

## THE OBSERVATION OF CONGENITAL RETROPERITONEAL LARGE SIZE NEUROBLASTOMA

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The article represents current literature data on epidemiological, clinical-morphological features and diagnostic criteria of neuroblastoma. The case of large congenital neuroblastoma with multiple metastases in the newborn child is presented. The histological picture and immunohistochemical profile of the tumor allowed us to consider this type of neuroblastoma as the least differentiated variant (subtype, “neuroblastoma rich in Schwann stroma”), with rapid progression and metastasizing started before the birth of the child. **Key Words:** neuroblastoma, congenital tumor, tumors in children.

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Neuroblastoma is an embryonal malignant tumor developing from the precursor cells of the sympathetic nervous system (sympathogonia). It constitutes 8–10% of all malignancies in children aged under 15 (7.8% in the USA, 9% in Germany, 9.3% in Belarus) [1–4], and in the structure of malignant extracranial tumors of childhood, according to some authors, is ranked first, ahead of leukemias [5].

More than 90% of tumors develop in children aged under 5 years, the peak of the disease occurs during the first year of life [6]. At the same time, the cases of neuroblastoma are described in adults and even in the elderly persons [7]. Neuroblastoma cases may be different by their clinical behavior with regressive, maturing or progressive types being delineated [8, 9]. It is believed that regressive type characterized by generally favorable prognosis dominates in the children of the first year of life [10, 11].

In 70% of patients over 1 year, metastases to lymph nodes, liver, bone marrow and bones are revealed with the overall 5-year survival being less than 40% [12]. In such cases, successful treatment cannot be achieved, even using intensive modes of high-dose therapy in combination with autologous bone marrow transplantation, or stem cells transplantation [13].

Microscopically, neuroblastoma is composed mainly of small rounded cells, with small rounded or oval nuclei surrounded by a narrow rim of cytoplasm (“naked nuclei”). The cancer cells are arranged irregularly, loosely or densely, depending on the amount of stroma. The rosette patterns (Homer Wright pseudorosettes) consisting of a halo of cancer cells surrounding a central region containing neuropil may be also seen. Axis cylinders usually cannot be found in the tumor. In addition to the above-described cell elements, a characteristic feature of this type of tumor is the presence of thin nerve fibers, but their detection in routine techniques used in the practical pathohistology, is almost impossible. Meanwhile, the presence of delicate nerve fibers is credible, pathognomonic,

diagnostic sign. In connection with this sign, in most of the classic guides, the differential diagnosis of this type of tumors is recommended to be used as additional method of impregnation with silver salts [14–16].

Currently, immunohistochemical methods are widely used for the differential diagnosis of neuroblastoma with detection of neuronal markers such as neuron-specific enolase (NSE), synaptophysin, chromogranin A, CD56, CD57. It should be noted that the expression of S-100 protein and neurofilament proteins occurs in more differentiated variants of tumors (ganglioneuroblastoma and ganglioneuroma) and Schwann stroma of low-grade neuroblastoma (subtype, “neuroblastoma that rich in Schwann stroma”) [17–20].

We present the case of congenital neuroblastoma of the retroperitoneal space, with large metastases, unrecognized *in utero*.

Baby T., a female, was treated at Children’s City Clinical Hospital with the diagnosis: congenital malignant tumor of the retroperitoneal space. The pregnancy of the mother was uneventful, the child was born in the City Clinical Maternity Hospital from the VII pregnancy (the third natural delivery, weight — 2550 g, height — 44 cm, Apgar grade — 7/7 points. After the birth, the child’s condition worsened progressively, so she was moved to the intensive care unit of City Clinical Children’s Hospital. While being in the hospital, the child’s condition remained severe due to the progression of respiratory distress, the growing phenomena of malnutrition, partial intestinal obstruction.

The baby was examined clinically and instrumentally. X-ray examination determined large size tumor formation in the abdominal cavity, with displacement loops of small bowel to the right. To clarify the diagnosis, biopsy of the tumor was performed.

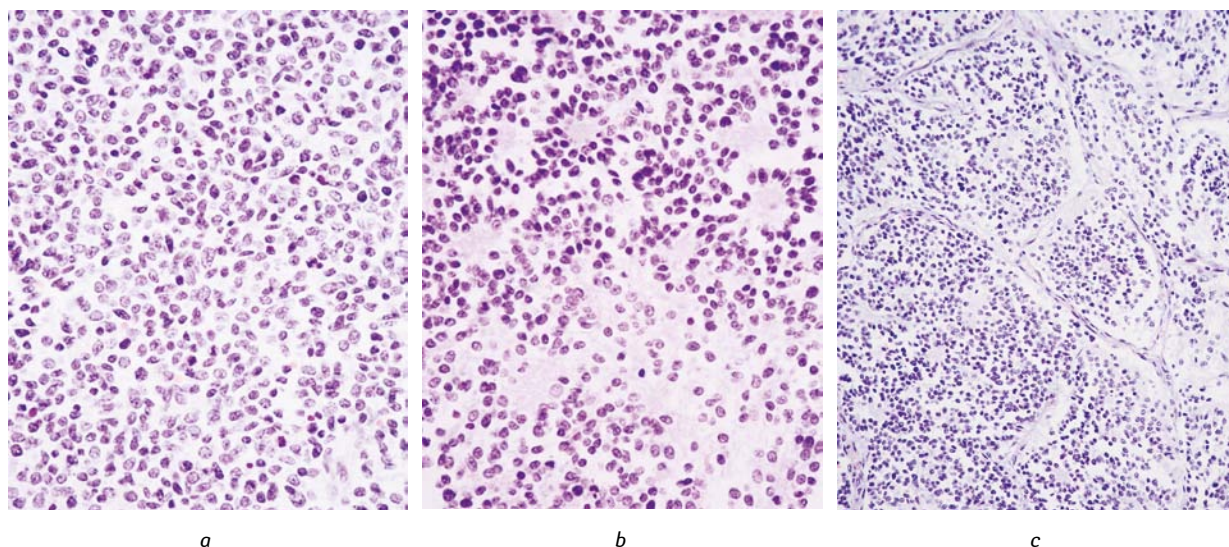
Microscopic examination of tumor biopsy revealed small mostly rounded cells with a narrow rim of cytoplasm and small round nuclei. Sometimes, the oval cells were evident (Fig. 1, a). The cellular elements located randomly, occasionally forming pseudorosette of Homer Wright (Fig. 1, b). Foci of necrosis and

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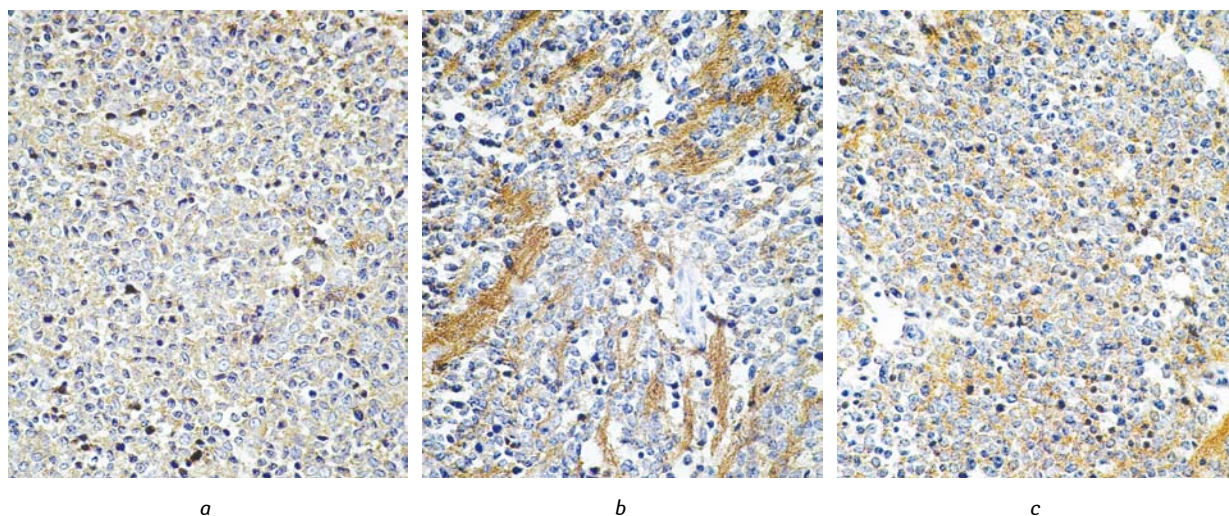
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Abbreviation used: NSE – neuron-specific enolase.



**Fig. 1.** Microscopic structure of the tumor. Hematoxylin and eosin stain. *a* — cellular composition of the tumor; *b* — formation of Homer Wright pseudorosettes; *c* — alveolar structures in the tumor.  $\times 400$  (*a*, *b*),  $\times 100$  (*c*)



**Fig. 2.** Immunohistochemical profile of the tumor. *a* — expression of CD57 by tumor cells; *b* — lack of S-100 expression in tumor cells, expression of S-100 in the stromal component of the tumor; *c* — expression of NSE by tumor cells and stromal component,  $\times 200$

hemorrhage were often seen in tumor tissue. At some sites, a well-defined stroma was evident forming a thin anastomosing alveolar structures (Fig. 1, *c*).

The above morphological and clinical data allowed to define the tumor as neuroblastoma, after which the child was assigned to symptomatic therapy. Treatment was not successful and on the 35 day after birth the child died.

On autopsy, in the left retroperitoneal space a grayish-white mucus-like tumor sized  $10.5 \times 7 \times 6.5$  cm with numerous focuses of decay and hemorrhages was discovered. The tumor extended into, left adrenal gland and left kidney, connecting with the head and body of the pancreas. The loops of the small bowel were displaced to the right by the tumor.

In the skin of the anterior abdominal wall, thighs, face, and neck area, dense whitish nodes sized from 0.5 to 1.5 cm in diameter were revealed a, which were interpreted as metastases of the tumor. The microscopic picture of the tumor and metastases was fully consistent with that described above.

To confirm the diagnosis, immunohistochemical examination with monoclonal antibodies to CD57, S-100, and NSE was performed. The reaction with CD57 in the majority of cancer cells was positive, S-100 was not expressed in cancer cells, but strong expression of S-100 was evident in the stromal component of the tumor. The expression of NSE was observed in the cellular elements of the tumor and in the stroma (Fig. 2).

Therefore, immunohistochemical studies confirmed the diagnosis previously made. Given the lack of S-100 expression in tumor cells and its pronounced expression in stromal component of the tumor, this neuroblastoma case should be attributed to the least differentiated variant (subtype, “neuroblastoma rich in Schwann stroma”) [17–20]. Apparently, the low differentiation of the tumor resulted in rapid progression, copious metastasis even before the birth of the child. At the same time, it should be noted that usually poorly differentiated variants of neuroblastoma are not characteristic of children of the first year of life [10, 11].

## REFERENCES

1. **Fediakova YuS.** Epidemiology and biology of neuroblastoma (literature review). *Detskaya Onkologiya* 2009; (3–4): 32–5 (in Russian).
2. **Men TKh, Poliakov VG, Aliiev MD.** Epidemiology of malignancies in children of Russia. *Onkopediatria* 2014; (1): 7–12 (in Russian).
3. **Heck JE, Ritz B, Hung RJ, et al.** The epidemiology of neuroblastoma: A review. *Paediatr Perinat Epidemiol* 2009; **23**: 125–43.
4. **Colon NC, Chung DH.** Neuroblastoma. *Adv Pediatr* 2011; **58**: 297–311.
5. **Kaatsch P.** Epidemiology of childhood cancer. *Cancer Treatment Rev* 2010; **36**: 277–85.
6. **Irwin MS, Park JR.** Neuroblastoma: Paradigm for precision medicine. *Pediatr Clin North America* 2015; **62**: 225–56.
7. **Starchenko II.** Clinico-morphological observations of adrenal neuroblastoma in adults. *Visnyk Problem Biol Med* 2013; **2**: 60–3 (in Russian).
8. **Chu CM, Rasalkar DD, Hu YJ, et al.** Clinical presentations and imaging findings of neuroblastoma beyond abdominal mass and a review of imaging algorithm. *Br J Radiol* 2011; **84**: 81–91.
9. **Shimada H.** International neuroblastoma pathology classification. *Pathology* 2012; **44**: 11–2.
10. **Kaschanov DYu, Tamazian GV, Kriuchko NV, et al.** Malignant neoplasms in children of the first year of life. *Vopr Hematologii/Onkologii Immunopatologii in Pediatria* 2010; **9**: 14–21 (in Russian).
11. **Pizzo PA, Poplack DG.** Neuroblastoma. In: *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2016: 777–8.
12. **Park JR, Eggert A, Caron H.** Neuroblastoma: biology, prognosis, and treatment. *Hematol/Oncol Clin North America* 2010; **24**: 65–86.
13. **Pinto NR, Applebaum MA, Volchenboum SL, et al.** Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol* 2015; **33**: 3008–17.
14. **Shimada H, Ambros IM, Dehner LP.** Terminology and morphologic criteria of neuroblastic tumors: recommendations by the International Neuroblastoma Pathology Committee. *Cancer* 1999; **86**: 349–63.
15. **Kushner BH.** Neuroblastoma: A disease requiring a multitude of imaging studies. *J Nucl Med* 2004; **45**: 1172–88.
16. **Erlanson RA, Nesland JM.** Tumors of the endocrine/neuroendocrine system: an overview. *Ultrastruct Pathol* 1994; **18**: 149–70.
17. **Grabovyi OM, Zaretskyi MB.** Feasibility and difficulties in histological assignment of solid tumors in children. *Klin Onkol* 2012; (1): 153–7 (in Ukrainian).
18. **Dabbs DJ.** *Diagnostic Immunohistochemistry: therapeutic and genomic applications*, Expert Consult: Online and Print. 4th Ed. Philadelphia: Elsevier, 2014: 762–829.
19. **Duijkers FA, Gaal J, Meijerink JP, et al.** High anaplastic lymphoma kinase immunohistochemical staining in neuroblastoma and ganglioneuroblastoma is an independent predictor of poor outcome. *Am J Pathol* 2012; **180**: 1223–31.
20. **Bielle F, Fréneaux P, Jeanne-Pasquier C, et al.** PHOX2B immunolabeling: a novel tool for the diagnosis of undifferentiated neuroblastomas among childhood small round blue-cell tumors. *Am J Surg Pathol* 2012; **36**: 1141–9.