, even below 1 year. Incidence depends on the epidemiological situation in the area of patient's

residence and his/her socioeconomic situation. Hydatid cysts are most often found in the liver and lungs. Adrenal location is rare. Imaging shows non-echoic cysts of various sizes, single or multiple, containing septa or not. An image of a proliferous cyst is pathognomonic for infection with this parasite. Calcifications may appear within cystic walls, especially when tapeworm larvae die [5,13].

Differential diagnosis of solid lesions of adrenal glands depends mainly on child's age.

General adrenal enlargement in newborns and neonates is found in adrenal cortical hyperplasia manifested as adrenogenital syndrome.

Bilateral adrenal enlargement with retained shape of the gland and presence of calcifications are characteristic for Wolman's disease – a rare autosomal recessive storage disease presenting with hepatosplenomegaly, diarrhea, vomiting and anorexia resulting in death in infancy [14–16]. Imaging studies may show enlarged lymph nodes and thickening of the walls of small intestine [16].

Adrenal cancer and adrenal adenoma occurs in older children, at the same age as in neuroblastoma (<5–6 years) although less often. They may be difficult to differentiate even in histopathological examination [3,7,18]. Clinically they present with symptoms of increased secretion of adrenocortical hormones (precocious puberty, Cushing's syndrome, Conn's syndrome, feminization in boys, virilization in girls). In diagnostic imaging they may resemble neuroblastoma. In ultrasound examination they typically appear as well-demarcated, round or oval, sometimes encapsulated solid lesions, rather homogenous but possibly containing foci of necrosis and calcifications. In CT the lesion is well-demarcated, heterogeneous (containing areas of necrosis or hemorrhage), with a thin capsule that undergoes enhancement following contrast administration. Adrenal cancer infiltrates lymph nodes, kidneys, liver, diaphragm, renal veins, gives distant metastases to the lungs, bones and brain.

Ganglioneuroblastoma originates from sympathetic ganglion cells. In terms of malignancy it is an intermediate form between ganglioneuroma and a neuroblastoma. It is most common in children between 2 and 4 years old, very rarely found in children above 10 years old. In diagnostic imaging it appears as an encapsulated, solid or mixed solid-cystic lesion often containing calcifications [19].

A rare benign tumor arising from sympathetic plexuses – ganglioneuroma – is often asymptomatic and reaches large sizes. Average age at diagnosis is 7 years. This tumor can develop as a result of spontaneous or chemotherapy-induced maturation

of neuroblastoma or its metastases. About 35% of tumors are located in the retroperitoneal space and 21% in adrenal glands. Ganglioneuroma is most often an incidental finding but, like a neuroblastoma, may exhibit hormonal activity. In diagnostic imaging it appears, similar to neuroblastoma, as a well-demarcated oval or lobular solid mass surrounding large vessels. In CT examination the tumor is homogenous, 20% may contain spots of calcification. Because of great similarity to neuroblastoma, final diagnosis can be made only on the basis of histopathological examination [14,19,20].

Tumor deriving from adrenal cortex, a pheochromocytoma, very rarely occurs in children – most often between the 8th and 10th year of life [3] – and produces symptoms of permanent or paroxysmal hypertension, headaches, sweating, nausea and vomiting. In diagnostic imaging it appears as a round, well-demarcated solid lesion undergoing intense enhancement following application of contrast medium in CT examination.

A rhabdomyosarcoma is the next, following Wilms' tumor and neuroblastoma, most common solid lesion and, at the same time, the most common soft tissue sarcoma in children [5,20]. There are two incidence peaks: between the 1st and 7th year of life and at puberty. The most frequent locations within the abdominal cavity are the urinary bladder and prostate, retroperitoneal space is less common. In CT examination the tumor is heterogeneous, with density similar to the density of muscles. It undergoes heterogeneous enhancement following application of contrast. Areas of necrosis are often visible but calcifications within the lesion are rare [20]. Rhabdomyosarcoma is locally invasive, infiltrates adjacent tissues and gives distant metastases to the lungs, CNS, bone marrow and bones.

Non-Hodgkin lymphomas may occur on both sides of the diaphragm, spreading along large vessels and causing retroperitoneal lymph node enlargement. In CT enlarged lymph nodes present as homogeneous masses, poorly enhancing after application of contrast medium. They rarely contain calcifications or areas of necrosis [20]. Adrenal lymphomas are very rare.

Conclusions

1. The value of diagnostic imaging and laboratory tests in differential diagnosis of adrenal gland lesions is limited.
2. One should remember about malignant tumors of adrenal glands in children.
3. Surgical resection should be considered in the diagnostic algorithm of adrenal gland lesions.
4. The final diagnosis is always based on histopathological examination.

References:

1. Kawashima A, Sandler CM, Ernst RD et al: Imaging of Nontraumatic Hemorrhage of the Adrenal Gland, *RadioGraphics*, 1999; 19: 949–63
2. Masiakos PT, Gerstle JT, Cheang T et al: Is Surgery Necessary for Incidentally Discovered Adrenal Masses in Children? *J Pediatr Surg*, 2004; 39(5): 754–58
3. Chybicka A, Sawicz-Birkowska A: *Onkologia i hematologia dziecięca*. PZWL, Warszawa, 2008
4. Balwierz W: Nerwiak zarodkowy współczulny w Zalecenia postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych. <http://www.onkologia.zalecenia.med.pl> (accessed 06.08.2011)
5. Marciński A: *Ultrasonografia pediatryczna*. Sanmedia, 1994
6. Pinarli GF, Danaci M, Tander B et al: Bilateral adrenal cystic neuroblastoma with superior vena cava syndrome and massive intracystic haemorrhage. *Pediatr Radiol*, 2004; 34: 746–49

7. Hendry GMA: Cystic Neuroblastoma of the Adrenal Gland, *Pediatr Radiol*, 1982, 12: 204-6
8. Kurtz AB, Hilbert P: Ultrasound Case of the Day. *Radiographics*, 1989; 9(2): 361-64
9. Atkinson GO, Zaatari GS, Lorenzo RL et al: Cystic Neuroblastoma in Infants: Radiographic and Pathologic Features. *AJR*, 1986; 146: 113-17
10. Brzewski M, Biejat A, Rumińska M et al: Miejsce ultrasonografii w algorytmie diagnostyczno-lecznym noworodków z wylewem do nadnerczy. *Ultrasonografia*, 2008; 8(35): 32-37
11. Luo CC, Huang CS, Chao HC et al: Intra-Abdominal Cystic Lymphangiomas in Infancy And Childhood. *Chang Gung Med J*, 2004; 27(7): 509-14
12. Li Y, Zhong Z, Zhao X: Primary Mature Teratoma Presenting as an Adrenal Tumor in a Child. *Urology*, 2011; 78(3): 689-91
13. Eckert J, Gemmell MA, Meslin F-X et al: WHO/OIE Manual on Echinococcosis in Humans and Animals: a Public Health Problem of Global Concern <http://whqlibdoc.who.int/publications/2001/929044522X.pdf>
14. Westra S, Zaninovic AC, Hall TR et al: Imaging of the Adrenal Gland in Children. *Radiographics*, 1994; 14: 1323-40
15. Jankowska I, Pawłowska J, Socha J et al: Cholestaza u dzieci. *Ped Wsp Gastroenterol Hepatol, Żywnie Dziecka*, 2001; 3(4): 309-14
16. Fulcher AS, Narla LD, Hingsbergen EA: Pediatric Case of the Day. *Radiographics*, 1989; 18: 533-35
17. Agrons GA, Loneragan GJ, Dickey GE et al: Adrenocortical Neoplasm in Children: Radiologic-Pathologic Correlation. *Radiographics*, 1999; 19: 989-1008
18. McHugh K: Renal and adrenal tumours in children. *Cancer Imaging*, 2007; 7: 41-51
19. Loneragan GJ, Schwab CM, Suarez ES et al: Ganglioneuroblastoma, and Ganglioneuroma: Radiologic-Pathologic Correlation. *Radiographics*, 2002; 22: 911-34
20. Xu Y, Wang J, Peng Y et al: CT characteristic of primary retroperitoneal neoplasm in children. *Eur J Radiol*, 2010; 75:321-28