

CLINICOMORPHOLOGICAL OBSERVATION OF REFRACTORY HEPATOBLASTOMA: A CASE REPORT

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The clinical case of refractory hepatoblastoma with lethal outcome followed by pathomorphological verification has been analyzed. The true causes of hepatoblastoma development remain unknown. The prognostic factors of the disease require detailed study in complex investigations that would include histological, clinical, laboratory, and immunohistochemical characteristics. However, comparing clinical and histopathological parameters with CD10 expression could have a diagnostic role and may be useful in understanding tumorigenesis and prognostic analysis of a given tumor.

Key Words: hepatoblastoma, prognostic factors, immunohistochemical characteristics, CD10.

DOI: 10.32471/exp-oncology.2312-8852.vol-42-no-3.14855

Hepatoblastoma (HB) is the most common malignant embryonic liver tumor, ranking third among most common tumors in children after neuroblastoma and nephroblastoma [1]. HB accounts for 50% of liver tumors and 1.3% of malignant neoplasms in children. Noteworthy, the incidence rate is 1.6 cases per 1 million population, tending to increase worldwide. There are two age peaks of morbidity: the first one is immediately after birth or in the first month of life, the second one falls on the 16–18th months of life. Given that the HB incidence is the highest immediately after birth, an increase in the incidence of antenatal diagnosis and histological similarity of HB with embryonic tissue indicates the initiation of the development of the disease during pregnancy [2].

Morphologically, the tumor is mainly unifocal, in a pseudocapsule, which is not an absolute barrier to tumor invasion beyond it. The right lobe of the liver is affected by 3 times more often than the left one. HB is diverse in its histological structure. Six morphological forms of the tumor are distinguished. The epithelial type includes the following histological variants: purely fetal, combined fetal-embryonic, macrotrabecular, small-cell undifferentiated. There is also a mixed epithelial-mesenchymal type of HB, which includes fibrous connective tissue, osteoid material, skeletal muscle fibers, squamous epithelial cells and cells with melanin, and a mixed type with a teratoid component. The most favorable form in terms of prognosis of the disease is the fetal variant of HB [3].

The study was aimed at the analysis of the clinical case of refractory HB with lethal outcome, followed by pathomorphological verification.

CASE REPORT

We reported the case of the 2-year-old male patient D., born to a primigravida mother. In his mother's words, the pregnancy and labor was un-

remarkable. The weight at birth was 3550 g. Before 1 year old, the child experienced acute respiratory disease. Vaccinations were made according to the schedule, allergological anamnesis was not burdened. From the age of 20 months, there were complaints of asymmetry of the anterior abdominal wall. At the local hospital, a liver tumor was detected. Computed tomography (CT) revealed enlargement of the liver due to the neoplasm in the left lobe and hypertrophy of the right lobe. In segment of liver (Sg) IVa, SgIII, a bulky solid neoplasm was detected, surrounded by a capsule measured 8.9 × 6.7 × 8.6 cm (267.0 cm³). The neoplasm retracted the left lobar portal vein. The right lobar portal vein was hypertrophied. The hepatic and non-hepatic bile ducts were not dilated. The gallbladder was not enlarged. The portal and splenic veins were insignificantly dilated. Enlargement of group 12 lymph nodes was detected.

The patient was referred to the National Cancer Institute for further examination and treatment and hospitalized at the Department of Pediatric Oncology. Upon comprehensive examination, the diagnosis was made: Undifferentiated malignant tumor (hepatoblastoma?) Left lobe of the liver (SgIVa, SgIII). PRETEXT II, T3NxM0, stage IIIA. Clinical group 2.

The patient underwent surgery: atypical resection SgIVb, SgIII. The findings of histological and immunohistochemical studies (cytokeratin pan, alpha-1-fetoprotein, Ki67, CD10) of postoperative material revealed HB with foci of extramedullary hematopoiesis. According to the established diagnosis, the patient received specific treatment in compliance with the clinical protocol.

Chemotherapy was performed under the control of CT and α-fetoprotein (AFP) determination. The data of control CT revealed the progression of the disease after the first block of chemotherapy and the patient was assigned to the high-risk group and received a specific intensive treatment (cisplatin, carboplatin, doxorubicin). The control CT showed: synchronous segment of lung (S) 2, S3, S4, S9 masses to 0.6 cm of the right lung; SgIVb heterogeneous

Submitted: September 5, 2019.

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Abbreviations used: AFP – α-fetoprotein; CT – computed tomography; HB – hepatoblastoma; S – segment of lung; Sg – segment of liver.

mass measured 1.8×1.6 cm; SgVIII mass measuring $3.1 \times 2.7 \times 2.9$ cm. Final conclusion: the diminished foci in SgIVb and SgVIII were preserved; metastasis in the right lung without dynamics.

The severity of the patient's condition after the sixth cycle of chemotherapy and its progressive deterioration, the level of tumor markers (continuing elevation of AFP: 283.3 ng/ml; 353.4 ng/ml; 13063 ng/ml; 715254 ng/ml), laboratory results (moderate anemia, elevation of transaminases to the levels by more than 5 times higher) showed clinical and biochemical progression of the disease. Multidisciplinary consultation decided to discontinue specific treatment of the patient and to conduct symptomatic therapy at the place of residence.

The patient was hospitalized at the Oncohematological Department of Poltava Municipal Children's Clinical Hospital. During the entire stay in the ward, the condition of the child remained extremely severe due to prominent intoxication. Symptomatic treatment was carried out, but the patient's condition progressively worsened and the baby died thereafter.

The autopsy showed numerous aggregations and 100 ml of clear yellowish liquid between the anterior abdominal wall, liver and diaphragm. The liver was flabby, measuring $14 \times 12 \times 11$ cm, weighing 786 g; smooth capsule; in section the parenchyma was colored yellow-red. Numerous nodules of 4×5 cm and smaller were found in the liver. Lungs dimensions: right — $15 \times 6 \times 5$ cm weighting 166 g; left — $14.5 \times 5.5 \times 4.5$ cm weighting 150 g. In the section, the lung tissue was colored dark-pink with numerous nodules of grey color of 0.5–1.0 cm in diameter. The stomach was enlarged, filled with liquid contents resembling coffee grounds. No specific changes have been identified in other organs.

Histological investigation of the autopsy material revealed nodules in the liver with a structure of HB. The tumor consisted of epithelioid cells, forming atypical trabecular, tubular and acinar structures, represented by two types of cells. Some cells have orbicular nuclei and light or fine-grained cytoplasm, other cells were small in size, orbicular with a small cytoplasmic rim. Dilated bile capillaries with the phenomena of cholestasis were noted in the tumor. Hepatocytes were preserved in the state of fatty dystrophy; sinusoids were anemic (Fig. 1).

The nodules in the lungs also had the structure of HB. According to the histological structure of the tumor, a combined fetal-embryonic epithelial type of HB was diagnosed.

Immunohistochemical picture of tumors, shown in Fig. 2, was characterized by a moderate focal, depending on the areas of the histological structure of the carcinoma, AFP expression (Fig. 2, a), and low cytokeratin Pan expression was observed in the trabecular structures of the tumor, in its absence in the areas with the acinar structure (Fig. 2, b). The proliferative activity of tumor cells was low, which was determined by immunohistochemical reaction with

Ki-67 (Fig. 2, c). The CD10 marker revealed bile ducts between hepatocytes in the liver tissue, and expressed focally in the cytoplasm of hepatocytes (Fig. 2, d).

On the basis of the revealed changes at autopsy and the findings of histological and immunohistochemical investigation of the autopsy material, a pathoanatomical diagnosis was made: The underlying disease is HB of the left lobe of the liver with metastases in the right lobe and lungs; state of health after surgery (atypical resection SgIVb/III); complications of the underlying disease: cerebral edema, ascites, bilateral hydrothorax, cholemic gastrointestinal bleeding, dys trophy and anemia of the internal organs.

The level of embryonic AFP in blood serum is an important indicator in the diagnosis and differential diagnosis of tumor in children. Elevated serum AFP is observed in 90% of HB cases. According to a few studies [3, 4], the AFP level of 100 to 1,000,000 ng/ml at the initial diagnosis is associated with a better prognosis than < 100 or $> 1,000,000$ ng/ml. The reported patient presented with the initial AFP level of 283.3 ng/ml, which was consistent with the indicators for good prognosis in specific treatment. This was also confirmed by other risk determination criteria [5]: PRETEXT II, absence of metastases in the lungs, and extrahepatic spread according to CT. However, the reported patient experienced a progression of the disease despite the treatment: AFP level was elevated simultaneously with the reduction in the size of the primary tumor and metastatic lesions appeared in the lungs. Therefore, for prognostic purposes it is desirable to use other criteria of progression and prognosis of tumor in combination with existing ones.

Few publications confirm the role of CD10 in HB, and CD10 expression could be one of the prognostic factors [6, 7]. Carcinoma progression is in some way dependent on the disruption of CD10 regulation in the stromal cells and tumor parenchyma, so its expression can be used to evaluate the favorable or adverse effects of treatment. The reported patient presented a high expression of CD10 in the tumor tissue, which was combined with resistance to chemotherapy even in the presence of other favorable prognostic indicators.

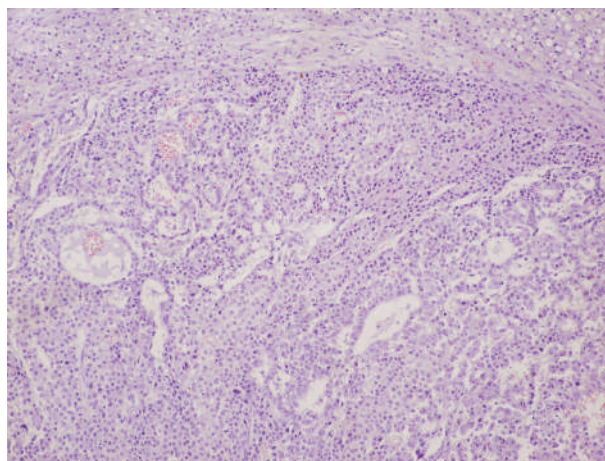


Fig. 1. Microscopic structure of the tumor. Hematoxylin and eosin stain. $\times 100$.

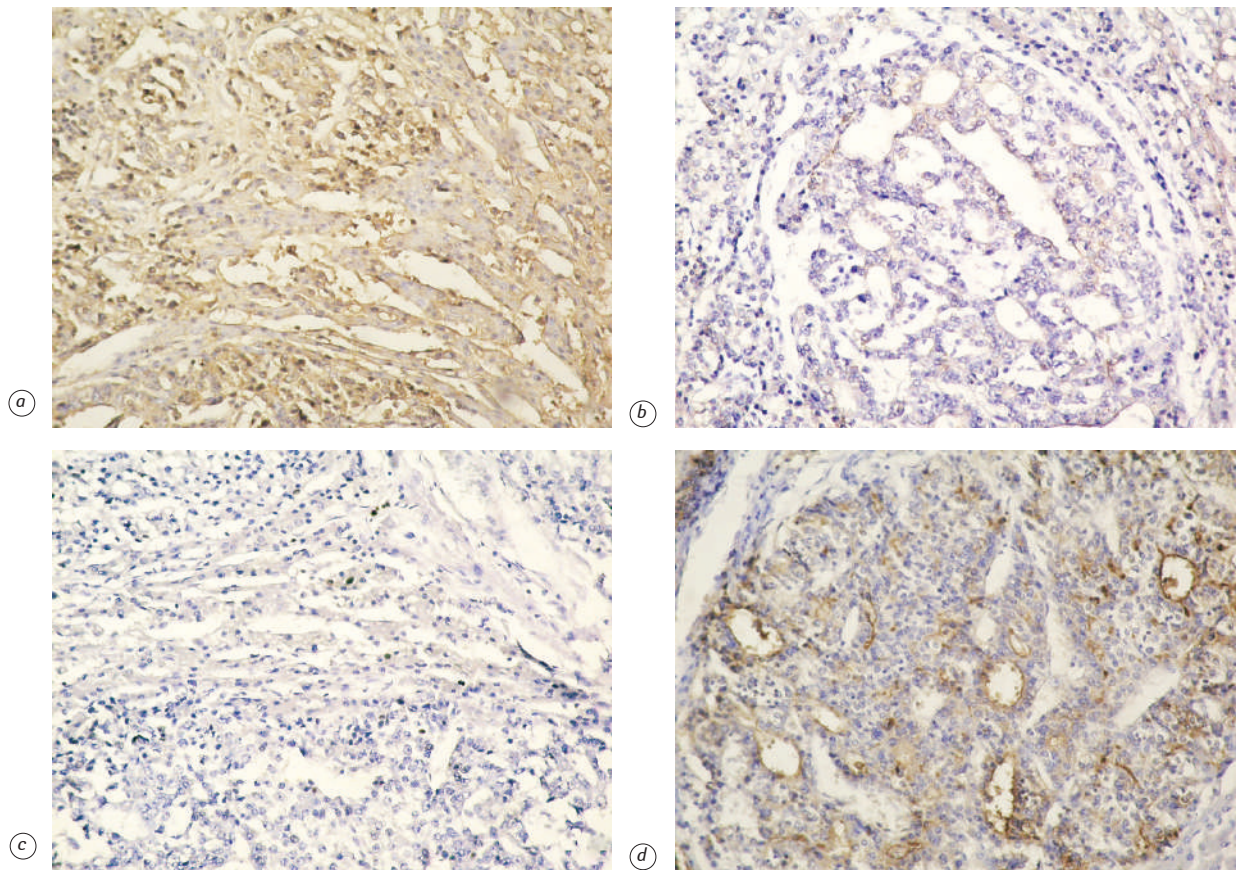


Fig. 2. Immunohistochemical profile of the tumor: *a* — expression of AFP by tumor cells; *b* — expression of Pan cytokeratin in tumor cells; *c* — low nuclear expression of Ki-67; *d* — CD10 expression in tumor tissue, $\times 200$.

Therefore, comparing clinical and histopathological parameters with CD10 expression may be useful in prognostic analysis of HB. However, its exact role in the progression and HB resistance is not well established. The prognostic factors of HB require detailed study in complex investigations that would include histological, clinical, laboratory, and immunohistochemical characteristics. This will expand our knowledge of tumor biology and improve diagnostic, prognosis and treatment methods.

REFERENCES

1. Starchenko II, Dyachenko LV, Prylutskyi OK, *et al.* The observation of congenital retroperitoneal large size neuroblastoma. *Exp Oncol* 2019; **41**: 1–3.
2. Zhang Y, Zhang WL, Huang DS, *et al.* Clinical effectiveness of multimodality treatment on advanced pediatric hepatoblastoma. *Eur Rev Med Pharmacol Sci* 2014; **18**: 1018–26.
3. Bosman F, Carneiro F, Hruban R, Theise ND (eds). WHO Classification of Tumours of the Digestive System. 4th edn. IARC Press: Lyon: 2010. 314 p.
4. Koh KN, Park M, Kim BE, *et al.* Prognostic implications of serum alpha-fetoprotein response during treatment of hepatoblastoma. *Pediatr Blood Cancer* 2011; **57**: 554–60.
5. Kiruthiga KG, Banumathi R, Soumitra S, *et al.* Histological and immunohistochemical study of hepatoblastoma: correlation with tumour behaviour and survival. *J Gastrointest Oncol* 2018; **9**: 326–37.
6. Zhang Q, Ming J, Zhang S, *et al.* A rare case of adult hepatoblastoma with neuroendocrine differentiation misdiagnosed as neuroendocrine tumor. *Int J Clin Exp Pathol* 2013; **6**: 308–13.
7. Mishra D, Sunita S, Narayan G. Role of B cell development marker CD10 in cancer progression and prognosis. *Mol Biol Int* 2016; 2016: 4328697.