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 leptomenigeal hyperpigmentation. Since then some 20 cases of cutaneous and leptomenigeal 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 binocular 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 binocular 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 monoplegia. 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

TABLE I

REPORTED CASES OF CEREBRAL MELANOMA WITH EXTENSIVE CUTANEOUS NAEVI

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

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.

MICROSCOPY Sections of the cutaneous naevi taken from several sites showed the histological appearance of pigmented intra-dermal naevi. There was no microscopic evidence of malignant change in any of the sections taken, nor was there evidence of malignancy in sections through

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

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. 2. Macroscopic appearance of tumour in right temporal lobe.

FIG. 3. Section of tumour showing melanin containing cells. $\times 350$.

(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 melanomata. 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.

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