Brain Tumor Pathol (2002) 19:93–96

CASE REPORT

M.C. Sharma · M. Agarwal · A. Suri · S. Gaikwad
P. Mukhopadhyay · C. Sarkar

A melanotic desmoplastic medulloblastoma: report of a rare case and review of the literature

Received: January 23, 2002 / Accepted: July 29, 2002

Abstract A 28-year-old man had a desmoplastic medulloblastoma in the vermis and left cerebellum. This tumor was composed of nodular, reticulin-free zones (pale islands) surrounded by densely packed, highly proliferative cells that produced a dense intercellular reticulin network. Some of the cells were heavily pigmented, and this pigment proved to be melanin. Adult age, desmoplastic nature, and melanin pigmentation are some of the rare features of this tumor that need documentation. Further, this pigment was in the primitive cells, unlike in the published cases, in which it was present in the tubular or tubulopapillary component. To the best of our knowledge, this is the first published case of desmoplastic pigmented medulloblastoma, and the patient is the oldest reported to have this tumor.

Key words Melanotic medulloblastoma · Pigmented · Melanin · Desmoplastic · Adult · PNET · Central nervous system · Tumor

Introduction

Neoplasms containing melanin pigment have been reported in various sites in the central and peripheral nervous system. The first case of melanotic medulloblastoma was described by Fowler and Simpson.[1] Since then 10 cases (Table 1) of melanotic cerebellar tumors[1–10] have been described, which were histologically similar to melanotic neuroectodermal (MNET) tumors occurring extracranially.[11,12] Stowen described a pigmented tumor that was probably of this category, the details of which are not available.[13] Some authors have designated them as melanotic prognoma,[13,14] whereas others have called them a variant of medulloblastoma.[1,2] All of them occurred in the first decade of life, except for one case,[5] and were histologically akin to melanotic neuroectodermal tumor of infancy, which occurs extracranially.

We report a rare case of melanotic medulloblastoma which, in contrast to the previous published cases, occurred in a 28-year-old man and had the histologic findings of a desmoplastic medulloblastoma.

M.C. Sharma · M. Agarwal · C. Sarkar (✉)
Department of Pathology, All India Institute of Medical Sciences, New Delhi-110029, India
Tel. +91-11-659-3371; Fax +91-11-686-2663
e-mail: sarkarcs@hotmail.com/sarkarch@medinst.ernet.in

A. Suri
Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi, India

S. Gaikwad
Department of Neuroradiology, All India Institute of Medical Sciences, New Delhi, India

P. Mukhopadhyay
Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India

Case report

A 28-year-old man presented with chief complaints of incoordination of the right upper limb for the last 6 months and headache and vomiting for the last 3 months. Fundus examination revealed bilateral papilledema. Cerebellar signs were present on the right side. A contrast-enhanced computed tomographic (CECT) scan revealed an enhancing mass lesion involving the right cerebellum and vermis. MRI showed a heterogeneous mass. On contrast injection, the solid component showed homogeneous enhancement (Fig. 1). The solid component appeared isointense on T2 W1. A preoperative diagnosis of a medulloblastoma was made. Through right suboccipital craniotomy, gross total decompression of a grayish-white, well-defined, soft, fleshy, moderately vascular tumor was performed, and the tumor was subject to histopathological examination.

The patient did well after surgery and underwent chemotherapy and radiotherapy. The dose of radiotherapy given as craniospinal irradiation was 40 Gy in 20 fractions per week to the whole brain, followed by a boost of 16 Gy in 8 fractions for 10 days to the posterior fossa. The dose to the spinal cord was 30 Gy in 20 fractions for 4 weeks. The

Table 1. Summary of information on all published cases of pigmented medulloblastomas

Study	Age (yr)/sex	Site	Metastasis	Therapy	Follow-up	Outcome
Fowler and Simpson 1962[1]	2½/M	Vermis and cerebellum, 4th ventricle	Subarachnoid spread	S	2 mo	Died
Rubinstein and Northfield 1964[2]	8/F	Vermis	Metastasis to spine	S	2½ yr	Died
Best 1973[3]	1/M	Posterior fossa, bilateral cerebellar pineal gland	Subarachnoid spread	S + RT	1.5 mo	Died
Sung et al. 1973[4]	3/M	Vermis	Metastasis to spine Cerebral hemisphere	S	2.5 mo	Died
Hahn et al. 1976[5]	21/M	Vermis, left cerebellum	Metastasis to spinal cord	S + RT	Not mentioned	Alive
Boesel et al. 1978[6]	4/M	Vermis	Subarachnoid spread	S + RT + CT	6 mo	Alive
Jimenez et al. 1987[7]	9/M	Right cerebellum	Recurrence twice	S + RT	8 mo	–
Dolman 1988[8]	2½/M	Vermis, 4th ventricle	Metastasis to cerebrum, spinal cord	S + CT + RT	8 mo	Died
Garcia-Bragado et al. 1990[9]	6/M	Vermis	–	–	11 mo	Died
Baylac et al. 1997[10]	3½/M	Vermis	2nd malignancy glioblastoma multiforme	S + RT	10 yr	Died
Present case	28/M	Vermis and right cerebellum	None	S + RT + CT	1 mo	Alive

S, Surgery; RT, radiotherapy; CT, chemotherapy

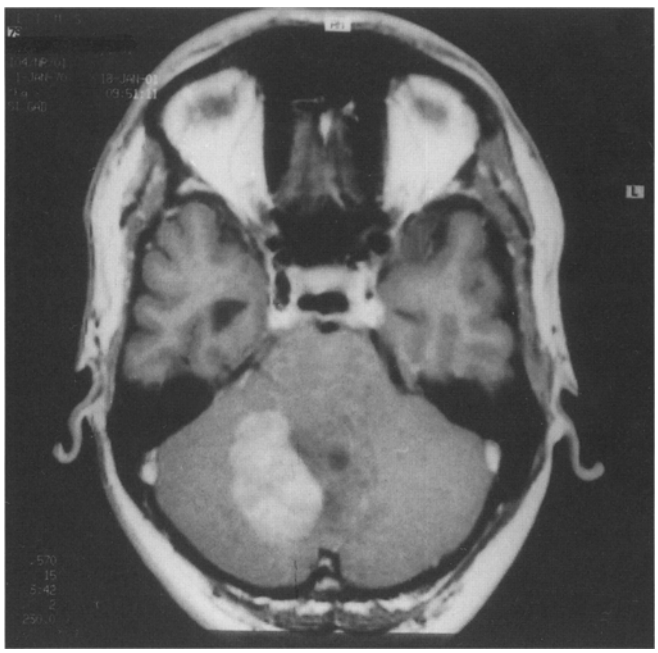

Fig. 1. Axial T1-weighted post-contrast image showing heterogeneous mass in the right cerebellar hemisphere. The solid component is nodular and homogeneously enhancing

patient received chemotherapy and is well 12 after months of surgery.

Pathological examination

The tissue consisted of multiple small fragments, which were soft and grayish-white. These were fixed in 10% neutral buffered formalin and paraffin embedded. Five-micron-thick sections were cut and stained with hematoxylin and eosin (H&E), periodic acid-schiff (PAS), Ziehl-Neelsen stain, Fontana Masson (FM) for melanin, Gomori silver impregnation for reticulin, Pearl's reaction for iron, and potassium permanganate bleach for melanin.

Immunohistochemistry

Five-micron-thick sections were cut, and immunohistochemical staining was performed by the streptavidin conjugate complex immunoperoxidase method. The antisera used were glial fibrillary acidic protein (GFAP; dilution 1:5000), synaptophysin (1:50), neuron-specific enolase (NSE; 1:100), cytokeratin (CK; pan cytokeratin 1:50), epithelial membrane antigen (EMA; 1:50), vimentin (1:100), S-100 protein (1:100), HMB-45 (1:50), neurofilament (1:50), MIB-L1 (1:20), and p53 (1:50). All antibodies except MIB-1 and p53 were obtained from M/s Dako Patt, Denmark. MIB-1 (1:50) and p53 (1:50) antibodies were procured from M/s Immunotech, France.

Results

Microscopic examination of H&E stained sections revealed nodular (pale islands) surrounded by densely packed, highly proliferative cells (Fig. 2a). The nodules showed reduced cellularity and marked nuclear uniformity (Fig. 2b). The nuclei of cells between nodules were more irregular and hyperchromatic. The nodular areas were reticulin poor, but the internodular areas were reticulin rich (Fig. 2c). No tubular or papillary component was seen. In some areas,

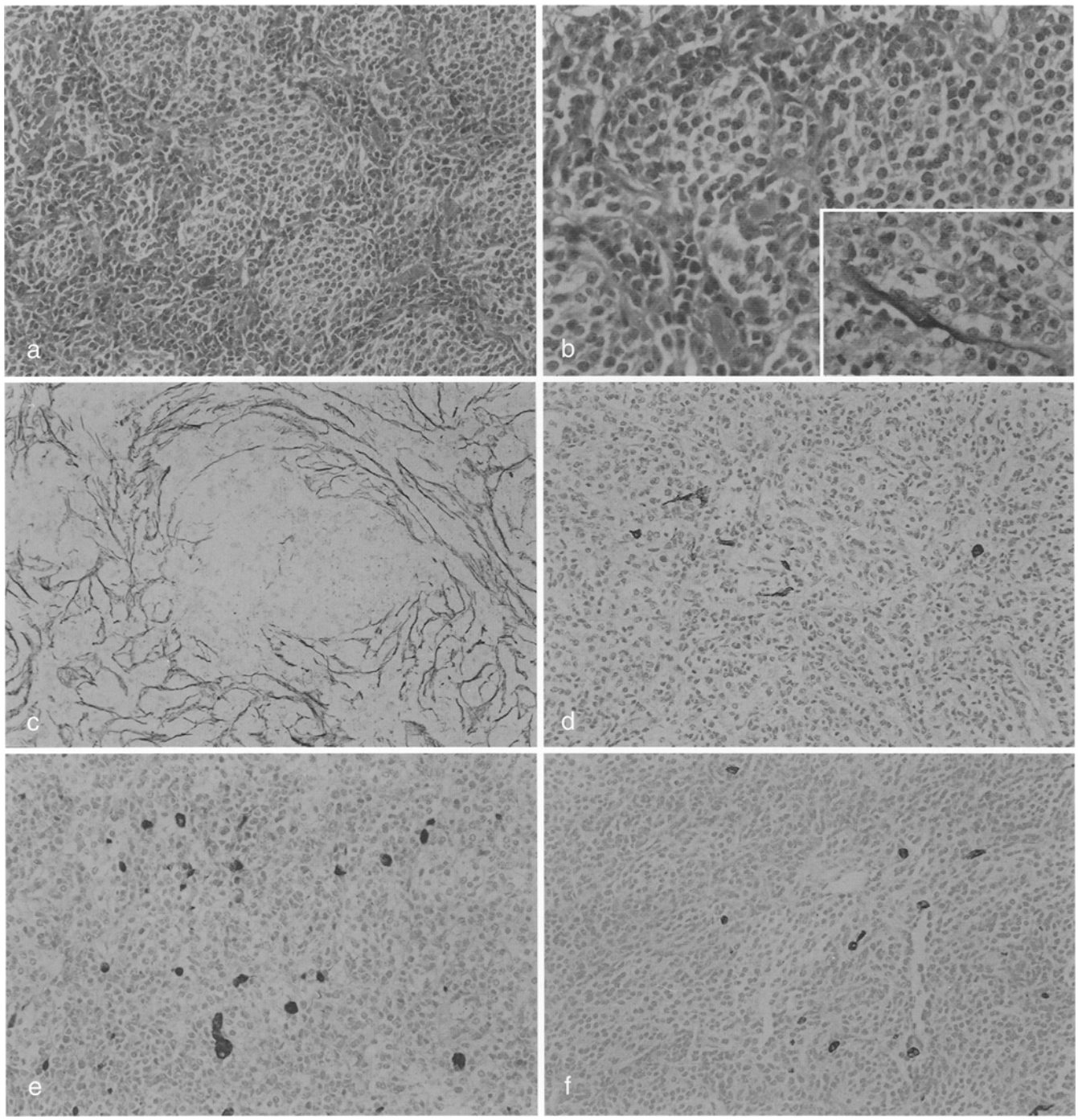

Fig. 2. **a** Photomicrograph showing pale islands surrounded by darkly stained cells, some of them containing brown pigment. (H&E, ×40). **b** Higher magnification demonstrating pale islands and pigment-containing cells. (×100). **Insert**: Some of the pigmented cells show long cytoplasmic processes. **c** Reticulin staining demonstrating reticulin-free pale islands and reticulin-rich surrounding areas. (×40). Pigment cells are immunoreactive to S-100 protein (**d**), HMB 45 (**e**), and synaptophysin (**f**)

especially in the internodular region, there were a large number of cells with brownish pigment. These pigment-containing cells were also seen focally in the nodular areas. The pigment-containing cells varied from oval to spindle-shaped, and some of them had long dendritic processes (Fig. 2b, inset). This pigment became more prominent with Fontana Masson's stain but was nonreactive with PAS, Ziehl-Neelsen stain, and a stain for iron. This pigment bleached with potassium permanganate. Both pigmented and nonpigmented cells were negative for GFAP, CK, and EMA. Some of the pigmented cells were positive for vimentin, S-100 (Fig. 2d), HMB-45 (Fig. 2e), and synaptophysin (Fig. 2f). The percentage of cells staining with MIB-1 L1 was 13.3%, but the cells did not express p53.

Based on histology, special staining, and immunohistochemistry, a diagnosis of melanotic desmoplastic medulloblastoma was made.

Discussion

Melanotic tumors of the central nervous system[15] are ependymomas, choroid plexus papillomas and carcinomas, primitive pineal tumors, medulloepitheliomas, astrocytomas, and medulloblastomas. The non-neuroepithelial pigmented intracranial tumors reported in the literature are schwannoma, meningioma, melanoma, and melanocytoma. In many of these tumors the pigment is melanin, whereas in others it is neuromelanin. In the case under discussion, this pigment was determined to be melanosomal melanin, since the pigment stained black with FM, bleached with potassium permanganate, and was reactive with HMB-45 and S-100. Lack of staining with PAS and Ziehl-Neelsen stain excluded the possibilities of lipofuscin and neuromelanin.

Melanin pigmentation has been described in medulloblastomas, and about 10 cases of this variant have been published.[1–10] All patients were male except for one.[2] All cases occurred in the first decade of life, except for one equivocal case that occurred in a 21-year-old man.[5] Our patient is the oldest. Survival varied from 2 months to 2.5 years, despite different treatment modalities, such as surgery, radiotherapy, and chemotherapy, except for one patient who survived for 10 years and died of a second malignancy.[10] In the case under discussion, the follow-up has been too short (12 months) to comment on the course of the disease.

Review of the published cases revealed that the melanotic component of the tumors consisted of tubules or papillae. In only three cases, the histology was that of a classic medulloblastoma.[5–7] In contrast, this was a typical case of desmoplastic medulloblastoma, and pigmented cells were seen around the nodules as well as focally in the nodules. These pigmented cells formed a significant part of the tumor, rather than a mere association or inclusion of melanin-forming cells occurring normally in leptomeninges. This tumor has a striking histological resemblance to a medulloblastoma and not to a pigmented neuroectodermal tumor of infancy. The latter tumors occur in infancy or early childhood in the maxilla and show a tubulopapillary or alveolar pattern. They behave in a relatively benign fashion. The MIB-1 L1 was high in our patient, but p53 gene protein expression was not seen.

The melanotic medulloblastoma and melanotic neuroectodermal tumor of infancy are probably of neural crest origin, because of the presence of melanin and differentiating neurons. This hypothesis is further supported in the case of the MNET by the presence of vanilmandelic acid and the presence of tight junctions in the absence of desmosomes, which are considered consistent with neural crest origin.[16,17] Kalimo et al.[18] reported a case of pigmented medullomyoblastoma and suggested multipotential differentiation of a primitive neuroectodermal tumor. They proposed that both neuroectodermal and mesenchymal components are of neural crest origin. This type of divergent differentiation has also been reported in peripheral primitive neuroectodermal tumors.[19]

References

1. Fowler M, Simpson DA (1962) A malignant melanin forming tumour of the cerebellum. J Pathol Bact 84:307–311
2. Rubinstein LJ, Northfield DWC (1964) Medulloblastoma and so-called "arachnoidal cerebellar sarcoma." A critical re-examination of a nosological problem. Brain 87:379–414
3. Best PV (1973) A medulloblastoma-like-tumour with melanin formation. J Pathol 110:109–111
4. Sung JH, Mastri AR, Segal EL (1973) Melanotic medulloblastoma of the cerebellum. Report of a case. J Neuropathol Exp Neurol 32:437–445
5. Hahn JF, Sperber EE, Netsky MG (1976) Melanotic neuroectodermal tumors of the brain and skull. J Neuropathol Exp Neurol 35:508–519
6. Boesel CP, Suhan JP, Sayers MP (1978) Melanotic medulloblastoma. Report of a case with ultrastructural findings. J Neuropathol Exp Neurol 37:531–543
7. Jimenez CL, Carpenter BF, Robb IA (1987) Melanotic cerebellar tumour. Ultrastruct Pathol 11:751–759
8. Dolman CL (1988) Melanotic medulloblastoma: a case report with immunohistochemical and ultrastructural examination. Acta Neuropathol 76:528–531
9. Garcia-Bragado F, Cabello A, Guarch R, et al (1990) Melanotic medulloblastoma. Ultrastructural and histochemical study of a case. Arch Neurbiol (Madr) 53:8–12
10. Baylac F, Martinoli A, Marie B, et al (1997) An exceptional variety of medulloblastoma: melanotic medulloblastoma. Ann Pathol 17:403–405
11. Krompecher E (1918) Zur Histogenese und Morphologie der Adamantinome und sonstiger kiefergesch Wuelste. Beitr Path Anat 64:169–197
12. Sharma MC, Mahapatra AK, Gaikwad S (1996) Pigmented neuroectodermal tumour of infancy: immunohistogenetic consideration. JAPI 44:278–280
13. Stowens D (1996) Pediatric pathology, 2nd edn. Williams and Wilkins, Baltimore
14. Stowens D (1957) A pigmented tumour of infancy: the melanotic prognoma. J Path Bact 73:43–51
15. Sharma MC, Arora R, Khanna N, et al (2001) Pigmented pleomorphic xanthoastrocytoma: report of a rare case with review of literature. Arch Path Lab Med 125:808–811
16. Borello ED, Gorlin RJ (1966) Melanotic neuroectodermal tumour of infancy – a neoplasm of neural crest origin: report of a case associated with high urinary excretion of vanillmandelic acid. Cancer 19:196–206
17. Cutler LS, Chaudhry AP, Topazian R (1981) Melanotic neuroectodermal tumour of infancy. An ultrastructural study, literature review and re-evaluation. Cancer 48:157–170
18. Kalimo H, Paljarvi L, Ekfors T, et al (1987) Pigmented primitive neuroectodermal tumor with multi-potential differentiation in cerebellum (pigmented medullomyoblastoma): a case with light and electron microscopy, and immunohistochemical analysis. Pediatr Neurosci 13:188–195
19. Eusebi V, Damiani S, Pasquinelli G, et al (2000) Small cell neuroendocrine carcinoma with skeletal muscle differentiation. Report of three cases. Am J Surg Pathol 24:223–230