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CASE REPORT

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Pigmented medulloepithelioma: report of a case and review of the literature

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Abstract A 9-year-old male child had a IV ventricular medulloepithelioma of classical histology, showing tubulopapillary and undifferentiated areas. The unusual feature, however, was the presence of melanin pigmentation in the cells, which was further confirmed by electron microscopy. So far 28 cases of medulloepithelioma have been reported in the English literature. However, none of them showed melanin pigmentation. To the best of our knowledge this is the first case of pigmented medulloepithelioma in the English literature.

Key words PNET · Medulloepithelioma · Pigmentation

Introduction

Medulloepithelioma, a tumour postulated as the most primitive multipotential neoplasm of the central nervous system, with features resembling those of the primitive medullary plate and neural tube, is very rare. Since Bailey and Cushing [2] described this tumour in 1926, 28 cases have been reported in the English literature [Table 1], with the entire range of differentiation varying from neural, glial, bone, cartilage and skeletal muscle [1]. Most (26) were intracranial, and 1 each in the cauda equina and sciatic nerve. Some of these cases have been well accepted as medulloepitheliomas, whereas others have not [25]. We describe a case of pigmented medulloepithelioma in the IV ventricle in a 9-year-old boy. To the best of our knowledge, this is the first such case being reported in the English literature.

Case report

A 9-year-old boy presented at the outpatient clinic in the Department of Neurosurgery of this hospital with complaints of headache, impaired consciousness and vomiting of 1 week's duration. On examination the child was drowsy but followed commands. There was bilateral papilloedema and the pupillary reaction to light was normal. Motor functions, pain and touch sensations were intact.

Routine haematological tests and serum chemistry showed no abnormality. Unenhanced CT scan of the head revealed an isodense tumour in the IV ventricle with a surrounding hypodense area (Fig. 1a). On contrast injection, the tumour was uniformly enhancing with a small hypodense area (Fig. 1b). A clinical diagnosis of medulloblastoma was entertained. A suboccipital craniotomy was performed, allowing near-total excision of the IV ventricle tumour, which was infiltrating the vermis. Postoperatively the patient's condition deteriorated and he died of pulmonary infection after 2 weeks.

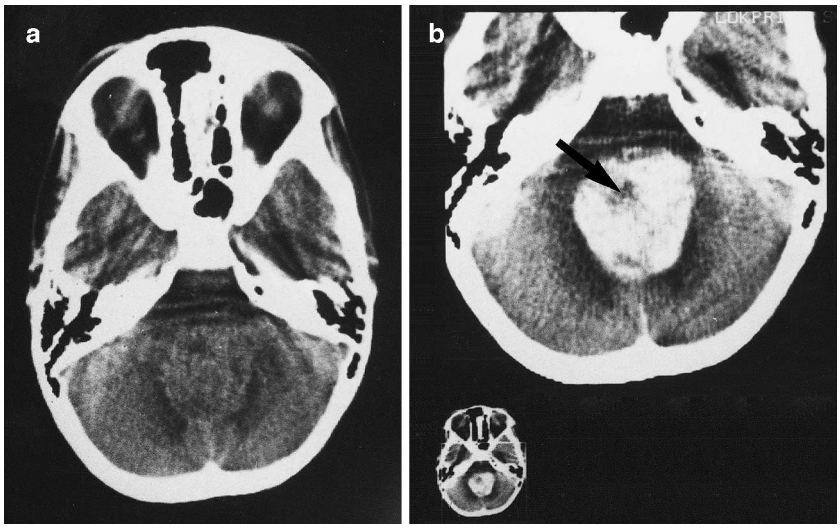

Fig. 1 **a** Unenhanced CT scan (posterior fossa cut) shows an isodense tumour in the IV ventricle, with peritumour oedema. **b** On contrast injection this tumour enhances uniformly with a small hypodense area (*arrow*)

Pathological examinations

The tissue consisted of multiple small fragments, which were soft and greyish white. These were fixed in 10% neutral buffered formalin. Sections (5 μm thick) were stained with haematoxylin and eosin (H&E), periodic acid–Schiff (PAS), phosphotungstic acid haematoxylin (PTAH), Nissl, Van Gieson, modified Gomori for reticulin, melanin bleach and Fontana Masson stains.

Immunohistochemistry

For the immunohistochemical demonstration of cellular antigens 5-μm paraffin sections were treated with corresponding antisera from DakoPatts (Glostrup, Denmark) and stained with the avidin–biotin complex (ABC) immunoperoxidase method. The various antisera used were: glial fibrillary acidic protein (GFAP) 1:25000, neuron-specific enolase (NSE, 1:500), S-100 protein (1:500), Cytokeratin (CK, 1:50), epithelial membrane antigen (EMA, 1:50) and alpha fetoprotein (AFP, 1:300).

Electron microscopy

Specimens were also processed for electron microscopy. For this, tissue was fixed in 2.5% glutaraldehyde, post-fixed in 1% osmium tetroxide and embedded in epoxyresin. Semithin sections of 1 μm were examined to find a representative area of the tumour, and ultrathin sections were double-stained with uranyl acetate and lead citrate.

Results

Microscopic examination of H&E-stained sections revealed tubulo-papillary structures in a loose myxomatous stroma (Fig. 2). The tubules varied in size and were lined with multilayered cuboidal to high columnar cells. Some of these tall columnar cells showed apical cytoplasmic blebs (Fig. 3). The nuclear chromatin was coarsely granular with prominent nucleoli. Mitotic activity was very brisk and at places mitoses were abluminal. There were focal areas of undifferentiated cells. In addition, many of the cells had black pigment in the cytoplasm, which was removed with melanin bleach and became more prominent with Fontana Masson stain. PAS stain revealed well-defined external and ill-defined internal limiting membranes in the tubules. PTAH stain revealed no glial differentiation.

Immunohistochemistry showed some of these cells to be positive for NSE. However, the tumour was negative for GFAP, S-100 protein, CK, EMA and AFP. Electron microscopy revealed melanosomes and premelanosomes in various stages of development (Fig. 4). No blepharoplasts, cilia, microvilli or intercellular junctions of zonulae adherentes were seen.

Discussion

Medulloepithelioma is a highly malignant primitive neuroectodermal tumour resembling the primitive neural tube of the 4- to 6-week embryo. Bailey and Cushing first described this entity in 1926 [2], but it was not accepted as a distinct entity until 1957, when Treip [24] published a case of medulloepithelioma of the mid-brain. Morphological features of this tumour were better delineated by Karch and Urich [15] in 1972.

In 28 cases reported in the literature (Table 1), the age ranged from 29 days to 23 years (average age 3.9 years), and the majority of the tumours occurred in the 1st decade of life. There was no sex predilection. There were 15 in a supratentorial location, 6 in the posterior fossa, 2 in the brain stem [12, 23] and 1 each in the III ventricle [11], basal ganglia [22], mid-brain [24], sacral canal [15] and in relation to the sciatic nerve [17]. The majority of the tumours were in or near the ventricles, usually solid, often

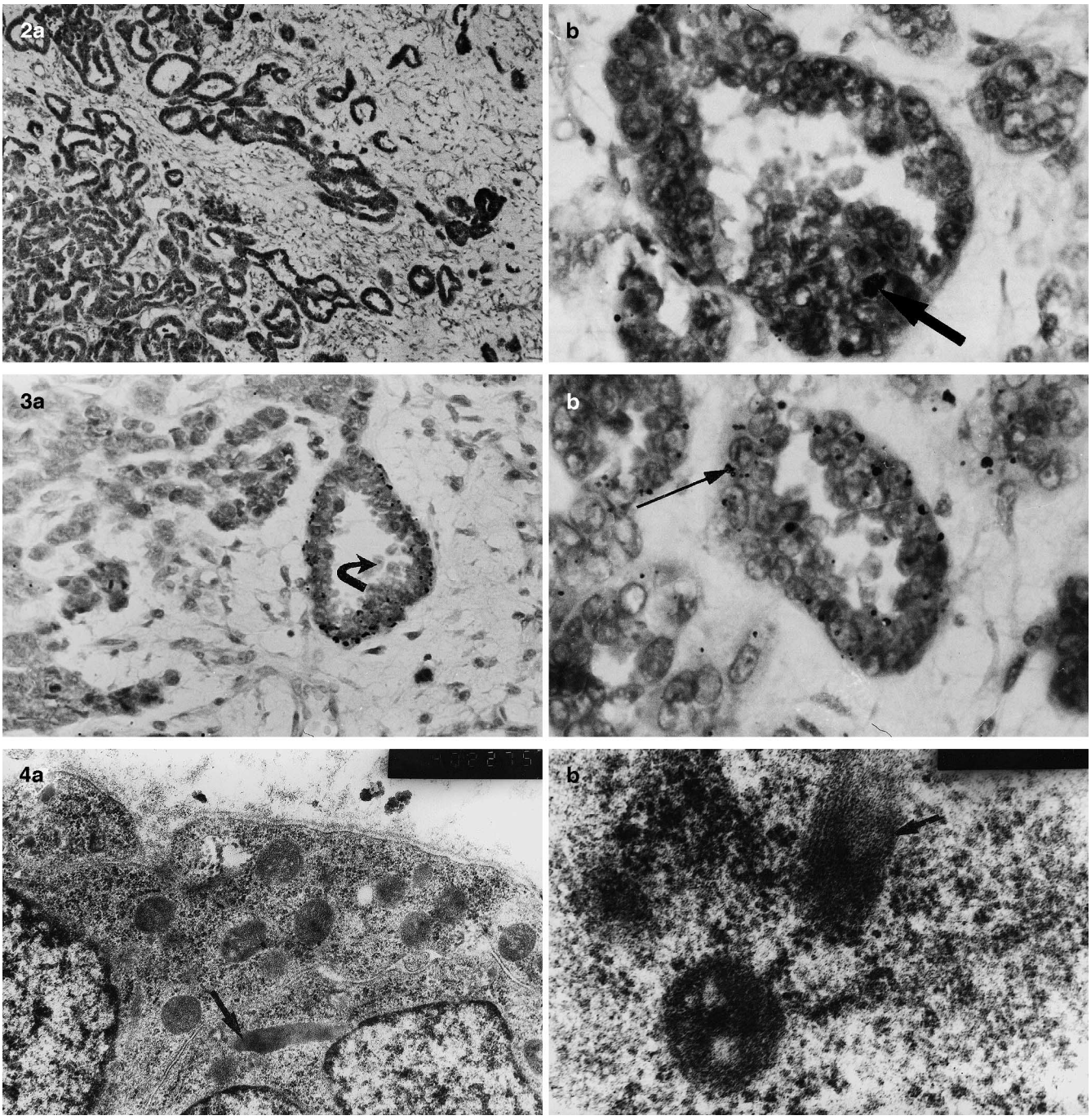

Fig. 2 Photomicrographs showing **a** tubules of variable sizes in the loose myxomatous stroma (H&E, ×40). **b** The tubules are lined by tall columnar cells with pseudostratification of the lining epithelium. Note frequent mitoses (H&E, ×200)

Fig. 3 Photomicrographs showing **a** apical cytoplasmic blebbings (*arrow*) in some of the tubules (H&E, ×100). **b** Note also melanin pigment in some of the cells (H&E, ×700)

Fig. 4 Electron micrographs showing melanosomes and premelanosomes (*arrow*) in the cells (**a** ×58,000; **b** ×140,000)

infiltrating locally and with areas of necrosis and haemorrhage. Cyst formation seemed to be infrequent [1, 12, 14, 19]. The case under discussion is that of a 9-year-old boy, and the tumour was located in the IV ventricle, with infiltration into the vermis. In the published literature CT findings are described for 2 cases; in 1 the tumour was partly solid and cystic [1], whereas the other showed two large cysts with solid mural nodules [19]. In our case, the CT scan showed a uniformly enhancing tumour, which was

Table 1 Summary of information on all known cases of medulloepithelioma (*RT* radiotherapy, *S* surgery, *C* chemotherapy)

Serial no.	Authors/year [ref.]	Age	Sex	Location	Survival	Therapy
1.	Hirsch and Oldberg 1938 [13]	9 years	M	IV ventricle	Not known	Not known
2.	Bailey et al. 1939 [3]	10 months	–	Cerebellum	2 weeks	Not known
3.	Treip 1957 [24]	8 months	M	Mid-brain Right cerebellum	8 months	No treatment
4.	Fujita 1958 [11]	2.5 years	F	III ventricle	8 months	Not known
5.	Zimmerman 1958 [28]	5 years	M	Left temporal lobe	Not known	S + RT
6.	Van Epps et al. 1967 [27]	5 years	M	Right temporal lobe	6 months	S + RT
7.	Fowler 1968 [10]	3 years	F	Left parietal lobe	5 months	S + RT
8.	Deck 1969 [9]	16 months	F	Right parietal lobe	5 days	S
9.	Dastur and Lalitha 1969 [8]	15 years	F	Frontal lobe	No follow up	S
10.	Lolova et al. 1972 [16]	23 years	F	Right fronto-temporal	>5 years	S + RT
11.	Jellinger 1972 [14]	7 months	F	Right parieto-occipital	2 months	No treatment
12.	Karch and Urich 1972 [15]	3 years	M	Right parieto-occipital	4 months	S
		2 years	M	Left temporal	5 months	RT
		15 months	F	Cauda equina	>10 years	S + RT
13.	Best 1974 [4]	2 years	M	Cerebellum	2 weeks	S
14.	Gullotta and Entzian 1975 [12]	20 months	M	Brain stem	2 months	Not known
15.	Tani and Higashi 1975 [23]	15 months	–	Brain stem	Not known	Not known
16.	Pollak and Freide 1977 [18]	15 months	F	IV ventricle	11 months	S + RT
17.	Scheithauer and Rubinstein 1979 [22]	12 years	F	Left basal ganglia	35 months	RT + C
18.	Sato et al. 1980 [21]	29 days	F	Cerebellum	2 weeks	No treatment
19.	Nakamura et al. 1982 [17]	6 months	M	Sciatic nerve	7 years	S
20.	Auer and Becker 1983 [1]	2.5 years	F	Left parieto-occipital	11 months	S + RT
21.	Bonnin et al. 1984 [5]	15 months	M	IV ventricle	“Short”	S
22.	Poot 1986 [19]	4 months	M	Right cerebrum	Not mentioned	S
23.	Caccano et al. 1989 [7]	Three cases	–	Cerebrum	–	–
24.	Troost et al. 1990 [25]	3 years	M	Left parieto-occipital	9 months	S
25.	Present case	9 years	M	IV ventricle	2 weeks	S

found to be solid at surgery. Survival varied from days to more than 10 years (average survival 2.3 months). Subarachnoid spread, radioresistance and a high rate of recurrence all contributed to a poor prognosis. Two patients who did survive without recurrence for more than 7 years and 10 years had tumours located close to the filum terminale and the sciatic nerve, respectively [15, 17]. In addition, 1 patient [16] survived for 5 years with two recurrences and there was metastasis in the submandibular lymph nodes along with infiltration of temporalis muscle at the site of operation. The patient described by Van Epps [27] also developed metastases at the craniotomy site and cervical lymph nodes. The cases reported by Bonnin et al. [5] and Treip [24] were associated with Wilms’ tumour of the kidney and meningeal lipoma respectively.

The complete spectrum of differentiation of neural tube derivatives has been reported in the literature, varying from neuroblastic, glial or both [14–16] and even mesenchymal tissue, striated muscle, cartilage and bone [1]. However, none of the 28 cases reported in the literature so far have shown melanin pigmentation, as in the case under discussion. The melanotic nature of the pigment is substantiated by melanin bleach and Fontana Masson stain. Further, this was confirmed by electron microscopy, which revealed melanosomes and premelanosomes in the tumour cells.

The various differential diagnoses of a medulloepithelioma include germ cell tumours (embryonal carcinoma and endodermal sinus tumour), teratoma, papillary ependymoma and choroid plexus carcinoma [6]. The germ cell tumours are excluded by immunohistochemistry for alpha fetoprotein (AFP) and cytokeratin, which were negative in this case. Moreover, PAS staining revealed no PAS-positive diastase-resistant globules. Primary choroid plexus carcinoma is usually positive for cytokeratin and rarely shows glandular or tubular differentiation, whereas this case showed internal and external limiting membranes and, in places, characteristic apical cytoplasmic blebbing of the columnar cells, as described in the literature [6]. The possibility of teratoma was unlikely because derivatives of all three germ layers were not seen. The presence of limiting membranes together with the absence of cilia, microvilli and blepharoplasts rules out the possibility of papillary ependymoma. Moreover, immunohistochemistry for GFAP was negative.

Pigmented tumours of the neuroectodermal derivatives described in the literature include ependymoma, cerebellar medulloblastoma, choroid plexus carcinoma, olfactory neuroblastoma, schwannoma, meningioma and pigmented neuroectodermal tumour of infancy [20]. Melanin pigment is a transient feature in the human fetal pineal gland and is occasionally also expressed in pine-

oblastomas. On the basis of these observations, it may be postulated that melanin pigmentation represents another expression of cellular differentiation in the neuroectodermal tumours. The expression of melanin pigment may constitute a transitory phenomenon in the neoplastic development, as observed by Vandenberg et al. [26] in a tumour fraction of the OTT-6050 transplantable mouse teratoma. They noted that as differentiation towards neuroepithelial derivatives increases, the amount of melanosomal melanin decreases.

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