Malignant cerebral melanoma complicating giant pigmented naevus: a case report

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The giant pigmented naevus is the most florid expression of cutaneous hyperpigmentation. Examples may be seen in illustrations of physiognomic works of the eighteenth century (Fanconi, 1956). To date over 200 cases of extensive cutaneous pigmentation have been recorded in the literature, and the pathogenesis, clinical course and pathology have recently been reviewed (Reed, Becker, Becker, and Nickel, 1965).

Rokitansky in 1861 described a patient with a giant pigmented naevus and leptomeningeal hyperpigmentation. Since then some 20 cases of cutaneous and leptomeningeal hyperpigmentation have been reported and recently reviewed (Fox, Emery, Goodbody, and Yates, 1964; Reed et al., 1965). Excluding those cases in which either skin malignancy or metastases elsewhere in the body were present, there exist in the literature seven case reports of primary intracerebral melanoma complicating the condition of extensive cutaneous pigmentation (Table I). The rarity of this association prompted us to report another case.

CASE REPORT

The patient, a 15-year-old Polish girl, a binovular twin, was admitted on 7 November 1966 to a gynaecological unit. She presented with amenorrhoea of two months’ duration. In response to further questions to the relatives, a history of increasingly severe bilateral retro-orbital headache and anorexia over the preceding month was obtained. Family history was non-contributory; in particular the patient’s binovular twin sister was free of skin blemishes and well in every respect.

She was apyrexial, listless, and apathetic. There was marked neck-stiffness and Kernig’s sign was positive. There were no other localizing neurological signs. The striking feature was the presence of a giant, hairy, pigmented naevus of the ‘cape’ variety. It involved the posterior cervical and occipital regions and extended symmetrically over both shoulders (Fig. 1). In addition, multiple large pigmented naevi were scattered over the rest of the body.

INVESTIGATIONS Cerebrospinal fluid: clear and colourless, 32 red blood cells and 21 lymphocytes per c.mm; protein 210 mg and sugar 36 mg/100 ml.; Pandy test positive, W.R. negative, Lange curve normal. No organisms were seen by Gram staining, and no acid fast bacilli were detected. The blood haemoglobin was 15.2 g/100 ml., white cell count 8,400 c.mm with a normal distribution, ESR 7 mm in the first hour (Westergren). Radiography of the chest and skull were normal.

ELECTROENCEPHALOGRAM (9 November 1966): 'The patient was drowsy at the time of recording. The alpha rhythm was very unstable at 7-9 c/s, and appeared less in amount on the right side. Several bisynchronous and symmetrical generalized paroxysms of anteriorly predominant high voltage delta activity at 1-2 c/s were seen. Between the paroxysms the activity over the left hemisphere returned to a lower voltage mixture of theta and faster frequencies, whereas over the right hemisphere very irregular, moderate voltage delta activity persisted and was mixed with theta activity in the lower range. No constant focal features were seen, but the right hemisphere slow wave abnormality was most marked in the temporal region. Arousal responses on auditory stimulation occurred readily on the left, but were either absent or suppressed over the right hemisphere.'

SUBSEQUENT PROGRESS The clinical signs and CSF findings suggested a provisional diagnosis of tuberculous meningitis, and treatment for this was commenced and continued for four days. In one routine CSF specimen black spots were observed, but as the significance of this finding was not appreciated at the time, microscopic and chemical examinations were not carried out.

The patient became increasingly drowsy, and on the fourth hospital day focal neurological signs appeared. The right pupil became larger than the left, though both reacted briskly to light. There was a left homonymous superior quadrantic field defect, together with a left lower facial weakness and a minimal left upper monoparesis. A right common carotid angiogram, performed on the sixth hospital day, showed the typical appearance of a moderately vascular tumour in the right temporal lobe.

The patient’s condition rapidly deteriorated and she died on 15 November, the eighth day following admission, before craniotomy could be carried out.

NECROPSY FINDINGS (16 November 1966, Dr. P. G. Lynch.) Gross findings outside the skin and central
nervous system were unremarkable. The skin showed the pigmentary changes previously described. There was no evidence of cutaneous, ocular, or visceral malignancy.

The brain weighed 1,510 g and showed flattening of the gyri. There was coning of the cerebellar tonsils and medulla into the foramen magnum. A large, solid, soft pigmented tumour measuring 6 cm in diameter was present in the right temporal lobe (Fig. 2). It extended into the posterior horn of the right lateral ventricle, where it appeared to communicate with the choroid plexus which was heavily pigmented. There was some adjacent ependymal pigmentation. The leptomeninges at the base of the brain and elsewhere showed no abnormal pigmentation. Throughout the entire length of the spinal cord, small brownish, granular lesions were seen inside the dura.

**TABLE I**

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Skin</th>
<th>Eyes</th>
<th>Meningeal pigmentation</th>
<th>Cerebral pigmentation</th>
<th>Spinal cord</th>
<th>Site of cerebral tumour</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oberndorfer, 1903</td>
<td>8 m</td>
<td>F</td>
<td>Numerous pigmented naevi involving over half of the body surface</td>
<td>Not mentioned</td>
<td>Black spots over brain, partly in cortex</td>
<td>Thalami, striae acousticae</td>
<td>No pigment</td>
<td>Cerebellum</td>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Berblinger, 1915</td>
<td>9 m</td>
<td>F</td>
<td>190 large, hairy, pigmented naevi. Neurofibromatosis</td>
<td>Normal</td>
<td>Basal leptomeningeal hyperpigmentation</td>
<td>Perivascular invasion of brain substance</td>
<td>Pigment-free tumour cells surrounding cord</td>
<td>Gyrus hippocampi. Also glioma of pons with melanin-containing cells and free melanin</td>
<td></td>
</tr>
<tr>
<td>Bjørneboe, 1935</td>
<td>37 M</td>
<td>F</td>
<td>Giant ‘bathing trunk’ naevus and numerous hairy naevi scattered elsewhere over the body. Neurofibromatosis</td>
<td>Not examined at necropsy, Fundoscopy normal</td>
<td>Absent</td>
<td>Absent</td>
<td>Normal</td>
<td>Left frontal lobe</td>
<td>Cerebral tumour</td>
</tr>
<tr>
<td>Willis, 1948</td>
<td>46 F</td>
<td>F</td>
<td>Pigmented patches right side of face and temporal area, pigmentation of the right and also slightly the left sclera</td>
<td>Normal</td>
<td>Extensive patches of hyperpigmentation at base of brain</td>
<td>Cerebral surface surrounding tumour</td>
<td>Not mentioned</td>
<td>Medial aspect of right hemisphere. 4 cm in diameter</td>
<td>Cerebral tumour</td>
</tr>
<tr>
<td>Fanconi, 1956</td>
<td>5 m</td>
<td>M</td>
<td>Multiple large, hairy pigmented naevi</td>
<td>Not examined</td>
<td>Basal hyperpigmentation with thickening of tissue</td>
<td>Perivascular infiltration into brain substance; spotty pigmentation over cerebral cortex, also dentate nuclei and brain stem</td>
<td>Meningeal hyperpigmentation</td>
<td>Pons</td>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Musger, 1963</td>
<td>20 F</td>
<td>F</td>
<td>Giant ‘cape’ naevus and numerous other scattered naevi</td>
<td>Not examined</td>
<td>Diffuse leptomeningeal pigmentation; pigmentation of the ependyma</td>
<td>Several small melanotic tumours in the brain substance</td>
<td>Discolouration of the spinal meninges</td>
<td>Left frontal lobe, plum sized</td>
<td>Cerebral tumour</td>
</tr>
<tr>
<td>Reed et al., 1965</td>
<td>7 F</td>
<td>F</td>
<td>‘Bathing trunk’ naevus and two smaller naevi over the scalp</td>
<td>Not examined</td>
<td>Diffuse leptomeningeal pigmentation</td>
<td>Superficial layers of cerebral cortex and pons, also medulla and cerebellum</td>
<td>Not mentioned</td>
<td>Left temporal lobe</td>
<td>Epilepsy, vomiting, left facial paralysis</td>
</tr>
<tr>
<td>Present case</td>
<td>15 F</td>
<td>F</td>
<td>Giant ‘cape’ naevus and numerous smaller, hairy naevi scattered over the rest of the body</td>
<td>Normal</td>
<td>Absent</td>
<td>Subependymal pigmentation and hyperpigmentation of choroid plexus</td>
<td>Patchy pigmentation in subarachnoid space</td>
<td>Right temporal lobe</td>
<td>Cerebral tumour</td>
</tr>
</tbody>
</table>
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of the optic nerves as well as the olfactory nerves and bulbs. Pigmentation is usually heavy over the anterior perforated substance. Melanin-containing cells may also extend along the cerebral fissures and along the dorsal surface of the spinal cord. Convex, protruding parts of the brain tend to remain free of pigment.

Since melanin-containing cells in the skin and meninges have a common origin, it is not surprising that hyperpigmentation frequently coexists at both sites. Over 200 cases of extensive cutaneous pigmentation and over 100 cases of primary melanosis of the central nervous system are described in the literature. Hyperpigmentation present in both the skin and the central nervous system is recorded in 20 cases. The frequency of this association has led some authors to refer to it as a neurocutaneous syndrome, and the term neurocutaneous melanosis has been applied to this condition (Van Bogaert, 1948; Touraine, 1949; Fox et al., 1964; Reed et al., 1965). In this connection it is of interest that two cases of neurofibromatosis (Berblinger, 1915; Björneboe, 1935), one case of Sturge-Weber syndrome (Giampalmo, 1940), and one case of pial telangiectasia

FIG. 1. 'Cape' distribution of the pigmented naevus.

the posterior halves of both eyes. The right temporal tumour showed the characteristic appearance of malignant melanoma (Fig. 3). Large numbers of tumour cells were present in the subarachnoid space surrounding the brain. Sections taken at several levels along the spinal cord showed anaplastic, pigment-containing cells in the subarachnoid space, with extension into the space surrounding the nerve roots.

DISCUSSION

Melanocytes are derived from the neural crests during early embryonic development and become widely distributed during subsequent development, coming to lie chiefly along surface membranes (Rawles, 1948). Virchow (1859) credits Valentin with the first description of melanin-containing cells in the leptomeninges covering the cervical spinal cord. It is estimated that they occur in 85% of normal leptomeninges (Fox et al., 1964). Baader (1935) has studied the preferential sites of leptomeningeal pigmentation in detail. Melanocytes are likely to be found on the ventral surfaces of the lower medulla and upper cervical cord, and in the fissures on the ventral surface of the brain stem, particularly the interpeduncular fossa. They may occur on the upper part of the optic chiasm and along the lengths

FIG. 2. Macroscopic appearance of tumour in right temporal lobe.
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FIG. 3. Section of tumour showing melanin containing cells. × 350.

(Wilcox, 1939) have been described in association with neurocutaneous melanosis.

The incidence of malignancy in meningeal melanosis is difficult to assess because often anaplastic cells show little or no invasiveness. Fox et al. (1964) estimate that 88 out of a total of 101 cases of meningeal melanosis showed malignant change histologically, but the formation of a malignant melanomatous tumour is much less common and occurs in only about a third of the cases. Nevertheless, its incidence is about twice that given for malignant change in the skin (Reed et al., 1965).

It is apparent from Table I, in which are summarized the pertinent clinical and pathological details of the eight reported cases of primary malignant cerebral melanoma associated with extensive cutaneous pigmentation, that there is no site of predilection for the melanoma. Death in all eight occurred below the sixth decade, when mortality of cutaneous melanoma is at its peak, thus stressing the distinction from that condition (Gibson, Burrows, and Weir, 1957). The three infants presented clinically with progressive hydrocephalus. When a cerebral melanoma develops in childhood or adulthood, the clinical course is that of a rapidly expanding tumour. Only five of the eight cases had a giant pigmented naevus. It is felt, however, that extensive cutaneous pigmentation, whether or not accompanied by a giant pigmented naevus, constitutes a distinct entity.

The leptomeninges of the present patient were macroscopically unpigmented. In this respect our case is similar to Berblinger's (1915). It has been argued that leptomeningeal hyperpigmentation must be considered an essential prerequisite for the diagnosis of a primary malignant cerebral melanoma on the grounds that the tumour may be secondary to a lesion at some other site, even if this is not found at necropsy. (Bouton, 1958; Fox et al., 1964). The argument whether, in the absence of malignancy elsewhere in the body, a cerebral melanoma is primary or secondary is impossible to resolve, and this difficulty is further underlined by the patient reported by Lua (1914). In this case undoubted secondary intracranial melanomatosis gave rise to diffuse leptomeningeal pigmentation and multiple cerebral melanomas. We believe that the fact that normal meninges contain melanocytes, a potential source of hyperpigmentary and malignant changes, coupled with the frequent failure to find a primary lesion at necropsy, would argue strongly that primary melanosis and primary malignant melanoma do exist within the cranium.

Although familial cases of giant pigmented naevi have been reported (Van Bogaert, 1948), the condition is usually non-hereditary. It is interesting that this patient's binovular twin sister is free of skin blemishes. Siemens and Waardenburg (1927) reported identical twins, one of whom had a 'cape' type giant pigmented naevus together with at least 62 similar but smaller naevi. The other twin was free of abnormal cutaneous pigmentation.

In conclusion, meningeal melanosis should be suspected in patients with giant or extensive pigmented naevi, and the development of signs indicative of an intracranial space-occupying lesion is highly suggestive of a complicating malignant cerebral melanoma. The finding in the CSF of free melanin or melanin-containing cells, though rare, is diagnostic of meningeal melanosis but may occur in both primary and secondary melanomatosis (Russi, Robinson, and Nagler, 1953; Gibson et al., 1957; Kiel, Starr, and Hansen, 1961; Spens, Parsons, and Begg, 1962; Pappenheim and Bhattacharji, 1962). In retrospect we feel that, had we recognized the significance of the black flecks contained in one of the CSF specimens, we should have made a diagnosis of a right temporal melanoma in this patient during life.
SUMMARY

The case is reported of a 15-year-old girl with a giant pigmented naevus of the ‘cape’ variety associated with a right temporal malignant melanoma, and pigment cells in the sub-arachnoid space surrounding the spinal cord.

The authors wish to thank Dr. J. H. Friend for permission to publish the case, Dr. P. G. Lynch for making available the necropsy findings, and Dr. E. C. Hutchinson for helpful criticism of the paper.

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Malignant cerebral melanoma complicating giant pigmented naevus: a case report.
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*J Neurol Neurosurg Psychiatry* 1968 31: 628-632
doi: 10.1136/jnnp.31.6.628

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