June 2002: 57-year-old male with leptomeningeal and liver tumors

Contributed by: Monika Koenigsmann[1]; Günther Jautzke[3]; Matthias Unger[4]; Agota Théallier-Janko[1]; Thomas Wiegel[2]; Gisela Stoltenburg-Didinger[1]

[1] Departments of Neuropathology and [2]Radiotherapy, Free University Berlin, Germany.
[3] Department of Pathology, St.Gertrauden Hospital, Berlin, Germany.
[4] Department of Pathology, Martin-Luther Hospital, Berlin, Germany.

Clinical History, Radiology and Microscopic Description

In 1988 a 57-year-old male patient began having symptoms of fluctuating headaches and lack of concentration. In early 1990 he noticed a deviation of his tongue towards the right side as well as double vision, vertigo and an increase of his headaches. A cranial CT scan revealed a hyperdense mass in the area of the foramen magnum (Figure 1A). Upon surgery a tumor was completely removed.

On H&E staining the tumor showed high cellularity, with isomorphic tumor cells and partial arrangement in nests (Figure 2A). Cells were medium-sized, round-to-oval with rather isomorphic nuclei, sometimes with prominent nucleoli (Figure 2B). Intra- and extracellular brownish pigment could be distinguished (Figure 2B). Mitoses were rare. Immunohistochemistry was positive for S-100 and vimentin as well as HMB 45 (Figure 2C). Electron microscopy showed both highly differentiated and less mature melanosomes, and no desmosomes (Figure 2D).

Eight years later, the patient noticed again double vision, vertigo, and also diminished physical activity. Another 7 months later, in December 1998, a sudden deterioration of his general health occurred with right abdominal pain and recurrent herpes virus infections. Dexamethasone alleviated both the headache and the abdominal pain. A cranial CT scan this time showed a tumor mass in both the region of the previous operation and in the left cerebellar hemisphere (Figure 1B). An abdominal CT was highly suspicious for disseminated liver metastases.

Biopsy revealed an infiltration of the liver by a solid tumor with medium-sized cells with brown granulated pigment (Figure 3A). The tumor cells had round or oval nuclei, mild pleomorphism, and prominent nucleoli. Immunohistochemistry was positive for HMB 45 (Figure 3B) and tyrosinase (not shown). A distinction from regular hepatocytes was achieved by the HEP antibody (Figure 3C). A MIB-1 immunostain revealed only scattered proliferating cells (Figure 3D).

Percutaneous irradiation of the neurocranium at a total dose of 30 Gy using 6 MeV-photons was performed. Systemic treatment was intended with cisplatinum. However, a further dramatic deterioration of the patient's general state with frequent generalized seizures occurred a few days after the end of radiotherapy. Therefore, the patient did not receive any chemotherapy, dying 2 weeks later in a state of cerebral coma. Permission for autopsy was not obtained.

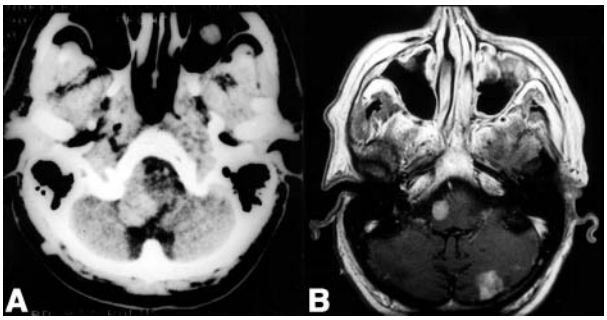

Figure 1.

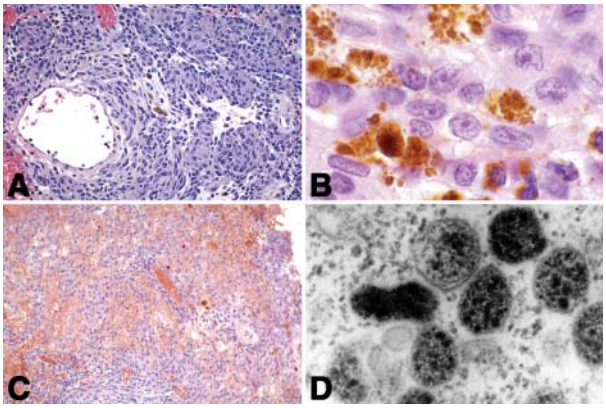

Figure 2.

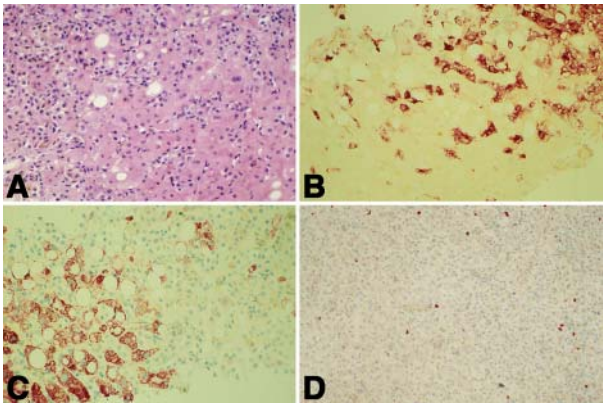

Figure 3.

Diagnosis

Metastasizing, melanocytic leptomeningeal tumor with histomorphological characteristics of a melanocytoma.

Discussion

We report a case in which the tumor morphologically resembles a benign melanocytoma, but which showed local recurrence as well as cerebral and hepatic metastases. To the best of our knowledge, this is the first case of a melanocytoma associated with hepatic metastasis.

Meningeal melanocytomas occur at every age, are usually unilocular and appear as nodes attached to the dura mater. They are mainly located in the posterior cranial fossa or the spinal canal (4, 11). Imaging studies of these tumors show homogeneous contrast enhancement (12).

Histologically, melanocytomas are hypercellular with cells arranged in nests or sheets. They have oval nuclei, prominent nucleoli and finely dispersed chromatin. Mitoses are rare. Necrosis, hemorrhage and CNS invasion are usually absent. It is necessary to differentiate primary melanotic tumors of the CNS not only from malignant melanoma metastases, but also from other pigmented CNS tumors such as melanotic meningiomas and melanotic schwannomas. They can be diagnosed by immunohistochemistry and electron microscopy: S-100, vimentin and HMB-45 are positive in meningeal melanocytomas and in schwannomas. In contrast to melanocytomas or schwannomas, meningiomas are EMA-positive. Electron microscopy reveals basal lamina formation around cell groups in melanocytomas, while in schwannomas the basal lamina surrounds every single cell. Melanocytomas contain melanosomes at varying differentiation stages. In contrast to meningiomas, there are no desmosomes (1, 5, 8, 10, 13).

The histological diagnosis of melanocytoma is no guarantee for a good clinical outcome (8), because meningeal melanocytomas can take an aggressive or repetitive course according to some case reports (1, 3, 6, 7, 9). The correct diagnosis of melanocytic CNS tumors is a diagnostic challenge. Primary melanocytic CNS tumors have a highly variable biological behaviour, their clinical course ranging from benign to highly malignant with the meningeal melanocytoma at one end and the malignant melanoma at the other end of the spectrum. In our case it remains elusive whether a transition has taken place, which has not become morphologically apparent.

There are reports of leptomeningeal melanomas with long-term survival and even permanent cure. Metastases of melanomas often show extensive necrosis, marked cell polymorphy and numerous mitoses. The differentiation between a low-grade melanocytoma and a high-grade melanoma cannot always be made histologically. An attempt to differentiate the extremes morphologically was published by Brat et al (2). A study with an adequate number of cases and close clinical follow up would be necessary to gain a better understanding of the nature of the tumor (1).

The biological behavior of this rare tumor might become more predictive by analyzing the distribution of progression-associated melanotic antigens (PAMA) such as VLA-2, ICAM-1, HLA-DR, vitronectin receptor, and transferrin receptor.

References

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Abstract

Cases of the Month, April to June, 2002

The April 2002 Case of the Month (COM). 35-year-old healthy man developed a mass in the right parotid gland. A superifical parotidectomy was performed for a 4.5 × 1.5 × 1.5 cm mass involving the intraparotid facial nerve. Grossly the tumor was multinodular, smooth and yellow with normal surrounding salivary gland. Microscopically, the tumor showed expanding nodules composed of proliferating fibroblasts, Schwann cells, and perineural-like cells in a myxoid stroma. Normal peripheral nerve twigs were identified in the periphery of the tumor. There was no increased mitotic activity, cellularity or nuclear pleomorphism. S-100 immunohistochemical stain was positive. The tumor was diagnosed as a solitary plexiform neurofibroma. Plexiform neurofibromas in this area have been described in children with von Recklinghausen's disease or neurofibromatosis 1 (NF 1). Plexiform neurofibromas typically involve deep seated nerve trunks and is considered pathognomonic for NF 1. This unusual case represents a solitary variant of plexiform neurofibroma presenting as a parotid mass in an adult patient without a personal stigmata or family history of NF 1.

The May 2002 COM. A 38-year-old man presented with new onset seizures and a 69-year-old woman presented with bilateral headaches and episodes of syncope. Both were found to have extra-axial masses that were contrast-enhancing and thought to be meningiomas. Both had complete resection. Microscopic examination revealed an inflammatory lesion composed of plasma cells, scattered lymphocytes and numerous large histocytic cells, which exhibited emperipolesis and were CD1a negative, but positive for CD68 and S100. The diagnosis of Destombes-Rosai-Dorfman Disease (DRDD) was rendered. Both cases had good long-term outcome. The differential diagnosis of inflammatory masses in the dura (plasmacytoma, lymphomas, plasma cell fibroma, angiofollicular hyperplasia [Castleman's-disease] and Langerhan's cell histiocytosis) are discussed.

The June 2002 COM. A male patient presented at the age of 57 years with a benign meningeal melanocytoma. Eight years later, the patient had a local recurrence of the tumor, cerebral metastases and liver metastases. This demonstrates that a correct diagnosis of melanocytic CNS tumors remains a challenge together with elucidating predictive markers for biological behavior. To the best of our knowledge, this is the first case of a melanocytoma associated with hepatic metastasis.

For a more complete discussion of these cases, additional micrographs and information regarding submission of cases, please access the WWW at: *http://www.brainpathology.com*. We welcome comments about these or similar cases our readers may have encountered.