



Primary leptomeningeal melanocytosis – A case report with an autopsy diagnosis

Primarna leptomeningealna melanocitoza

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Abstract

Introduction. Primary melanocytosis of the leptomeninges is a rare tumor, most likely originating from the melanocytes in the leptomeninges. The average survival is only about 5 months. **Case report.** A 61-year-old woman presented with headache, amaurosis and hallucinations lasted for two months, and she had been treated at the Clinic for Psychiatry and Clinic for Infectious Diseases. The cerebrospinal fluid analysis showed a lower level of glucose and a higher level of proteins. Small shaded areas of basal leptomeninges and hydrocephalus were found by computed tomography and magnetic resonance imaging. The autopsy showed a dark brown mass on basal leptomeninges with blurred boundaries. No pigmented skin lesions were found. Histopathological analysis revealed a primary leptomeningeal melanocytosis. **Conclusion.** Primary leptomeningeal melanocytosis is a rare tumor, difficult to diagnose. This case is being presented for its specificity, since this diagnosis is not frequently seen in practice.

Key words:

meningeal neoplasms; diagnosis; tomography, x-ray computed; magnetic resonance imaging; autopsy; 6 enzyme-linked immunosorbent assay.

Apstrakt

Uvod. Primarna melanocitoza leptomeningi predstavlja redak tumor, koji najverovatnije nastaje od melanocita koji se nalaze u leptomeningama. Prosečno vreme preživljavanja iznosi samo oko pet meseci. **Prikaz bolesnika.** Prikazana je bolesnica stara 61 godinu koja je imala dvomesečne tegobe – glavobolju, amaurozu i halucinacije, a lečena je u Klinici za psihijatriju i Klinici za infektivne bolesti. Analizom cerebrospinalne tečnosti nađen je snižen nivo glukoze i povišen nivo proteina. Kompjuterizovanom tomografijom i magnetnom rezonancijom viđena su mala zasenčenja bazalnih leptomeningi i hidrocefalus. Obdukcijom na bazalnim leptomeningama uočena je tamnobraon masa sa nejasnim granicama. Pigmentne kožne lezije nisu nađene. Histopatološkom analizom dijagnostikovana je primarna leptomeningealna melanocitoza. **Zaključak.** Primarna leptomeningealna melanocitoza je redak tumor koji se teško dijagnostikuje. Specifičnost ovog rada je u tome da prikazuje bolesnicu sa oboljenjem koje se retko sreće u praksi.

Ključne reči:

meninge, neoplazme; dijagnoza; tomografija, kompjuterizovana, rendgenska; magnetska rezonanca, snimanje; autopsija; elisa.

Introduction

Primary melanocytic neoplasms of the central nervous system originate from melanocytes of leptomeninges, and can occur as diffuse or solitary, benign or malignant tumors. This group of tumors also includes diffuse melanocytosis and melanomatosis, melanocytoma and malignant melanoma¹.

Limas and Tio² first described these lesions in 1972, while before, they had been referred to as melanotic meningioma. Approximately 110 cases of meningeal melanocytosis have been reported^{3,4}. The annual incidence of meningeal melanocytoma is estimated to be one case per 10 million population, and females are affected more often than males

(female: male ratio 1.5 : 1)^{1,5}. Meningeal melanocytosis may manifest at any age, but most patients are in the 5th decade of life^{6,7}.

This case is being presented for its specificity, since the disease is not frequently seen in practice.

Case report

The problems of a 61-year-old female patient had lasted for two months, accompanied with headache, amaurosis and hallucinations. At the beginning of February, she was transferred to the Clinic for Infectious Diseases, Clinical Centre Niš, from the Clinic for Psychiatry, Gornja Toponica,

doubting of an inflammation process of the central nervous system (lumbar puncture: glycorachy 0.0 mmol/L). A month before admission to the Clinic for Infectious Diseases, the patient had complained of an occipital headache, low back pain and pain in the right leg. The patient had an outpatient treatment with symptomatic therapy. In the meantime, the patient started speaking with no fluency, hallucinations appeared and people around her noticed she could not see. Diagnosed with acute hallucinatory syndrome, the patient was observed at the Clinic for Psychiatry, where, apart from a lumbar puncture, computed tomography and nuclear magnetic resonance of the brain were done showing reductive changes without focal lesions.

At the Clinic for Infectious Diseases, the following results were obtained: sedimentation values were 4, 12, 22 mm/h, urea, creatinine, electrolytes without major changes, the value of lactate dehydrogenase (LDH) was 966 U/L, leukocytes $30.9 \times 10^9/L$, and neutrophils 86.5%, 89.0%, 90.1%; hematocrit value was 31.27%. The patient was anti-HIV negative. A lumbar puncture was done for three times and the cytological results were normal. The first time the level of glycorachy was 0.5 mmol/L with serum glucose 5.3 mmol/L, and proteinorachy was 0.85 g/L; the second time the level of glycorachy was 0.3 mmol/L with serum glucose 6.8 mmol/L; the third time the level of glycorachy was 1.1 mmol/L with serum glucose 6.1 mmol/L. Bone marrow biopsy discarded hematological malignancy. The control computed tomography of the brain revealed dilated ventricular system (the third and lateral ventricle) and small shaded areas of basal leptomeninges. At a consultative examination, a neurosurgeon determined there were no indications for a neurosurgical intervention. The neurologist determined spastic paraparesis, sphincter incontinence and amaurosis as a consequence of hydrocephalus. Finally, an ophthalmologist determined cortical amaurosis. The enzyme-linked immunosorbent assay (ELISA) test on tuberculosis (TB) (liquor) was done and proved to be negative.

During hospital treatment, antibiotic, tuberculostatic, antiedematous and symptomatic therapy had been given. For a short period of time, the patient was taking psychiatric medication. Due to the received therapy, the hallucinatory syndrome started to wear off, but instead spastic-type paraparesis and incontinence developed, which indicated a control computed tomography of the brain. She was afebrile all the time. At the beginning of March, the general condition got worse, tension decreased with tachycardia 120/min. After tension correction, she still had tachycardia with hypoproteinemic edema and her state of mind worsened to sopor state with tachy/dyspnea (to 38/min). In a week's time, the state of the patient worsened, she fell into coma, with acid-base imbalance and significant tachycardia. In spite of reanimation measures, cardio-respiratory failure occurred accompanied with fatal outcome (*exitus letalis*).

At autopsy, a dark brown mass with blurred boundaries was found on basal leptomeninges (Figure 1). No pigmented skin lesions were found, as well as any changes on other organs. Histopathological analysis revealed a leptomeningeal melanocytosis (Figure 2). Immunohistochemical analysis

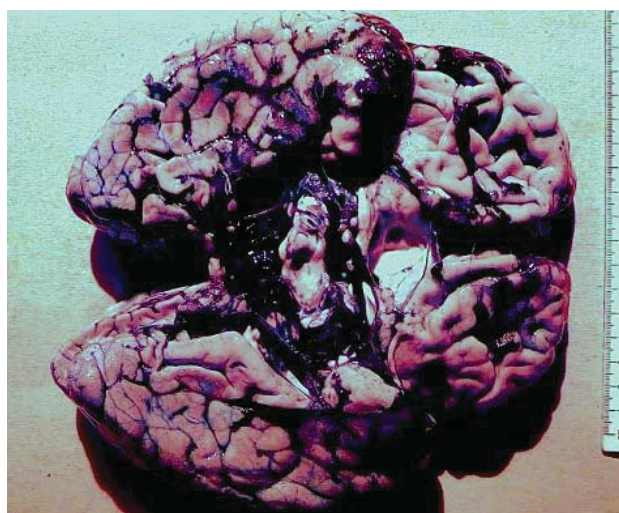


Fig. 1 – Dark brown areas on the leptomeninges of the brain basis

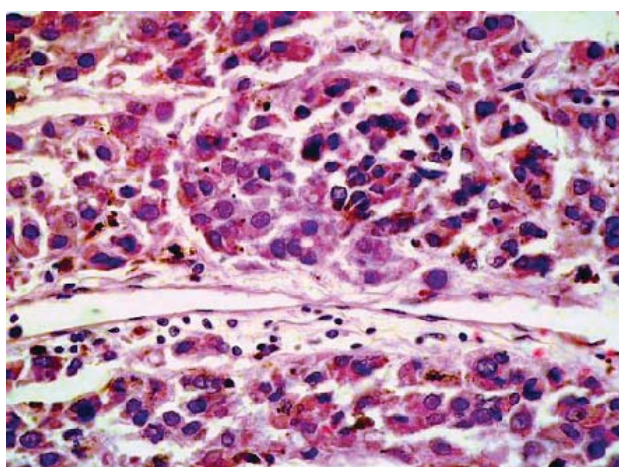


Fig. 2 – Melanin presented in the cytoplasm of tumor cells (hematoxylin and eosin, $\times 40$)

demonstrated the expression of melanocytic marker proteins, melan A (Figure 3) and β -hydroxy β -methylbutyrate (HMB) 45 (Figure 4), but an absence of meningotheial cell markers, endothelial monocyte antigen (EMA) (Figure 5). The Ki-67 index was approximately 10% (Figure 6).

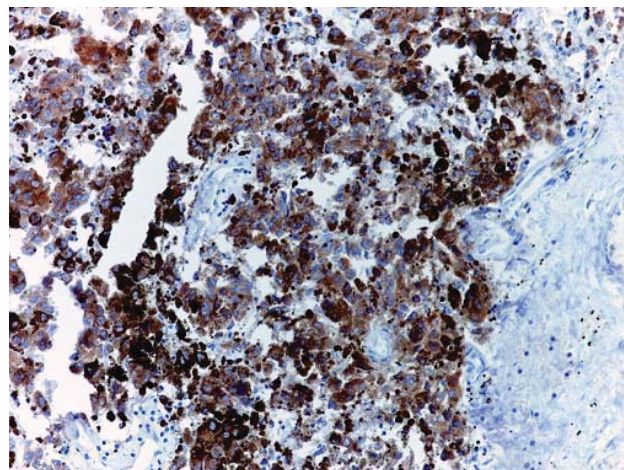


Fig. 3 – Melan A positivity of tumor cells ($\times 20$)

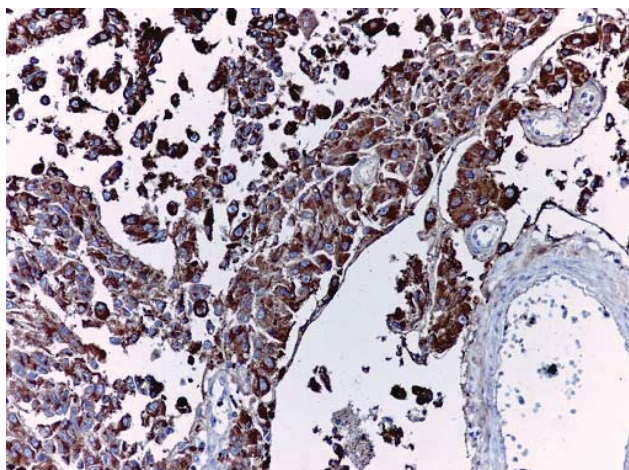


Fig. 4 – β -hydroxy β -methylbutyrate (HMB) 45 positivity of tumor cells ($\times 20$)

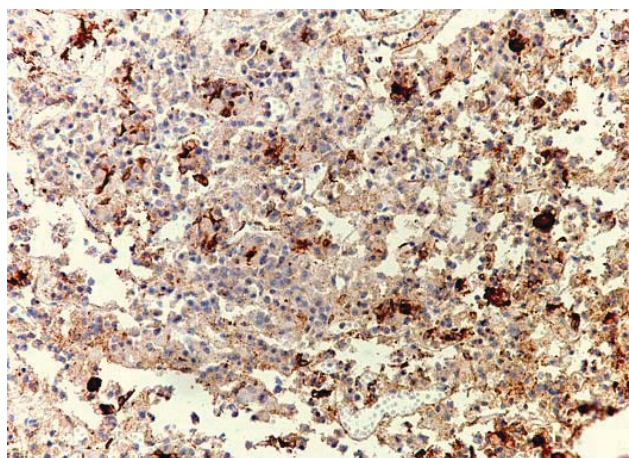


Fig. 5 – The tumor cells were negative for endothelial monocyte antigen (EMA) ($\times 20$)

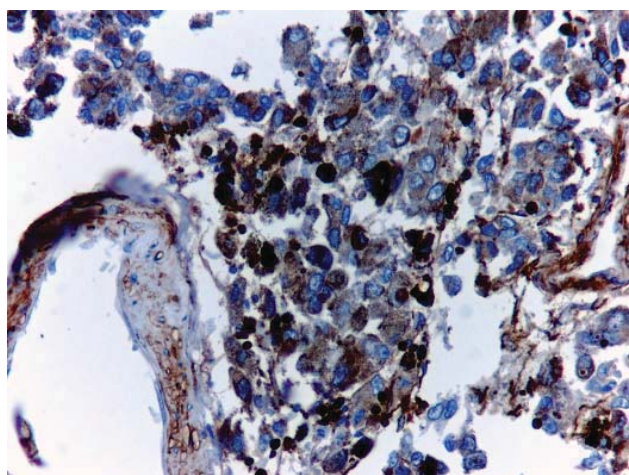


Fig. 6 – The Ki-67 index was approximately 10% ($\times 40$)

Discussion

Leptomeningeal melanocytosis is a very rare tumor of the central nervous system. The pathogenesis has not been clear enough yet, but it is supposed that melanocytes populate this area from the neural crest, so it is their proliferation

that causes the disease^{8,9}. Certainly, there is a predisposition from birth, but it is a question of time when it is going to manifest clinically. Very often, these lesions in the central nervous system go together with skin changes, but they can also be solitary as in our case^{10,11}.

There are diffuse and solitary forms of this tumor. Diffuse tumors are more often found in children, opposite to solitary ones, that are found in adults^{12,13}. Diffuse forms of melanocytoses and melanomatoses infiltrate supra- and infratentorial leptomeninges and the surface of the brain parenchyma. The areas they are localized the most are cerebellum, pons, medulla and temporal lobe¹.

Diffuse melanocyte lesions are presented as dense black content in the subarachnoid area or as a dark blurry change on the meninges. Melanocytomas and a malignant melanoma are solitary masses which can occur as black, red-brown, blue or macroscopic non-pigmented changes¹.

In terms of diagnostics, encephalography, myelography, arteriography and computed tomography are used, but the best results are achieved with magnetic resonance. Cerebrospinal fluid analysis showed higher values of proteinorachy, lower values of glycorachy, a greater number of lymphocytes, but tumor cells also.

In terms of differential diagnostics, it can be doubted of a meningioma, schwannoma, medulloblastoma, choroid plexus papilloma and astrocytoma¹¹.

The microscopic characteristics of the primary leptomeningeal melanocytosis are basically identical to melanocytosis in other places. The tumor consists of epithelial cells or spindle cells in their characteristic nest arrangement¹³. Most of benign and malign melanocytic lesions contain melanin pigment, finely distributed in tumor cells or roughly in the tumor stroma – in the cytoplasm of macrophages (melanophages). Rarely, melanocytoses and primary melanoma do not contain melanin; in such cases the diagnosis is given with the help of the electronic microscope or immunohistochemical methods.

At most published cases, the diagnosis was given post-mortally⁹. It is accompanied with a number of symptoms by vegetative, motor and central nervous system, in terms of headache, vomiting, visual field loss, lethargy and hemiparesis. Very often, the meningeal signs are positive, most often Kernig's one. As a consequence of high intracranial pressure, hydrocephalus may occur^{10,11}.

Our 61-year-old patient had had problems for two months, including headaches, amaurosis and hallucinations. The cerebrospinal fluid analysis showed a higher value of proteinorachy and a lower value of glycorachy. Some shaded areas on the brain basis and hydrocephalus were found by computed tomography. At autopsy, histopathological and immunohistochemical analysis revealed leptomeningeal melanocytosis.

The tumor was composed of epithelial cells in a characteristic nest arrangement. The grains of melanin were present in the cytoplasm. Infiltration of the surrounding tissue was not present.

Meningeal melanocytoma is characterized by positive immunoperoxidase staining for HMB-45, S-100 protein,

melan A and vimentin antibodies, and by a negative reaction to EMA^{1, 14–16}. In general, melanocytoma is a solitary tumor with discrete margins, lack of mitoses, and a low Ki-67 index (< 12%)¹⁶.

In 1999, Brat et al.¹⁷ analyzed 33 of these rare tumors (comprising nearly half of the reported tumors at that time) and proposed a three-tiered grading system. Approximately half of their cases consisted of well-differentiated lesions (melanocytomas), characterized by variably pigmented cells arranged in nests and fascicles. This group of tumors demonstrated rare mitotic figures, inconspicuous nucleoli, and absence of parenchymal invasion. With a medium follow-up period of 3 years, none of these tumors recurred. Most of the other half of the tumors in the study were composed of poorly organized, mitotically active cells, with more prominent nucleoli, necrosis, and parenchymal invasion. This group of tumors was classified as primary central nervous system melanoma. Although half of these tumors recurred between 2 and 76 months after surgery, all but one were alive at the time of this publication. In addition, 4 out of 5 totally resected melanomas did not recur. Three (10%) of the

tumors in the study could not be easily situated within either category and received the designation of intermediate-grade melanocytic tumor. Therefore, although the grading system proposed for primary central nervous system melanocytic tumors may be helpful in predicting the biologic behavior of these rare tumors, there is very significant overlap. In addition, with longer follow-up intervals, low-grade melanocytomas have shown a tendency toward radiographic recurrence^{17, 18}.

Conclusion

Primary pigmented lesions can be manifested both as benign and malignant neoplasms. Leptomeningeal melanocytosis is a rare tumor difficult to diagnose and treat.

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