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Rare embryonal tumor of the central nervous system in newborns: case report and comparative clinical analysis

A. S. Panina[1,A,B,C,D,F], P. V. Kuzyk[1,2C,E,F], T. V. Savchuk[1,B,C,E], V. A. Zhovnir[1,2E,F], A. Zh. Sadykova[3,E,F]

[1]Bogomolets National Medical University, Kyiv, Ukraine, [2]National Research Center for Radiation Medicine, Hematology and Oncology of the National Academy of Medical Sciences of Ukraine, Kyiv, [3]S. D. Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan

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Aim: to conduct a clinical and morphological analysis of a case of central nervous system (CNS) embryonic tumor not otherwise specified (NOS) and to determine its key pathogenetic features.

Materials and methods. A retrospective analysis was conducted of an autopsy case involving a deceased premature female neonate diagnosed with a CNS embryonal tumor, NOS. The material was obtained from the Division of Pathological Anatomy of the National Specialized Children's Hospital "Ohmatdyt" of the Ministry of Health of Ukraine. The morphological diagnosis was established based on macroscopic and microscopic examination.

Results. The findings indicate an intrauterine origin of the CNS embryonal tumor NOS and the presence of characteristic morphological features that correlate with aggressive tumor behavior, including multiple necroses, hemorrhages, and pseudorosettes formations composed of poorly differentiated cells. The study emphasizes the importance of fetal magnetic resonance imaging in complex cases of prenatal hydrocephalus as a diagnostic tool and for determining further pregnancy management strategies.

Conclusions. The presented case highlights the need for an interdisciplinary approach to the diagnosis and care of newborns with CNS embryonal tumors and the creation of prognostic models for delivery outcomes in the presence of this pathology.

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Рідкісна ембріональна пухлина центральної нервової системи в новонароджених: власний випадок і аналіз клінічних аналогів

А. С. Паніна, П. В. Кузик, Т. В. Савчук, В. А. Жовнір, А. Ж. Садикова

Мета роботи – проаналізувати клініко-морфологічний випадок ембріональної пухлини центральної нервової системи (ЦНС), що не визначена до інших категорій (NOS), та навести її ключові патогенетичні особливості.

Матеріали і методи. Здійснили ретроспективний аналіз випадку аутопсії померлої недоношеної новонародженої дитини жіночої статі з ембріональною пухлиною ЦНС NOS. Матеріал отримано у відділенні патологічної анатомії Національної дитячої спеціалізованої лікарні «Охматдит» МОЗ України. Морфологічний діагноз встановлено на підставі результатів макро- та мікроскопічного дослідження.

Результати. Результати дали змогу зробити висновок про внутрішньоутробне походження ембріональної пухлини ЦНС NOS і виявити характерні морфологічні особливості, що корелюють з агресивним перебігом пухлинного процесу (множинні некрози, крововиливи, псевдорозетки з низькодиференційованих клітин). Підтверджено доцільність застосування магнітно-резонансної томографії у складних випадках пренатальної гідроцефалії як засобу уточнення діагнозу та для визначення наступної тактики ведення вагітності.

Висновки. Наведений клінічний випадок акцентує на необхідності міждисциплінарного підходу до діагностики та лікування новонароджених з ембріональними пухлинами ЦНС, а також створення прогностичних моделей перебігу пологів, коли діагностовано цю патологію.

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Embryonal tumors of the central nervous system (CNS), not elsewhere classified (NEC), are a rare, diagnostically challenging, and clinically aggressive category of pediatric neoplasms. According to the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System (5th edition), CNS embryonal tumour NEC/NOS is a tumour arising in the CNS with embryonal morphology and immunophenotype and either lacking an alteration that would classify it as one of the molecularly defined CNS embryonal tumours (not elsewhere classified; NEC) or not susceptible to further analysis (not otherwise specified, NOS) [1]. These tumors are characterized by rapid growth, high cellularity, pronounced mitotic activity, and multiple areas of necrosis [2,3].

The overall survival rate of newborns with this rare tumor is generally low. Thus, the five-year overall survival rate recorded in retrospective cohorts ranges from 25 % to 30 %, reflecting the aggressive nature of these tumors and the difficulties in their treatment [4]. Such mortality rates are particularly associated with the frequent development of complications such as hydrocephalus due to obstruction of the cerebrospinal fluid outflow pathways, intracranial hemorrhages, neurological disorders due to mass effect or infiltration, and early dissemination in the CNS [2,5].

There is a notable correlation between histological features and clinical manifestations: tumors with higher mitotic indices and extensive necrosis tend to cause more rapid development of neurological symptoms [6]. However, the inability to assess the latter in fetuses complicates the clinical diagnosis of tumors which develop during the intrauterine period and are mainly found during autopsy. The consistency of clinical and morphological data is limited, so pathological observations play a critical role in refining the diagnosis and management tactics.

Aim

To conduct a clinical and morphological analysis of a case of central nervous system embryonic tumor not otherwise specified and to determine its key pathogenetic features.

Materials and methods

We retrospectively analyzed an autopsy case of a deceased premature female neonate diagnosed with a CNS embryonal tumor, NOS. The material was obtained from the Division of Pathological Anatomy of the National Specialized Children's Hospital "Ohmatdyt" of the Ministry of Health of Ukraine in accordance with a cooperation agreement between the university and the healthcare institution. No immunohistochemical or molecular studies were performed in this case. The diagnosis was established within the limits of available methods, based on macroscopic and microscopic findings using hematoxylin and eosin staining. The morphological diagnosis was made to the extent possible in the absence of immunohistochemical and molecular confirmation.

This retrospective study was approved by the Medical Ethics Committee of the National Research Center for Radiation Medicine, Hematology and Oncology, National Academy of Medical Sciences of Ukraine (Protocol No. 9, July 15, 2025). The study was conducted in accordance with national legislation, institutional regulations, and the principles of the Declaration of Helsinki. Human samples were obtained as by-products of routine diagnostic autopsies. Due to the retrospective design and complete anonymization of data, written informed consent from the parents was not required under applicable national and institutional guidelines.

Results

Child K. was born to a 35-year-old woman during her second pregnancy. The first pregnancy ended with the birth of a healthy child. The current pregnancy initially proceeded without complications, but in the first trimester, mild toxicosis and iron deficiency anemia developed, for which oral iron therapy was prescribed. Routine ultrasound screening at 20 weeks of gestation revealed no structural anomalies or intrauterine growth restrictions.

At 26 weeks of gestation, the woman presented with clinical signs of severe gestosis, including arterial hypertension (BP 160/100 mmHg), generalized edema, and proteinuria. She was hospitalized to the department of pregnancy pathology for close monitoring. During her hospital stay, a repeat prenatal ultrasound revealed significant bilateral hydrocephalus with ventricular dilatation up to 25 mm, polyhydramnios, and signs of fetal distress. Fetal echocardiography and Doppler studies indicated a reduced cerebroplacental ratio and abnormal umbilical artery flow (absent end-diastolic flow). No extracranial anomalies were detected.

Laboratory tests ruled out maternal infections, including TORCH-infections (Toxoplasma gondii, Rubella virus, Cytomegalovirus, Herpes simplex virus types I and II). Serological testing for HIV, hepatitis B and C, and syphilis was also negative.

At 29 weeks of gestation, due to the worsening maternal condition – including uncontrolled hypertension (BP 180/110 mmHg), elevated liver enzymes, thrombocytopenia, and signs of hemolysis – severe preeclampsia with impending HELLP syndrome was diagnosed. An emergency cesarean section was performed to save the mother's life.

A premature female neonate was delivered via lower-segment cesarean section. The newborn weighed 2550 g, measured 46 cm in length, and had Apgar scores of 2 at 1 minute and 3 at 5 minutes. The newborn was pale, hypotonic, and bradycardic at birth, with weak spontaneous respiratory effort. Immediate neonatal resuscitation was initiated according to international neonatal life support protocols. This included positive-pressure ventilation with oxygen, endotracheal intubation, external cardiac massage, and administration of epinephrine. Despite maximal supportive measures, the newborn's condition did not stabilize, and spontaneous cardiac activity ceased at 30 minutes of life.

The infant was referred for autopsy with the clinical diagnosis: congenital malformation (internal hydrocephalus, suspected holoprosencephaly), multiple organ failure syndrome, and prematurity.

Pathological examination. Skin is pale blue, with petechial hemorrhages in the area of lower extremities. The subcutaneous fat layer is satisfactorily developed and swollen. The umbilical cord remnant is tied with a ligature. The head is round in shape, enlarged in volume, with a circumference of 37 cm, a large fontanelle measuring 6 × 6 cm, and a sagittal suture that has separated, causing the medial edges of the parietal bones of the skull to be 3 cm apart. The brain tissue is significantly thinned to

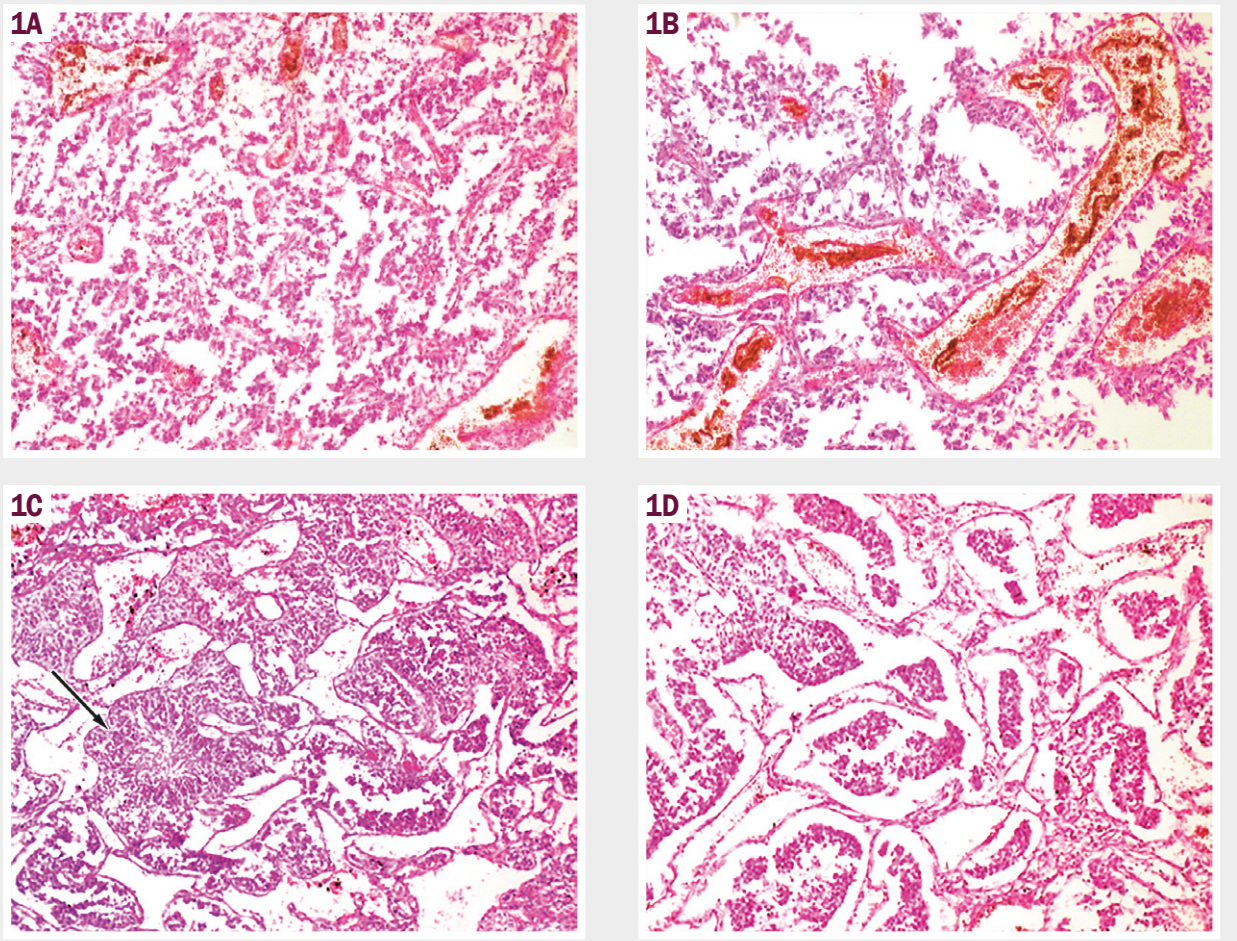

Fig. 1. Histopathological examination of an embryonal CNS tumor NOS; structural polymorphism observed in different fields of view (**A–D**). **A, B:** cords of atypical cells with sinusoid-like dilated stromal vessels; **C:** formation of pseudorosettes (arrow); **D:** alveolar structures and nests of atypical cells surrounded by delicate stromal septa, H & E. **A:** × 40; **B, C, D:** × 200.

1–2 mm, swollen, pale blue, without differentiation into gray and white matter. The superior sagittal sinus has no lumen from the crista galli to its middle part, and from the middle part to the confluens sinuum, the sinus is sharply widened to 1.5 cm. Expanded: confluens sinuum up to 3 cm, sinus transversus sinister and sinus sigmoideus sinister up to 1 cm in diameter. At the site of expansion of the superior sagittal sinus, fusion between it and the brain tissue is noted along the upper edge of the large hemispheres. In this place and on the medial surface of the hemispheres, the brain tissue is bluish-pink in color, with hemorrhages, soft-elastic consistency, and differed from normal tissue. The surface of the hemispheres with smoothed convolutions and sulci. Ependyma includes brownish deposits.

The structures of the corpus callosum, thalamus, and walls of the third ventricle are not differentiated. The brain stem is flaccid in consistency, with enlarged cavities of the fourth ventricle and cerebral aqueduct. The vascular plexuses are full of blood. The lateral ventricles are greatly enlarged and filled with liquid blood. The internal organs are pale, without any peculiarities. There is a large amount of transparent yellowish content in the pleural cavities. There is a small amount of transparent yellowish fluid in the abdominal cavity.

Microscopic examination. Thinning of the brain substance of the large hemispheres with violation of histoarchitectonics due to the predominance of glial elements, an increase in the number of vessels in one field of view. Perivascular and pericellular edema, necrotic and necrobiotic changes, perivascular-focal lymphoid infiltration were observed. The tumor had a polymorphic structure, consisting of poorly differentiated cells, which formed alveolar structures in some places, focal clusters of atypical cells surrounded by thin stromal bridges with a large number of dilated vessels, while in other fields of view there were strands of atypical cells, a large number of dilated vessels, multiple necroses, and pseudorosettes *(Fig. 1)*. Diagnosis: embryonic CNS tumor, NOS.

Thymus. Lobular structure and division into layers are preserved, inversion of layers, delymphatization and Hassall's corpuscles located in the cortical and medullary layers are observed; conclusion: accidental involution of the thymus, stage III.

Discussion

Embryonal CNS tumors, NOS, are usually localized in the frontal or parietal lobes of the cerebral hemispheres, less commonly in the brain stem and spinal cord. In 25–30 % of cases,

these neoplasms are associated with tumor implants (mainly in the subarachnoid space) [7,8,9].

Macroscopically, these tumors usually appear as solid gray-pink formations that are not clearly demarcated from normal brain tissue. Large lesions with cystic or necrotic areas are common [10,11,12]. Microscopically, they appear as hypercellular lesions consisting of poorly differentiated cells with round or oval nuclei with banded chromatin, high mitotic index, and frequent apoptotic bodies [7,8]. Sometimes they can also form pseudorosettes. Molecular drivers for this diverse group of tumors are still not understood, either because the molecular profile does not fit a defined CNS WHO diagnostic entity (NEC) or molecular classification cannot be performed (NOS).

Due to this, according to the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System (5th edition), when molecular analysis of CNS embryonal tumors fails to detect an alteration that allows specific classification or is unsuccessful, the designations “not elsewhere classified (NEC)” or “not otherwise specified (NOS)”, respectively, should be applied [1].

Our clinical and pathological observation concerns a premature girl born at 29 weeks of gestation who died within the first 30 minutes of life due to severe respiratory failure. Pathologically, the tumor was localized in the frontal lobes of the brain and had grown into the superior sagittal sinus, leading to obliteration of its lumen and the development of hydrocephalus; it was not possible to determine the clear boundaries of the tumor. Most likely, the tumor invaded the structures of the corpus callosum, thalamus, and walls of the third ventricle, which explained the inability to verify these structures at autopsy. Hemorrhages in the lateral ventricles indicated invasion of the cerebral vessels and were the cause of anemia detected at autopsy. Morphologically, the tumor met the criteria for an embryonic CNS tumor NOS according to the WHO classification – it consisted of undifferentiated cells with a high mitotic index, pronounced polymorphism, pseudorosettes, and multiple areas of necrosis. These morphological characteristics allow us to verify a highly malignant neuroepithelial tumor. In general, the morphological picture of the tumor we describe is typical for an embryonic CNS tumor NOS.

The discrepancy between the clinical and pathological diagnoses in this case could be due to the difficulty of diagnosing the neoplasm based on insufficient clinical data (ultrasound, which revealed hydrocephalus), as well as the difficulty of differentiating the diagnosis of an embryonic CNS tumor NOS from other pathologies that can cause hydrocephalus (e. g., TORCH infections, meningitis, or congenital defects of the cerebrospinal fluid pathways). In this case, due to the extreme degree of malignancy of the neoplasm (grade IV), the discrepancy between the clinical and pathological diagnoses was not clinically significant, but it further emphasized the importance of using alternative imaging methods, such as magnetic resonance imaging (MRI), for a more accurate differential diagnosis of fetal pathologies. Thus, hydrocephalus together with macrocephaly or polyhydramnios are often the first ultrasound markers that can be indications for a more detailed MRI examination [13].

A comparative analysis of our observation with similar cases from the literature allows us to identify key clinical and morphological patterns and differences. In the case described by E. Cambruzzi et al. [14], a premature newborn girl (gestational age 22 weeks) had a 0.9 cm tumor located in the right lateral ventricle. Microscopically, it was a high-grade malignant neoplasm with marked atypia, a solid pattern, and a high mitotic index (Ki-67 – 90 %). Despite high proliferative activity, this case, unlike ours and the case reported by R. Kapoor et al. [15], was not accompanied by significant hydrocephalus or massive mass effect, probably due to the smaller size of the tumor and earlier gestational age at the time of death. However, the presence of a thrombus in the right lateral and third ventricles may indicate hemorrhage, which is an indirect sign of potential tumor aggressiveness.

Another similar observation reported by R. Kapoor et al. [15] concerns a newborn girl who was found to have a large echogenic formation in the supratentorial region at 24–25 weeks of gestation, and later, at 35 weeks, an enlarged fetal head and a heterogeneous mass in the left hemisphere of the brain with multiple cystic areas were detected. In this case, right-sided hydrocephalus, associated polyhydramnios, placentomegaly, pericardial and pleural effusion were observed. Morphologically, the tumor consisted of proliferating neoplastic cells located perivascularly with the formation of focal pseudorosettes and focal necrosis. Mitotic activity was minimal, but the tumor showed rapid growth. The child died after spontaneous premature delivery.

Common clinical and morphological patterns identified in our observation and described by other authors indicate several important features of CNS embryonal tumors, NOS. All described cases concern premature babies (from 22 to 29 weeks of gestation), which confirms the intrauterine origin of these tumors and their early clinical onset in the perinatal period. Morphologically, the tumors show signs of high malignancy: pronounced cell undifferentiation, the presence of pseudorosettes, multiple areas of necrosis and hemorrhages in the brain parenchyma and ventricular cavities. These characteristics were present in our case and in studies conducted by other authors, which correlates with the aggressive course of the disease [16,17,18]. At the same time, in the case described by E. Cambruzzi et al., a high mitotic index was observed, but the absence of massive necrosis and hemorrhages, as well as the smaller size of the tumor, could have led to the absence of hydrocephalus [14].

Among the main complications, hydrocephalus is the most common that typically result from ventricular system compression by a tumor or due to hemorrhage. This complication occurs in approximately 17.3 % of newborns with CNS tumors and causes increased intracranial pressure with subsequent damage to brain tissue [19,20]. In our case and in the observation by R. Kapoor et al. [15], hydrocephalus was one of the leading manifestations, while in the case of E. Cambruzzi et al. [14], it was not recorded.

Additionally, such systemic manifestations of the tumor as polyhydramnios and non-immune hydrops fetalis, which were noted in our own observation and in the case reported by R. Kapoor et al., deserve particular attention. These conditions were accompanied by pericardial and pleural effusion, ascites, and were probably caused by both hypothalamic dysfunction and high cardiac output [21,22]. Non-immune hydrops fetalis can also cause “mirror syndrome” (Ballantyne syndrome), described in the observation by R. Kapoor et al. [15], in which the mother’s

condition “mirrors” the hydrops condition of the fetus, manifested by edema, hypertension, and proteinuria, which must be differentiated from preeclampsia [23]. This syndrome is an important trigger for termination of pregnancy and/or delivery for medical reasons [24].

Thus, the described case supports the inclusion of embryonal CNS tumors in the differential diagnosis of prenatally detected anomalies, particularly hydrocephalus, polyhydramnios, fetal hydrops, and cases of sudden neonatal death. Such cases highlight the critical role of pathological examination in verifying prenatal hypotheses and determining the causes of fatal outcomes. Multidisciplinary collaboration between perinatologists, neonatologists, neuropathologists, pediatric oncologists, and prenatal diagnostics specialists is essential to ensure accurate diagnosis and optimal management of such pregnancies. A comprehensive approach to monitoring high-risk pregnancies is a key for reducing neonatal morbidity and mortality, especially in the context of limited access to specialized perinatal monitoring programs [24].

Systematization of clinical and morphological data on CNS embryonal tumors, NOS is necessary for improving morphological classification, refining diagnostic criteria, developing prognostic approaches, and implementing effective clinical algorithms in neonatal neurooncology. Given the exceptional rarity and diagnostic complexity of embryonal CNS tumors in neonates, there is a clear need for multicenter collection and systematic analysis of such cases. The accumulated data will contribute to future updates in tumor classification, facilitate prenatal detection, and support the development of standardized management protocols in neonatal oncology and perinatal care.

Conclusions

1. CNS embryonal tumors, NOS, are the ones of intrauterine origin, as confirmed by their detection predominantly in premature infants. This indicates an early onset of the pathological process and its significant impact on the course of pregnancy and neonatal prognosis.

2. These tumors are characterized by high-grade malignancy, an undifferentiated cellular structure, the presence of pseudorosettes, extensive necrosis, and hemorrhages – features that reflect their aggressive behavior and poor prognosis.

3. The most common complications include hydrocephalus, intracranial hemorrhage, and non-immune hydrops fetalis (manifested by polyhydramnios, ascites, pericardial, and pleural effusions), which largely determine the severity of the clinical course and contribute to early neonatal mortality.

4. Given the limited specificity of standard prenatal ultrasonography, fetal MRI should be considered in cases of hydrocephalus of unknown etiology. Prenatal MRI may become the gold standard for detecting intracranial tumors. Effective management of such cases requires interdisciplinary collaboration among specialists in prenatal diagnostics, perinatology, neuropathology, and pediatric oncology.

5. Considering the rarity, aggressive clinical behavior, and diagnostic complexity of CNS embryonal tumors, NOS, multicenter case collection is crucial for advancing tumor classification and improving prenatal detection strategies in neonatal neuro-oncology.

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Information about the authors:
Panina A. S., MD student, Faculty of Medicine No. 1, Bogomolets National Medical University, Kyiv, Ukraine.
ORCID ID: 0009-0004-7830-444X
Kuzyk P. V., MD, PhD, Associate Professor of the Department of Pathological Anatomy, Bogomolets National Medical University; Pathologist at the National Research Center for Radiation Medicine, Hematology and Oncology, National Academy of Medical Sciences of Ukraine, Kyiv.
ORCID ID: 0000-0001-9352-4513
Savchuk T. V., MD, PhD, Associate Professor of the Department of Pathological Anatomy, Bogomolets National Medical University, Kyiv, Ukraine.
ORCID ID: 0000-0002-7218-0253
Zhovnir V. A., MD, PhD, DSc, Acting General Director of National Research Center for Radiation Medicine, Hematology and Oncology, National Academy of Medical Sciences of Ukraine, Kyiv.
ORCID ID: 0000-0002-6290-342X
Sadykova A. Zh., MD, PhD, Associate Professor of the Department of Childhood Diseases, S. D. Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan.
ORCID ID: 0000-0002-7780-6243

Відомості про авторів:
Паніна А. С., здобувачка магістерського рівня вищої освіти медичного факультету № 1, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.
Кузик П. В., канд. мед. наук, доцент каф. патологічної анатомії, Національний медичний університет імені О. О. Богомольця; лікар-патологоанатом, ДУ «Національний науковий центр радіаційної медицини, гематології та онкології Національної академії медичних наук України», м. Київ.
Савчук Т. В., канд. мед. наук, доцент каф. патологічної анатомії, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.
Жовнір В. А., д-р мед. наук, т. в. о. генерального директора, ДУ «Національний науковий центр радіаційної медицини, гематології та онкології Національної академії медичних наук України», м. Київ.
Садикова А. Ж., канд. мед. наук, доцент ЗВО каф. дитячих хвороб, Казахський національний медичний університет імені С. Д. Асфендіярова, м. Алмати, Республіка Казахстан.

Альона Паніна (Alona Panina)
panina0511@nmu.ua

References

1. International Agency for Research on Cancer. WHO classification of tumours of the central nervous system: Who classification of tumours. 5th ed. Who Classification of Tumours Editorial Board, editor. IARC; 2022. Available from: https://publications.iarc.fr/601
2. Rezaei N, Hanaei S, editors. Human brain and spinal cord tumors: From bench to bedside. Volume 2: The path to bedside management. Cham: Springer International Publishing; 2023. doi: 10.1007/978-3-031-23705-8
3. Santosh V, Rao S, Dasgupta A, Gupta T. Diagnosis and management of central nervous system embryonal tumors in the molecular era: A contemporary review. Int J Neurooncology. 2021;4(Suppl 1):S190-205. doi: 10.4103/ijno.ijno_427_21
4. Guidi M, Giunti L, Buccoliero AM, Santi M, Spacca B, De Masi S, et al. Use of high-dose chemotherapy in front-line therapy of infants aged less than 12 months treated for aggressive brain tumors. Front Pediatr. 2020;8. doi: 10.3389/fped.2020.00135
5. Kram D, Henderson J, Baig M, Chakraborty D, Gardner M, Biswas S, et al. Embryonal Tumors of the Central Nervous System in Children: The Era of Targeted Therapeutics. Bioengineering. 2018;5(4):78. doi: 10.3390/bioengineering5040078
6. Kwon SM, Kim JH, Kim YH, Hong SH, Cho YH, Kim CJ, et al. Clinical Implications of the Mitotic Index as a Predictive Factor for Malignant Trans-

formation of Atypical Meningiomas. J Neurosurg Soc. 2022;65(2):297-306. doi: 10.3340/jkns.2021.0114
7. Pietsch T. [Neuropathology of medulloblastomas and other CNS embryonal tumors: Precision diagnostics through the integration of genetic markers]. Die Pathologie. 2019;40(2):140-7. German. doi: 10.1007/s00292-019-0580-9
8. Pickles JC, Hawkins C, Pietsch T, Jacques TS. CNS embryonal tumours: WHO 2016 and beyond. Neuropathol Appl Neurobiol. 2018;44(2):151-62. doi: 10.1111/nan.12443
9. Stensvold E, Krossnes BK, Lundar T, Due-Tønnessen BJ, Frič R, Due-Tønnessen P, et al. Outcome for children treated for medulloblastoma and supratentorial primitive neuroectodermal tumor (CNS-PNET) – a retrospective analysis spanning 40 years of treatment. Acta Oncol. 2017;56(5):698-705. doi: 10.1080/0284186x.2017.1301679
10. Hwang EI, Kool M, Burger PC, Capper D, Chavez L, Brabetz S, et al. Extensive Molecular and Clinical Heterogeneity in Patients With Histologically Diagnosed CNS-PNET Treated as a Single Entity: A Report From the Children's Oncology Group Randomized ACNS0332 Trial. J Clin Oncol. 2018;36(34):3388-95. doi: 10.1200/jco.2017.76.4720
11. Ai R, Li J, Lai M, Cai L. RADT-27. Report of 9 Cases of Embryonal Tumors of The Central Nervous System with Multilayered Rosettes (ETMR). Neuro Oncol. 2024;26(Supplement_8):viii78. doi: 10.1093/neuonc/noae165.0311
12. Friedrich C, Warmuth-Metz M, von Bueren AO, Nowak J, Bison B, von Hoff K, et al. Primitive neuroectodermal tumors of the brainstem in children treated according to the HIT trials: clinical findings of a rare disease. J Neurosurg. 2015;15(3):227-35. doi: 10.3171/2014.9.peds14213
13. Bedei IA, Huisman TA, Whitehead W, Axt-Fliedner R, Belfort M, Sanz Cortes MS. Fetal Brain Tumors, a Challenge in Prenatal Diagnosis, Counselling, and Therapy. J Clin Med. 2022;12(1):58. doi: 10.3390/jcm12010058
14. Cambruzzi E, Pêgas KL, Nascimento GB, da Silva JN, Zandoná NB, Medeiros MS. Autopsy report and review of the 2016 WHO classification of congenital supratentorial embryonal tumors, not otherwise specified. Interdiscip Neurosurg. 2021;23:100913. doi: 10.1016/j.inat.2020.100913
15. Kapoor R, Bansal A, Aggarwal AK, Aggarwal A, Chaddha V, Kapoor S. A Rare Aggressive Fetal Intracranial Tumor. J Fetal Med. 2015;2(2):91-5. doi: 10.1007/s40556-015-0046-y
16. Kim SY, Tang M, Chih SY, Sallavanti J, Gao Y, Qiu Z, et al. Involvement of p38 MAPK and MAPKAPK2 in promoting cell death and the inflammatory response to ischemic stress associated with necrotic glioblastoma. Cell Death Amp Dis. 2025;16(1). doi: 10.1038/s41419-025-07335-3
17. Yee PP, Li W. Tumor necrosis: A synergistic consequence of metabolic stress and inflammation. BioEssays. 2021;43(7):2100029. doi: 10.1002/bies.202100029
18. Karsch-Bluman A, Benny O. Necrosis in the Tumor Microenvironment and Its Role in Cancer Recurrence. In: Birbrair A, editor. Tumor Microenvironment. Advances in Experimental Medicine and Biology. Cham: Springer; 2020. doi: 10.1007/978-3-030-35727-6_6
19. Al Shoufy M, Kafa G, Ibrahim B, Ibrahem H, Dakour A, Haidar A, et al. Exploring neonatal brain tumors: a narrative review about epidemiology, classification, and management. Ann Med Amp Surg. 2025;87(5):2838-46. doi: 10.1097/ms9.0000000000003229
20. Tully HM, Dobyns WB. Infantile hydrocephalus: a review of epidemiology, classification and causes. Eur J Med Genet. 2014 Aug;57(8):359-68. doi: 10.1016/j.ejmg.2014.06.002
21. Toniutti M, Sasso AL, Carai A, Colafati GS, Piccirilli E, Del Baldo G, et al. Central nervous system tumours in neonates: what should the neonatologist know? Eur J Pediatr. 2024;183(4):1485-97. doi: 10.1007/s00431-023-05404-3
22. Khairudin D, Alfirevic Z, Mone F, Navaratnam K. Non-immune hydrops fetalis: a practical guide for obstetricians. Obstet Gynaecol. 2023;25(2):110-20. doi: 10.1111/tog.12862
23. Albar OH, Maghfuri LM, Alhadri HY, Albahli FH, Omairah MH, Albahli HM, et al. Innovations in maternal-fetal medicine and neonatology: A multidisciplinary approach to enhancing care for high-risk pregnancies and premature infants. J Ecohumanism. 2024;3(8):12904-14. doi: 10.62754/joe.v3i8.6155
24. Malachynska M, Kuzyk P, Diegtiar O. Promoting healthy births and reducing infant mortality through national health system. Int J Health Sci. 2021;5(3):449-60. doi: 10.53730/ijhs.v5n3.1905