Neoplastična, hiperplastična ili ektopična meningotelijalna ostrva? – Prikaz slučaja i kratak pregled literature

Milenković Sanja[1], Berisavac Iva[2], Jovanović B Milan[3], Grubor Andrej[3]

[1]Služba kliničke patologije, Kliničko bolnički centar Zemun, Beograd, Srbija
[2]Služba neurohirurgije , Kliničko bolnički centar Zemun, Beograd, Srbija
[3]Služba za Otorinolaringologiju i maksilofacijalnu hirurgiju, Kliničko bolnički centar Zemun, Beograd, Srbija

Apstrakt

Prikazujemo slučaj istovremene pojave švanoma etmoidnog sinusa i meingotelijalne hiperplazije kod pacijentkinje bez neurofibromtoze. Postojanje švanoma i meningotelijalne hiperplazije je potvrđeno histopatološkom analizom i imunohistohemijskim bojenjima. Prelazna zona između ova dva entiteta nije utvrđena, ni makroskopski ni mikroskopski. Histološki i imunohistohemijski nalaz, kao i moguća patogeneza ove retke tumorske kombinacije je predmet diskusije.

Ključne reči: Švanoma, meningealne ćelije, sinonazalni tumori

Neoplastic, hiperplastic or ectopic meningothelial islands? - Case report and short review of the literature

Milenkovic Sanja[1], Berisavac Iva[2], Jovanovic B Milan[3], Grubor Andrej[3]

[1]Department of Pathology, Clinical Hospital Center „Zemun", Belgrade, Serbia
[2] Department of Neurosurgery, Clinical Hospital Center „Zemun", Belgrade, Serbia
[3]Department of Otorhinolaryngology, Clinical Hospital Center „Zemun", Belgrade, Serbia
[3]Faculty for Special Education and Rehabilitation, University of Belgrade, Serbia

Abstract

The case of concomitant occurrence of schwannoma of the ethmoid sinus and meningothelial hyperplasia in female patient without neurofibromatosis-2 is presented. The components of Schwannoma tissue and meningothelial hyperplasia cells islets were confirmed by histopathological and immunohistochemical examinations. Transitional zones of these two different tissues macroscopically as well as microscopically were not observed. Histological and immunohistochemical findings and possible pathogenesis of this uncommon tumor combination is discussed.

Key words: schwannoma, meningeal cells, sinonasal tumor

Introduction

Tumors arising from peripheral nerves or displaying differentiation along the lines of the various elements of the nerve sheath (Schwann cells, perineural cells, fibroblasts) are referred as Peripheral Nerve Sheath Tumors (PNSTs) (1). PNSTs may be subdivided into benign and malignant (MPNST) variants[1]. Term PNSTs replaces previously used designations, including Schwannoma, neurofibroma and perineurioma[2]. The most common sites for PNSTs are the proximal parts of lower and upper extremities, the paraspinal region of the trunk, and the head and neck region[1]. Only 4% of all PNSTs of the head and neck are present in the area of the paranasal sinuses[3]. The etiology of PNSTs is usually unknown. However, several hereditary disorders are known to predispose to benign and malignant PNSTs, notably neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2), both of which are inherited in an autosomal dominant fashion[4].

Meningiomas are common central nervous system tumors that originate from the meningeal coverings of the brain and the spinal cord. It seems that meningioma initiation is closely linked to the inactivation of one or more members of the protein 4.1 superfamily, including the neurofibromatosis type 2 gene product merlin/schwannomin, protein 4.IB (DAL-1) and protein 4.1R[5].

Potential "collisions" of schwannoma and meningioma within the same tumor are extremely rare[4]. Most of them are usually associated with von Recklinghausen's disease or neurofibromatosis type-2, NF-2[7]. Neurofibromatosis 2 (NF2) is an uncommon, autosomal dominant disorder in which patients are predisposed

to neoplastic and dysplastic lesions of Schwann cells (schwannomas and schwannosis), meningeal cells (meningiomas and meningioangiomatosis) and glial cells (gliomas and glial hamartomas)[8].

Here we described an interesting appearance of meningeal cell islets with schwannoma of ethmoidal sinuses in patient without NF-2. Histological and immunohistochemical findings and possible pathogenesis of this uncommon tumor combination is presented.

Material and methods

Tumor tissue of 2gr. weight was isolated from the patient and fixed in neutral formalin and embedded in paraffin by standard methods. Sections 5nm thick were stained routinely with Haematoxylin and Eosin. Standard histochemical stainings for Reticulin, Periodic Acid Schiff and Alcian blue were also performed.

Sections made from paraffin embedded tumor tissue were incubated with a panel of monoclonal antibodies which included S-100 protein, epithelial membrane antigen (EMA), carcino-embryonic antigen (CEA), vimentin, desmin, HMB45, synapthophysin and cytokeratin (all from DakoCytomation). Antibodies were revealed using avidin-biotin-peroxidase complex (ABC, DakoCytomation) and labelled streptavidin-biotin staining system (LSAB2, DakoCytomation). Binding was demonstrated using 3,3'-diaminobenzidine tetrahydrochloride (DAB, DakoCytomation) as chromogen and H_2O_2 (0,03%) as substrate, All sections were counterstained with haematoxylin.

Proliferative activity was explored by means of the MIB 1 (Ki67) antibody (DakoCytomation). The sections stained with Ki67 were evaluated in semiquantitative manner at high - power field magnification (HPF, X400). Total number of 1000 stained cells was counted.

Results

A 37- year old woman was presented with 1-year long history of headache propagated on the whole scalp, persistent eye flickering, and ambiguous vision of the right eye and feeling mass behind of the same eye. In particular, there were no stigmata of von Recklinghausen's disease and no familiar history of this disorder. Patient showed no clinical evidence of neurofibromatosis, and genetic test did not performed. Neuro-otological examination revealed normal patient's eyes movement without diplopia. Nystagmus at marginal movement to the right and weaker audition on the right ear were confirmed. Biochemical laboratory tests were normal. CT scan (Fig 1.) showed a nonhomogenous lesion of the right ethmoid sinus spreading outside into the periorbital region and up to anterior cranial base with orbital roof destruction.

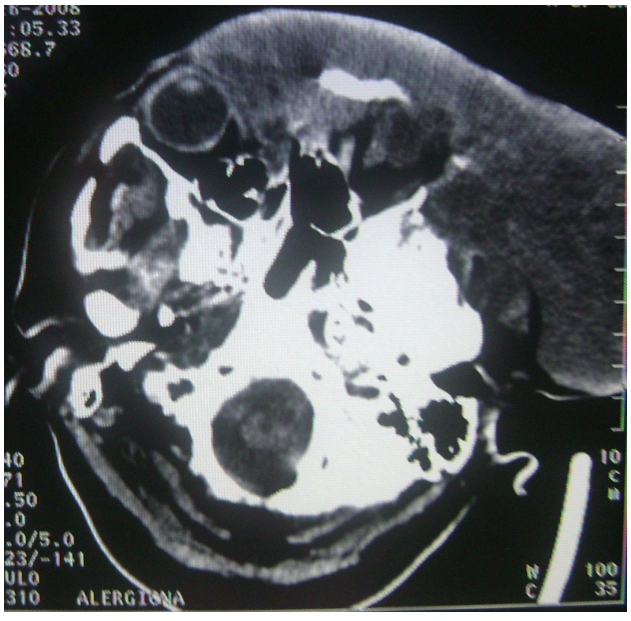

Figure 1. CT scan demonstrated a nonhomogenous density lesion of right ethmoid sinus with extensive outside propagation

The patient underwent a right-sided frontal craniotomy with gross total resection of the tumor. We performed right frontal craniotomy and removed the tumor completely. The dural defect were tented with fat tissue and closed with fascia lata. We used Palcosin order to close the defect of the orbital roof. The postoperative course of the patient was uneventful.

Microscopically the tumor consisted of two different histological components: a solid area of typical benign schwannoma and smaller portion with histological features of menigothelial hyperplasia cells. Histological examination demonstrated tumor with moderate hypercellularity, variable cellular pleomorphisms and low mitotic index (Fig. 2 and Fig. 5).

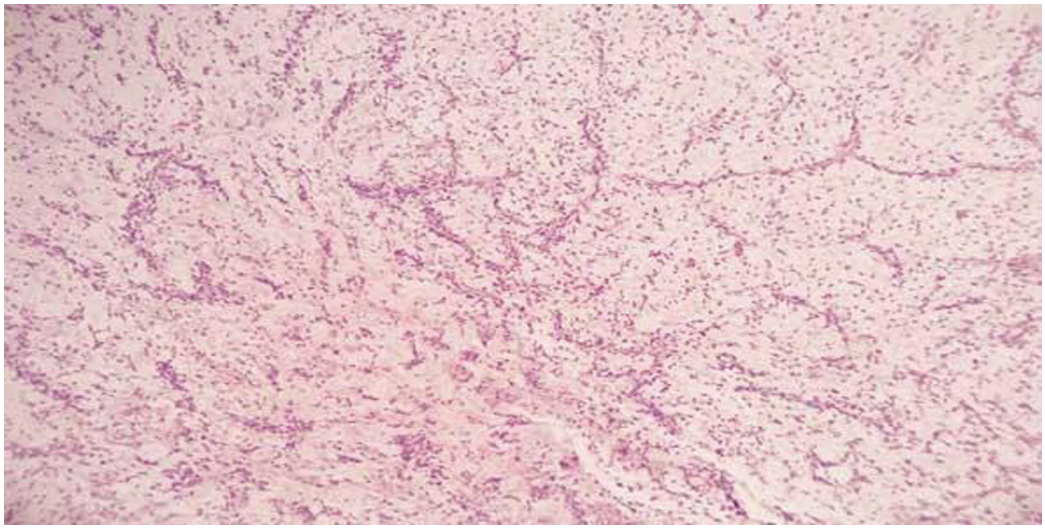

Figure 2. – H&E staining of tumor tissue showing moderate hypercellularity, variable cellular pleomorphisms, low mitotic index and dominate Antoni B areas (X10)

The islet cells have a typical meningothelial features and they are arranged in whorls with numerous psammoma bodies (Fig. 3).

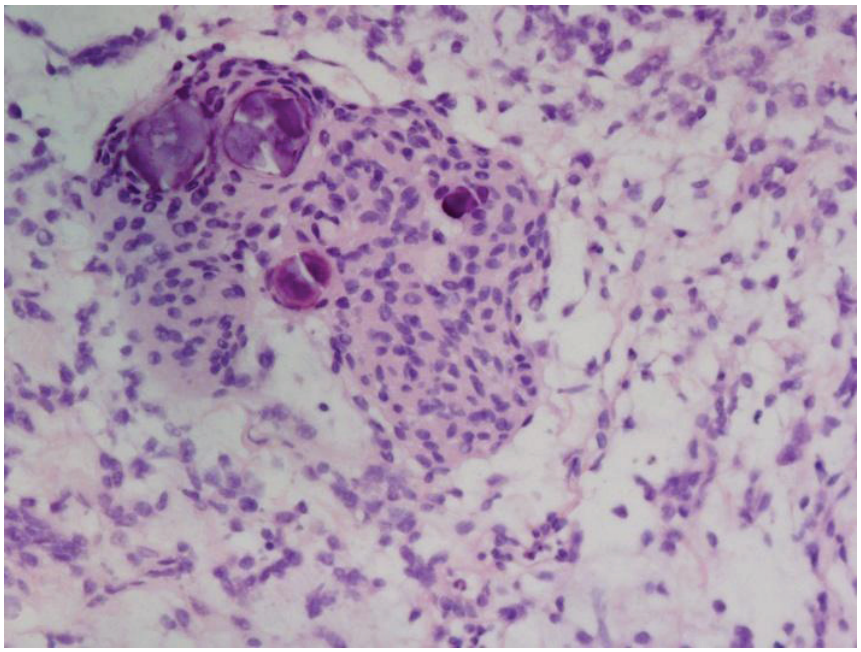

Figure 3. – H&E staining of tumor tissue showing strong perivascular cell arrangement (X10)

Myxoid areas dominate the tumor and the perivascular accentuation is evident (Fig. 2). Cytoplasm of the cells is pale and poorly defined. Nuclei have narrow outline focally bulked or wavy morphology. Nucleoli are inconspicuous. About 70% tumors cells were positive for S100 antibodies, but the menongothelial islands were negative (data not shown). On the other hand, all cells in meningothelial islands were EMA and Vimentin diffuse positive (Fig. 4).

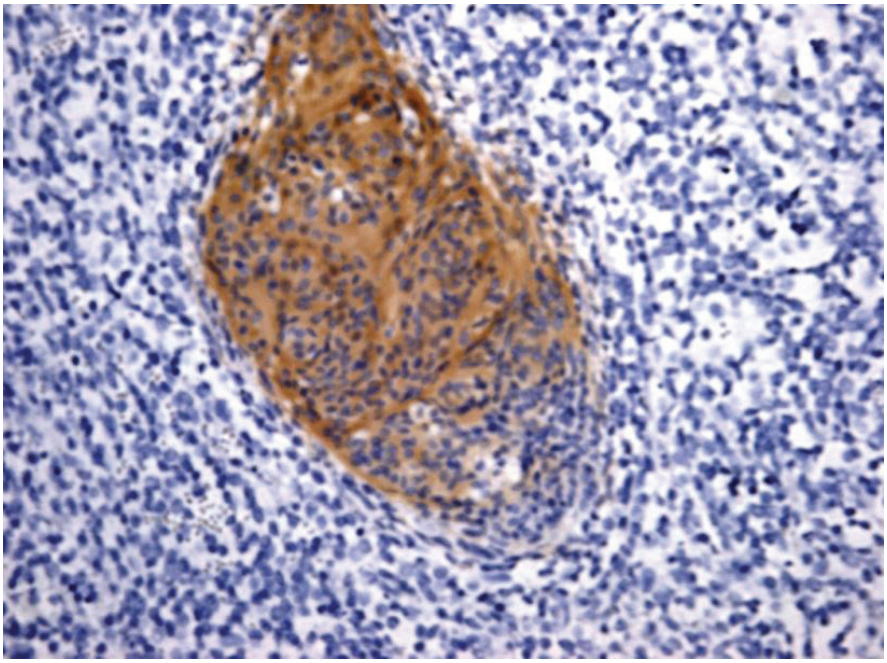

Figure 4. – EMA positive meningothelial islands (X10)

The number of Ki-67 positive nuclei in a solid meningeal area is lower than 1% but in the areas of the PNST the number of positive cells is almost 10% (Fig. 5).

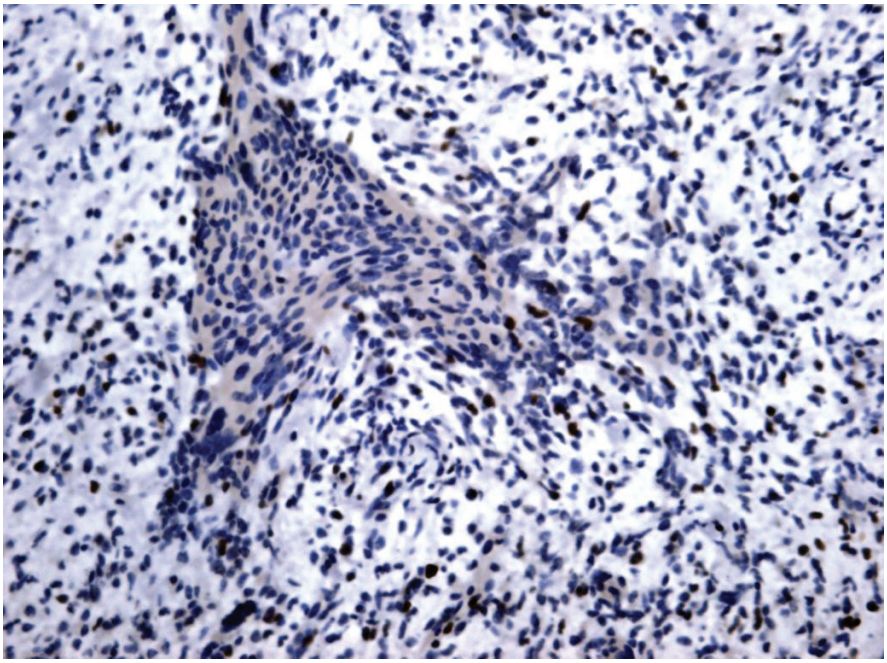

Figure 5. - Ki-67 positive nuclei in a solid meningeal area is lower than 1% (anti Ki67 x 20)

Discussion

Solitary PNST is the most common primary spindle cell sarcoma and predominantly appears in sinonasal tract. In the regions of the paranasal sinuses PNST may arise from the sheet of the common sensor branches of ophthalmic and maxillary branch trigeminal nerve.[5] It is relatively often to find metaplastic changes in nerve-sheath tumors, both benign and malignant. The presence of heterologous elements containing mesenchymal and/or epithelial components is a rare feature in human nerve-sheath tumors. We presented evidence for presence of meningothelial cell islets in PNST. Extracranial meningiomas are common in region of the optic nerve where represent 1 to 2% of all meningiomas[8]. In here presented case, histology revealed areas of spindle-shaped to oval cells arranged in a fasciculated or whorled pattern, indicating the Antoni A pattern of schwannoma, distinct feature that suggests neural differentiation. The compression of adjacent tissue induced by tumor growth was significant but bony erosion was not observed.

Probably the most interested issue arising from the tumor we described is the question of its origin. In spite the fact that the floor of the orbit is speared PNSTs could not arise from sheath of the optic nerve. The nerve is covered by arachnoidea and does not have a peripheral sheath of the Schwannomas cells. Gliomas of the optic nerve could be associated with meningothelial hyperplasia, which makes them difficult to be histologically distinguished from meningioma[9]. Reactive meningothelial hyperplasia that surrounds optic nerve glioma could be very prominent and may be severe enough to mimic orbital meningioma. Several theories have been proposed to explain described situation. One of the possible explanations is the "collision" of two independently different types of tissues. In some previous reports there have been described nine cases with collision tumors (meningiomas and schwannomas)[10, 11] but not a single case in the region of the paranasal sinuses. We also considered as one of possible explanations, ectopic meningeal hamartoma. This type of tumor is described as very rare lesion usually placed in the nasal region and in the scalp[12]. Meningeal cells may have a hamartomatous congenital origin and undergo transformation to neoplastic cells. At present there is no conclusive evidence to support this hypothesis. Third possible explanation might be occurrence of metaplasia inside of schwannoma. We excluded this possibility since metaplasia appears in malignant but not benign schwannomas like here presented.

It is quite difficult to differentiate between these neoplasms based on the histological examination alone, because there is an overlap in the histological features. Immunohistochemically, schwannomas are invariably S-100 protein positive and meningiomas are EMA positive[13]. Thus, S-100 protein alone might not reliably differentiate between fibrous meningioma and schwannomas. Given that schwannomas and meningioma are both positive for vimentin, this type of staining used to test the preservation of the antigenicity, is considered to be of no use in discriminating between these neoplasms. Vimentin is considered the principal intermediate filament in Schwann cells as well as the markers of meningeal cells[14]. No single immunoreactivity pattern is pathognomonic of schwannoma, and hence a combined use of immunostains (S-100 protein, EMA, vimentin) is of great help in distinguishing schwannoma from its histological mimickers[15].

Meningeal cells (cells of the arachnoidal cap) create an external layer of the arachnoidea and arachnoidal villuses. The thickness of this layer varies from one single row of flattened cells similar to fibroblasts to more than 10 rows of cells with epitheloidal appearance. In here described case report we clearly-demonstrated islets of the meningeal cells in PNSTs with more then 10 layers and numerous psammoma bodies. Meningeal cells islets are positive on immunostaining on the Vimentin and EMA as well as the meningioma cells,[6,16,17], but exact differentiation between meningothelial hyperplasia and true neoplasia on clinical and histopathological grounds alone still remains. A „meningothelial hyperplasia" is a reactive process characterized by a proliferation of a arachnoidal cap cells that is often non-invasive, multicentric, and at least focally reaches a thickness of 10 or more cell layers"[18]. Here presented tumor have several islands of the meningothelial cells which were not attached to the dura. Therefore, we considered it as non-neoplastic tumor. We also showed

that expression of Ki67 in MPNST reach almost 10%, while in meningeal islets is lower than 1%, which additionally demonstrate its non-neoplastic nature.

We believe that here described meningeal islets actually represent reactive meningothelial hyperplasia, condition in which schwannoma irritates the underlying meningothelium causing hyperplasia. Similar case of congenital supratentorial meningeal arteriovenous malformation with hemangioma that provoked massive meningeal cell hyperplasia was described by Nabeel at al[19]. To the best of our knowledge, here we reported the first case of meningeal hyperplasia which is invaded by schwannoma in the paranasal sinuses.

References

1. Kapadia S. Tumors of the nervous system. 2nd ed.: Marcel Dekker Inc; 2001.
2. Enzinger F.M. WSW. Malignant tumors of the peripheral nerves. 1 ed.: Mosby-Year Book; 1995.
3. DiNardo LJ, Rumsey RL. Management of malignant schwannomas of the paranasal sinuses and anterior skull base. Ear Nose Throat J. 1996 Jun;75(6):377-80.
4. Bruner JM. Peripheral nerve sheath tumors of the head and neck. Semin Diagn Pathol. 1987 May;4(2):136-49.
5. Perry A, Gutmann DH, Reifenberger G. Molecular pathogenesis of meningiomas. J Neurooncol. 2004 Nov;70(2):183-202.
6. Louis DN SB, Budka H, von Demling A, Kepes JJ. Meningiomas. Tumours of the Nervous System;Pathology & Genetics. International Classification of Tumors; 2000; Lyon. IARC Press; 2000. p. 172.
7. Louis DN, Ramesh V, Gusella JF. Neuropathology and molecular genetics of neurofibromatosis 2 and related tumors. Brain Pathol. 1995 Apr;5(2):163-72.
8. Liu JK, Forman S, Moorthy CR, Benzil DL. Update on treatment modalities for optic nerve sheath meningiomas. Neurosurg Focus. 2003 May 15;14(5):e7.
9. Cooling RJ, Wright JE. Arachnoid hyperplasia in optic nerve glioma: confusion with orbital meningioma. Br J Ophthalmol. 1979 Sep;63(9):596-9.
10. Geddes JF, Sutcliffe JC, King TT. Mixed cranial nerve tumors in neurofibromatosis type 2. Clin Neuropathol. 1995 Nov-Dec;14(6):310-3.
11. Elizabeth J, Menon G, Nair S, Radhakrishnan VV. Mixed tumour of schwannoma and meningioma in a patient with neurofibromatosis-2 : a case report. Neurol India. 2001 Dec;49(4):398-400.
12. Simpson RK, Jr., Goodman JC, George RE, Laurent JP, Cheek WR. Scalp hamartoma in identical twins. Pediatr Neurosurg. 1993 Mar-Apr;19(2):89-92.
13. Carneiro SS, Scheithauer BW, Nascimento AG, Hirose T, Davis DH. Solitary fibrous tumor of the meninges: a lesion distinct from fibrous meningioma. A clinicopathologic and immunohistochemical study. Am J Clin Pathol. 1996 Aug;106(2):217-24.
14. Gould VE MR, Moll I, Lee I, Schwechheimer K, Franke WW. The intermediate filament complement of the spectrum of nerve sheath tumors. Lab Invest 1986;55:463–74.
15. Giangaspero F, Fratamico FC, Ceccarelli C, Brisigotti M. Malignant peripheral nerve sheath tumors and spindle cell sarcomas: an immunohistochemical analysis of multiple markers. Appl Pathol. 1989;7(2):134-44.
16. Zamada T KD, Walker G Vimentin immunoreactiviti in normal and pathological human brain tissue. Acta Neuropathol. 1992;84:157-62.
17. Perry A, Lusis EA, Gutmann DH. Meningothelial hyperplasia: a detailed clinicopathologic, immunohistochemical and genetic study of 11 cases. Brain Pathol. 2005 Apr;15(2):109-15.

18. Maier H WJ, Sedivy R, Rossler K, Ofner D, Budka H Proliferation and DNA fragmentation in meningioma subtype. Neuropathol Appl Neurobiol. 1997;23(496-506).

19. Nabeel A, Lach B, Al-Shail E, Patay Z. Congenital supratentorial meningeal arteriovenous malformation with hemangioma and massive arachnoid cell hyperplasia. Childs Nerv Syst. 2005 Nov;21(11):995-9.

Coresponding author:
Sanja Milenkovic, MD PhD, Head of Department of Pathology
Department of Pathology,
Clinical Hospital Center „Zemun”,
Address: Vukova 9, 11080, Belgrade, Serbia
e-mail: kbczpatologija@open.teleko.rs
Tel: +381-11-37772692