Neuropathic malignant melanoma presenting as a trigeminal sensory neuropathy

Cranial neuropathies may occur as a complication of malignant melanoma of the head and neck and may be an important feature. We have not been able to find an account of this in the neurological literature. A 63 year old woman presented with a seven month history of altered sensation over the right cheek and nose; for five months the cheek and the roof of the mouth on the right side had been numb and a continuous dull pain had developed over the right face. There was no relevant medical history. There was no family history of neurological problems and the patient had not received cytotoxic medication in the past.

On examination there was mild infraorbital oedema on the right and a sense of loss to light touch and pin prick over the cheek, the side of the nose, the hard palate and upper gum on the right side. Movements of the mandible, face, tongue and palate were symmetric and sensation over the soft palate and posterior pharyngeal wall was normal. The rest of the clinical examination was normal.

Routine blood tests, a chest radiograph, and examination of the CSF were normal. Plain radiographs of the maxillary sinuses, fine section axial CT through the skull base and parasagittal sinuses (which included images of the nasopharynx) and MRI of the brain stem and middle cranial fossa were all normal. Examination under anaesthesia of the postnasal space and biopsies of the right lateral nasopharynx and the right fossa of Rosenmüller were normal.

Two months later the patient noticed enlargement of a lesion on the tip of her nose. This lesion had been present for as long as the patient could remember and until this time it had not changed or attracted her attention; medical staff had noticed the lesion when the patient first presented and had considered it to be benign in appearance. Examination revealed a well-shaped nodule on the tip of the nose measuring 13 mm by 10 mm with a purple red surface; no brown pigmentation was present to suggest a melanocytic lesion. Histopathological examination of a punch biopsy of the lesion revealed an amelanotic malignant spindle cell tumour. A biopsy of the skin of the right cheek was then performed and histopathological examination revealed thickened inflamed nerves with infiltration of the perineurium by cytologically malignant cells (figure). Immunocytochemical studies showed that both the spindle cells in the first biopsy and the larger cells in the perineurium of the dorsal nerves in the second biopsy were positive with polyclonal anti S-100 antibodies (figure, insert) and monoclonal HMB-45 antibodies. The pathological diagnosis was of a spindle cell neurotrophic malignant melanoma.

The swelling of the right cheek worsened and repeat CT of the head two months later showed a 20 mm by 15 mm mass superficial to the right maxillary antrum extending through to the infraorbital foramen. This was thought to be expanding tumour along the course of the infraorbital nerve and a palliative course of radiotherapy to the right side of the face was commenced. The patient died 11 months after presentation.

Electroencephalography during an episode of ictal crying shows a repetitive sharp wave discharge, maximal over the right temporal area.

right temporal area (figure), confirming the occurrence of partial seizures with ictal crying. He was loaded intravenously with phenytoin with resolution of the crying seizures. Brain CT showed periventricular leukomalacia and mild diffuse cerebral atrophy. Neurological examination showed a left hemiparesis, unchanged from previous examinations.

Crying can represent an affective behavioural manifestation of sadness or depression, or can occur as an ictal event or postictal phenomenon, or can occur in association with a non-epileptic seizure. Outbursts of involuntary and uncontrollable laughing or crying may also accompany the pathological emotion seen in patients with pseudobulbar palsy, which may occur in vascular, degenerative, or demyelinating diseases of the brain.

The neuroanatomical localisation of crying remains unknown. In most patients with crying seizures, the EEG has provided evidence of a frontotemporal seizure focus in the non-dominant cerebral hemisphere. Evaluation of our patient also showed the presence of a seizure focus in the temporal region of the non-dominant cerebral hemisphere, presumably caused by ischaemic cerebrovascular disease as there was no evidence of an intracranial tumour, vascular malformation, or infection. This is in support of the concept that the limbic areas in the non-dominant hemisphere are related more to the experiencing of negative emotions, such as fear and anxiety, than positive emotions such as happiness.1

To our knowledge, this is the first reported case of crying seizures after cerebral infarction. As sudden outbursts of uncontrollable crying may also accompany the pathological emotion seen in patients with pseudobulbar palsy, the differentiation of these two possibilities with EEG recordings should be considered.

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Subcutaneous nerve showing perineural infiltration with cytologically malignant cells (arrowed). Immunocytochemistry showed S-100 positivity (insert).

Nerve involvement by malignant melanoma is uncommon but it is a well described feature of the rare amelanotic spindle cell variant of melanoma, termed desmoplastic malignant melanoma.1 Nerve involvement may be of three types; local invasion of neural tissue, distant spread along perineurium (as in this case), or actual differentiation into neural tissue. Such tumours are termed neurotropic malignant melanomas but are recognized to be a variant of desmoplastic malignant melanoma.2 The common embryological origin of melanocytes, fibroblasts, and nerve cells from the neural crest supports speculation that melanocytes have the potential to differentiate into fibrous and neural tissue. Clinically the diagnosis of desmoplastic malignant melanoma is often overlooked because it may develop within a very long standing cutaneous lesion, as in this case, or present as a deep fibrous nodule without prominent overlying brown or black pigmentation. Initial diagnoses in one series included viral wart, basal cell carcinoma, pyogenic granuloma, and sebaceous cyst.3 Histopathological diagnosis may also be difficult. Absence or subtlety of pigmentation with prominent collagenous stromal tissue in the dermis give the tumours a deceptively benign, non-melanocytic appearance. Overlying epidermal lentiginous hyperplasia or the presence of melanocytic junctional proliferation may provide a valuable clue to the likely diagnosis. These features are sometimes absent4 and diagnosis often relies on the immunocytochemical demonstration of a melanocytic origin.5 Metastases may show more obvious features of a classical melanoma or retain the desmoplastic features of the primary lesion.6

Since desmoplastic melanoma was first described in 1971 over 200 cases have been reported.1 In one series of 45 patients cranial nerve involvement occurred in 10.7 Three patients presented with unilateral facial sensory loss, three presented with altered sensation over the face and a cutaneous lesion, and four developed trigeminal or facial neuropathies with recurrent disease. Centripetal spread of tumour cells along branches of the trigeminal and facial nerves, particularly the maxillary nerve and its branches in the face, orbit, and cavernous sinus, may lead to involvement of other cranial nerves. Although desmoplastic melanoma accounts for less than 1% of all cases of melanoma, the neural involvement is not always a feature. Cases with early cranial nerve involvement may be referred to neurologists before attention is drawn to a cutaneous lesion or to a history of their removal. The case illustrates the need to establish the nature of cutaneous lesions on the face in patients with cranial neuropathies, particularly where superficial branches of the fifth or seventh cranial nerves are involved at an early stage.

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Propranolol in startle induced epileptic seizures

Startle epilepsy is a rare but severe seizure disorder, most often seen in patients with severe brain damage and neurological or mental handicap, but occasionally in patients without signs of cerebral dysfunction.1 Epileptic seizures of predominantly tonic, tonic-psychomotor, or tonic-myoclonic semiology precipitated by sudden unexpected stimuli are among the constituent features of this condition. Frequency of seizures is high, with daily attacks in most patients, and falls are common. Spontaneous seizures also occur.

Treatment is difficult. Carbamazepine and benzodiazepines such as clonazepam have been found to be effective in some patients, whereas valproate seemed to be of less value and phenytoin or phenobarbitone were ineffective.

In the Epilepsy Center, Bethel, 24 adult patients with startle induced seizures have been studied and treated since 1980. Twelve of them received clonazepam and 20 received carbamazepine. As a new approach, propranolol was investigated in 11 patients. This was after experimental studies had shown an accentuation of the startle reflex by adrenergic substances;2 and some anticonvulsant activity. Kolbinger et al had demonstrated the efficacy of metoprolol in a case of startle epilepsy.

We started treatment with 80 mg propranolol, increasing the dose gradually up to 160 mg per day (in two patients up to 240 mg). With propranolol, one patient had no more startle induced seizures, two patients had a greater than 50% reduction in seizure frequency, and eight showed no improvement. There were no side effects and no development of tolerance. The three successfully treated patients remained on propranolol for 82, 19, and 120 months. In the remaining eight patients the drug was withdrawn after treatment failure was apparent. With clonazepam and carbamazepine, one and three patients remained free from startle induced seizures respectively, and one further patient with each drug showed a reduction of more than 50%. Five of seven patients with an initial response to clonazepam developed complete tolerance within two to 16 weeks.

Mean follow up for all patients who were successfully treated was 55 (range 12–120) months. The overall therapeutic outcome was poor. In only 21% of all patients (five out of 24) was a complete control of startle induced seizures achieved. Clonazepam and carbamazepine did not show better results than propranolol. We conclude that propranolol seems to be an additional and safe drug in the treatment of startle epilepsy with efficacy comparable with the standard regimen, but further experience is required.

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