UDC: 616-006.487-07
DOI: 10.52532/2663-4864-2020-1-55-33-35

B.B. ZHETPISBAEV[1], E.B. SATBAEVA[2], N.A. RYSKELDIEV[1], N.N. ASHIROV[1], E.S. GORSHKOVA[1]

[1]National Centre for Neurosurgery, Nur-Sultan, Kazakhstan;
[2]Kazakh Institute of Oncology and Radiology, Almaty, Kazakhstan

Olfactory neuroblastoma

The article describes a classic case of olfactory neuroblastoma in a 33-year-old female patient diagnosed with «nasal cavity neoplasm (polyp?)» who was referred to the National Centre for Neurosurgery JSC from the ENT Department of the City Hospital No. 1. The first symptoms of the tumor occurred during her pregnancy. The aggressive tumor has invaded the anterior cranial fossa and spread into the right half of the ethmoid sinuses and the orbit. The tumor diagnostics was complicated by the prevalence of symptoms of a nasal cavity neoplasm. The "olfactory neuroblastoma" diagnosis was verified by clinical observations, MRI, and pathomorphological studies. Histological examination of the tumor showed a typical structure of olfactory neuroblastoma. IHC examination showed an expression of neuronal differentiation markers. The degree of malignancy was determined by Hyams grading.

Keywords: *olfactory neuroblastoma, histopathology, immunohistochemistry (IHC), Hyams grading.*

Introduction: Olfactory neuroblastoma (nasal cavity esthesioneuroblastoma, ONB) is a rare tumor that develops from olfactory neuroepithelial cells located in the upper part of the nasal septum, ethmoid bone, and superior nasal concha [1].

ONB frequency is 3-15% [1-3]. The first mention of ONB in the scientific literature dates back to 1924. The review of scientific literary published in 1997 described 2145 ONB cases worldwide [4]. Since 1996 till today, separate cases of ONB were described in domestic literature [3, 5]. This tumor can occur at any age but is more often in adults [1, 3, 5].

ONB is a malignant tumor that grows into the paranasal sinuses, orbit, and cranial cavity. It often spreads to the regional lymph nodes and, in the case of intracranial spread, is metastasizing in subarachnoid cavities [3-5]. Developing in the upper part of the nasal cavity and ethmoid sinuses, it destroys the lateral wall and fills out the corresponding half of the nasal cavity. ONB penetrates the maxillary sinus, extends into the orbit cavity from ethmoid sinuses through the medial orbit wall, and penetrates the anterior cranial fossa via the sieve plate. A substantial tumor spread involves such structures as basis crania, sinus sphenoidalis, nasopharynx, oropharynx, laryngopharynx, soft tissues and bone structures of the upper jaw, pterygopalatine and infratemporal fossa, Turkish saddle, and frontal sinus; the process extends to the other half of the nasal cavity and paranasal sinuses [4-6, 9]. The majority of authors estimate the prevalence of ONB according to the S. Kadish classification (1976). Consequently, the authors outline the following three stages:

A – the tumor is limited by the nasal cavity;

B – the tumor affects the paranasal sinuses;

C – the tumor extends beyond the nasal cavity and paranasal sinuses;

D – the presence of regional and distant metastases.

Nonspecific nature of clinical symptoms at an early stage of this tumor development and low awareness of doctors about this rare pathology result in diagnostic errors and inadequate treatment [8, 9]. As the disease progresses, the symptoms become quite specific. The patients complain of unilateral nose obstruction, nasal bleeding, and anosmia, as well as the proptosis, diplopia, visual impairment, and severe headache.

Early diagnostics of ONB is challenging. ONB shall be differentiated from an inflammatory process, adenoids, debride, and nasal polyps. A comprehensive ONB diagnostics shall include the nasal cavity examination, rhinoscopy, X-Ray radiography, CT and MRI with contrast enhancement (in axial and frontal projections with use of T2-sequences for better delimitation of the lesion volume from the paranasal sinuses secretion), ultrasound examination of internal organs and soft tissues of the neck, as well as histopathological examination of biopsy material [3, 5, 8, 9]. A rhinoscopic examination reveals a soft polypoid formation of gray-pink color, bleeding in contact.

Histologically, ONB can be confused with many other neoplasms such as lymphoma, melanoma, rhabdomyosarcoma, Ewing's sarcoma, plasmacytoma, or nasopharyngeal carcinoma. This necessitates an IHC study [6-9]. Microscopically, the tumor has a lobular structure and consists of relatively homogeneous cells on a fibrillar matrix. In an IHC study, the tumor cells are positive to the neuron-specific enolase (NSE), synaptophysin (Syn); the reaction to chromogranin A (Chromogranin A) might be slightly intense.

In 1988, Hyams et al. have proposed a clinically significant classification which splits the ONB into low malignant (grade I-III) and highly malignant tumors (grade IV) [10, 11]. This classification takes into account such pathomorphological signs as the tumor structure, mitotic activity, nuclear polymorphism, fibrillar matrix, rosettes, and necrosis (Table 1).

Grade I tumors have a lobular structure with a visible neurofibrillary matrix. The cells are small, homogeneous, without mitotic activity; there are no necrosis foci; the Homer-Wright pseudorosettes are quite common. Grade II tumors usually have a less apparent matrix and significant cell atypia with mitoses. Grade III tumors can preserve lob-

ular structure; however, the signs of cell atypia and mitosis increase, there are more foci of necrosis, the true Flexner-Wintersteiner rosettes can be found. Grade IV tumors are the most undifferentiated and difficult to diagnose due to the loss of lobular structure, the presence of cell atypia, necrosis, and mitotic activity.

Table 1 – The Hyams grade of malignancy of olfactory neuroblastoma

Histological signs	Hyams grade			
Tumor structure	Lobular	Lobular	Heterogeneous	Heterogeneous
Mitotic activity	No	Yes	Visible	Apparent
Nuclei polymorphism	No	Moderate	Visible	Apparent
Fibrillar matrix	Visible	Yes	Minimal	Absent
Rosettes	Homer-Wright	Homer-Wright	Flexner-Wintersteiner	Flexner-Wintersteiner
Necrosis	No	No	+/-	Yes

ONB treatment includes the entire range of malignant tumor therapy [8, 9]. Surgical treatment depends on the location, size, and penetration of the tumor into other body segments, and the metastasis. Organ-preserving surgery is preferred without compromising radicalism. At early stages, minimally invasive intervention is performed through the transnasal endoscopic access [9]. Chemotherapy is often used at the preoperative stage, with the penetration of the tumor into neighboring tissues and metastasis. Due to ONB radiosensitivity, chemotherapy is often combined with radiation therapy (RT) as one of the main treatment methods. Remote RT, proton therapy, brachytherapy, and RF-surgery (cyberknife and Novalis) are also used. RT is efficient for regional metastases.

The observed clinical case is presented given the rarity of ONB in modern oncology.

Information about the patient: Patient B., 33 years old, was admitted to the CNS Pathology Department of the National Center for Neurosurgery (Astana, Kazakhstan) with complaints of recurrent headaches, nasal stuffiness, and nasal breathing difficulty. Anamnesis Morbi: sick since the beginning of 2019, when nasal stuffiness, difficulty in nasal breathing, and periodic fever were observed during pregnancy. She was treated and monitored by the ENT doctor at the place of residence. The brain CT has revealed the signs of nasal cavity formation (polyp?). The surgery in the scope of "Right-side endoscopic polysinusotomy" was performed at the ENT department of the City Hospital No. 1. Pathological study: "Pathomorphological picture is indicative of the olfactory neuroblastoma." Head and Neck MRI: "Signs of the anterior cranial fossa formation with invasion to the right half of ethmoid bone cells and the orbit" (figure 1).

Clinical picture: Due to the clinical diagnosis, the patient was transferred to the CNS Pathology Department of the National Center for Neurosurgery. Upon admission: general habitus – moderately severe. Consciousness – clear, GCS score 15. Karnowski grade – 70. Hyposmia. Ophthalmoptosis rightward. Pupils D = S. The photoreaction was alive. The eyeballs movement – in full range, painless. The face – symmetrical, nasolabial triangle – not smoothed. The function of phonation and swallowing was retained. The palatal reflex (+). The tongue was located in the center. No hypotrophy of the tongue muscles observed. The muscle strength was retained in all limbs - 5 points. The tendon reflexes in all limbs were alive, D = S. In the Romberg position was stable. Coordination tests – satisfactory. No meningeal signs.

Diagnostics and treatment: The council of physicians recommended surgical treatment, which was conducted in the scope of "Combined access (bifrontal access and the Mur access). Microsurgical removal of the main bone tumor with the use of a neuronavigation system."

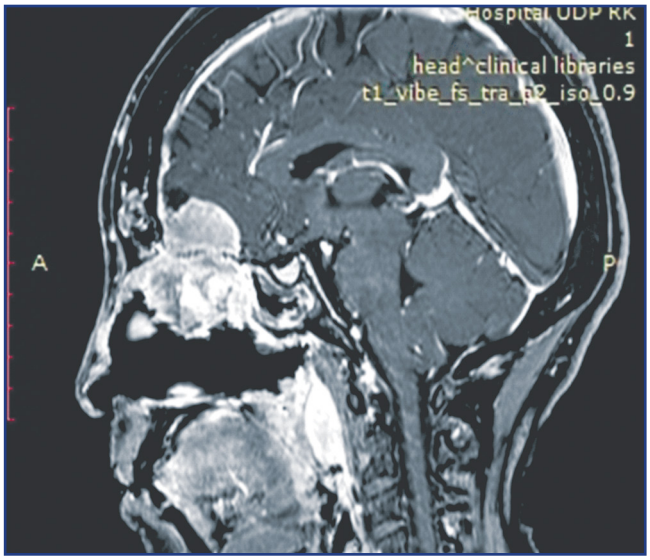

Figure 1 – T2-weighted image in a sagittal projection demonstrates the presence of formation of the anterior cranial fossa with invasion to the right half of ethmoid bone cells and the orbit

The biopsy fragments were referred for histopathological examination. The material was fixed for 24 hours in 10% neutral buffered formalin. After traditional processing, the preparations were stained by hematoxylin and eosin. The pathomorphological study was performed using the Axioscop 40 (Carl Zeiss, Germany) microscope, with total image magnification of X 100, X 200. The tumor tissue fragments demonstrated diffuse round-shaped cell formations with hyperchromic polymorphic nuclei and a few foci of pathological mitoses. The cell cytoplasm had the form of a narrow limbus. The cells formed lobular structures penetrated by fibrous fibers. The Homer-Wright rosettes and glomerular vascular proliferation with endothelial micro-proliferation were observed (figure 2).

IHC studies using the "*Dako*" imaging system followed a standard protocol. The tumor cells were diffusely positive to NSE and Synaptophysin, and negative to GFAP, Chromogranin A, CD45, CD99, Vimentin, S100, Melan A, Pankeratin (AE1/AE3), CK5/6 (Figures 3 and 4).

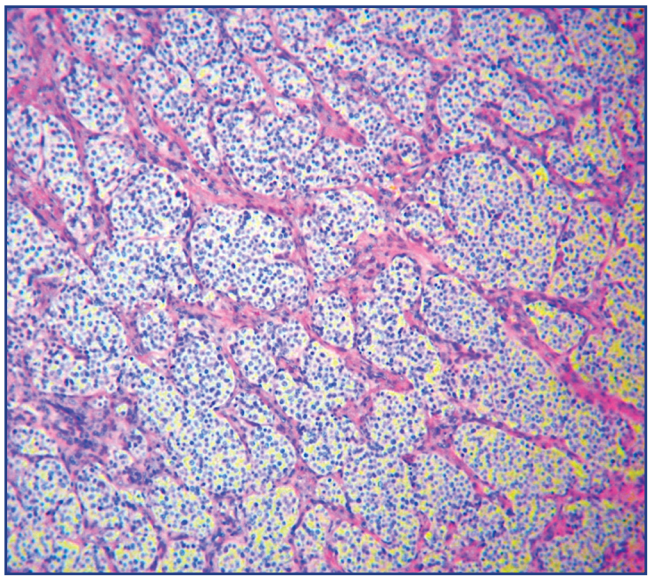

Figure 2 – Low-grade olfactory neuroblastoma, Hyams grade II. X 100. Stained with hematoxylin and eosin

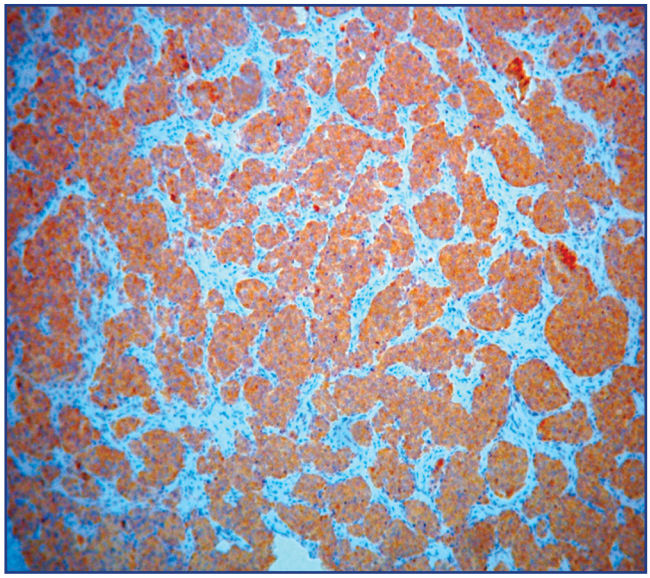

Figure 3 – Positive expression with NSE x100

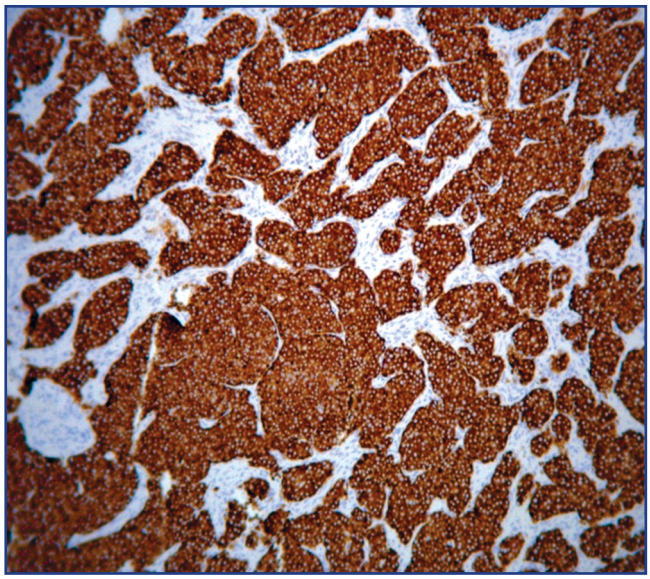

Figure 4 – Positive expression with Synaptophysin, x100

Results: "Olfactory neuroblastoma, Low-grade, Hyams grade II, ICD-O code 9522/3, with intracranial invasion, spread to the right orbit, under clinical subcompensation" was diagnosed based on the clinical, radiological, histopathological and IHC data.

Discussion: The article describes a classic case of olfactory neuroblastoma in a 33-year-old female patient. Tumor symptoms first occurred during pregnancy clinically manifested by symptoms of a nasal polyp. The tumor aggressiveness was evidenced by the invasion of the neoplasm into the anterior cranial fossa, the right half of ethmoid bone cells, and the orbit. The diagnosis was verified by histopathology and immunohistochemistry, with the determination of malignancy degree by Hyams.

Conclusion: This case is of great scientific and clinical interest due to the rare occurrence of the described pathology.

References:

1. Matsko D.E., Korshunov A.G. Atlas opukholey TsNS [Atlas of CNS tumors]. – SPb.,1998. – 134 p. [in Russian];

2. Matsko D.E. Neyrokhirurgicheskaya patologiya [Neurosurgical pathology]. – SPb, 2015. – 182–183 p. [in Russian];

3. Kairemo K.J., Jekunen A.P., Kestilä M.S., Ramsay H.A. Imaging of olfactory neuroblastoma – an analysis of 17 cases // Auris Nasus Larynx. – 1998. – Vol. 25 (2). – P. 173-179;

4. Mustafaev D.M., Svistushkin V.M., Sambulov V.I., Tsagadaeva S.B., Nosova O.A., Ratova A.V., Ershov P.S. Estezioneyroblastoma polosti nosa (ol'faktornaya neyroblastoma) [Estesioneuroblastoma of the nasal cavity (olfactory neuroblastoma)] // Rossiyskaya otorinolaringologiya [Russian Otorhinolaryngology]. – 2009. – Vol. 5. – P. 85–91 [in Russian];

5. Krylov A.S., Shiryaev S.V., Ryzhkov A.D., Mikhailova E.V., Goncharov M.O., Sevryukov D.D. OFEKT/RKT s 99mTc-Tekhnetrilom v monitoringe estezioneyroblastomy [SPECT / RKT with 99mTc-Technetril in monitoring estesioneuroblastoma] // Sib. Onkol. Zh. [Siberian Journal of Oncology]. – 2017. – Vol. 16 (2). – P. 97–102 [in Russian];

6. Zhetpisbaev B.B., Manekenova K.B., Omarov T.M., Abdulguzhina R.M. Sovremennyye podkhody k klassifikatsii opukholey TSNS i opredeleniye ikh stepeni zlokachestvennosti [Modern approaches to the classification of CNS tumors and the determination of their degree of malignancy] // Neyrokhirurgiya i nevrologiya Kazakhstana [Neurosurgery and Neurology of Kazakhstan]. – 20111. – № 4 (25). – P. 11-13 [in Russian];

7. Zhetpisbaev B.B., Kozhakhmetova A.O., Bayzhigitov B.B. Glioma nosa [Glioma of the nose] // Lab. Med. – 2017. – № 2 (21). – P. 29–32 [in Russian];

8. Tabolinovskaya T.D., Mudunov A.M., Aliyeva S.B., Orel N.F., Komarova L.E., Oganyan Ye.R., Pustynsky I.N., Khasanov R.A., Aketova T.A., Pirogova N.A. Estezioneyroblastoma (klinicheskoye techeniye, otdalennyye rezul'taty lecheniya) [Estesioneuroblastoma (clinical course, long-term treatment results)] // Diagnostika i lecheniye opukholey golovy i shei [Head and Neck Tumors Diagnosis and Treatment]. – 2016. – №1(6). – P. 32-39 [in Russian];

9. Merkulov O.A. Endoskopicheski assistirovannyy endonazal'nyy podkhod v khirurgicheskom lechenii estezioneyroblastomy u detey [Endoscopically assisted endonasal approach in the surgical treatment of esthesiuroblastoma in children] // Opukholi golovy i shei [Head and Neck Tumors]. – 2012. – № 1. – P. 37-41 [in Russian];

10. Van Gompel J.J., Giannini C., Olsen K.D., Moore E., Piccirilli M., Foote R.L., Buckner J.C., Link M.J. Long-Term Outcome of Esthesioneuroblastoma: Hyams Grade Predicts Patient Survival // J. Neurol. Surg. B. Skull. Base. – 2012. – Vol. 73(5). – P. 331-336;

11. Thompson L.D.R. Olfactory Neuroblastoma // Head and Neck Pathol. – 2009. – Vol. 3(3). – P. 252-259.