

Slowly progressive cranial nerve palsies

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Clinical records

The details of four patients treated at the Head and Neck Unit, Princess Alexandra Hospital, Brisbane, over a 1-year period are summarised in the table. All four patients presented with progressive trigeminal or facial nerve palsies following excision of cutaneous lesions from the head and neck.

Patient	Age (years)	Sex	Presentation	History of cutaneous head and neck malignancy	Specialties involved	Delay in diagnosis	Investigations	Final diagnosis	Management
Patient 1	40	male	3 years' progressive paraesthesia of the left upper lip and cheek	Nasal tip lesion removed with cryotherapy: no histology available	General practice, dermatology, otolaryngology	3 years	MRI	PNS (SCC) along V2	Intracranial/skull base surgery with postoperative radiotherapy
Patient 2	41	male	8 months' progressive left cheek paraesthesia, jaw pain and trismus	Excision of a left lower lip SCC 2 years previously: histology showed small nerve PNS, so postoperative radiotherapy given	General practice, maxillofacial, neurology, otolaryngology	6 months	MRI (showed hyperintensity of the left masseter consistent with denervation changes) Masseteric muscle biopsy	PNS (SCC) along V2 and V3 extending to the pons	Palliative radiotherapy
Patient 3	67	female	2.5 years' progressive left facial nerve palsy	Extensive facial SCCs, including an aggressive recurrent right cheek SCC treated with radical excision and radiotherapy	Neurology, ophthalmology, otolaryngology	2.5 years	MRI	PNS (SCC) along VII and V2	Intracranial/skull base surgery with postoperative radiotherapy
Patient 4	72	female	5 months' progressive left facial nerve palsy and left forehead and cheek paraesthesia	Two skin lesions excised from the right (contralateral to nerve palsies) nasolabial sulcus 20 years previously: no histology available	Otolaryngology	5 months	Initial MRI (Box 1) reported as "normal", although on retrospective review PNS was seen. Subsequent MRI (Box 2) showed extension of the tumour to the pons.	PNS (melanoma) along V2 and V3 extending to the pons	Palliative care

MRI = magnetic resonance imaging. PNS = perineural spread. SCC = squamous cell carcinoma. V2 = maxillary division of trigeminal nerve. V3 = mandibular division of trigeminal nerve. VII = facial nerve. ♦

The incidence of non-melanotic head and neck skin cancers in Queensland is among the highest in the world.¹ Perineural spread (PNS) from these lesions involves either small nerves, identified at pathological examination (incidental), or large nerves, presenting clinically as cranial nerve palsies. Basal cell carcinoma is the more common skin cancer, but incidental PNS is most frequently associated with squamous cell carcinoma.² In 32 out of 34 patients over a 5-year period, isolated major nerve PNS was due to squamous cell carcinoma (unpublished data). PNS from melanoma and microcystic adnexal carcinoma has also been described.^{3,4}

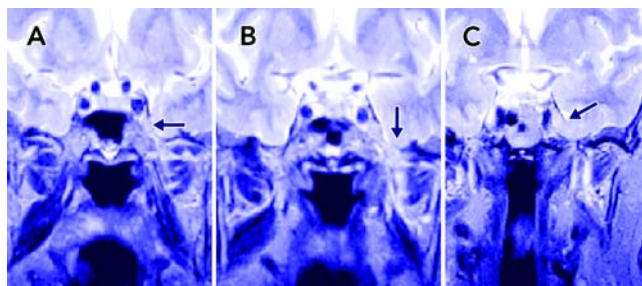
Because many clinicians are not familiar with PNS involving large cranial nerves, the diagnosis can easily be missed or delayed. The disease is associated with high treatment morbidity and poor prognosis once clinical or radiological evidence becomes apparent, with a 5-year survival rate of 20%–30%.⁵ Early detection of PNS in large cranial nerves is essential, as the condition is often unsalvageable once the tumour has spread through the skull base.

The facial and trigeminal nerves are most commonly affected,⁶ although forehead tumours can gain access to the orbit via the ophthalmic nerve.⁷ Symptoms of trigeminal nerve infiltration include formication, dysaesthesia, paraesthesia,

numbness and pain (often severe and "electric shock-like" in nature).⁸ Slowly progressive facial nerve palsy may represent seventh cranial nerve infiltration or infiltration within the parotid, whereas diplopia and visual impairment indicate advanced orbital disease. These symptoms can mimic other diagnoses, such as Bell's palsy or trigeminal neuralgia, but almost always manifest as slowly progressive and irreversible palsies. Close follow-up of patients to ensure resolution of symptoms is mandatory.

The four patients we have described illustrate delays between clinical presentation and diagnosis. These delays could have been avoided by establishing the link between unresolving cranial nerve palsies and excision of cutaneous lesions from the head and neck. Patients 2 and 3 had a history of aggressive squamous cell carcinoma of the face treated with radical excision and postoperative radiotherapy. Advanced, recurrent skin squamous cell carcinomas have a higher incidence of PNS, particularly when located close to a cranial nerve, and should alert the clinician to the possibility of neural metastasis.⁹ Tumour size before excision, postoperative defect size, subclinical extension and Moh's micrographic surgery levels are significantly larger in patients with PNS than in patients without PNS.¹⁰

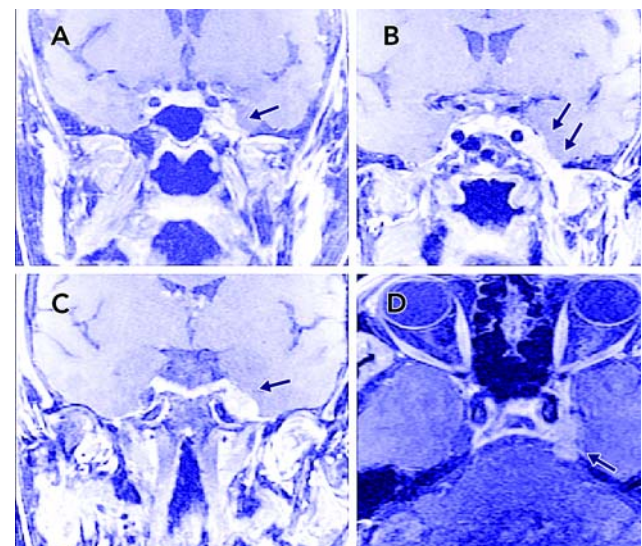
1 Coronal T2-weighted MRI images of Patient 4



These images were reported as "normal", although retrospective review shows perineural spread of melanoma with thickening and nodularity along the left V2 (A), V3 (B) and the trigeminal ganglion (C). MRI = magnetic resonance imaging. ♦

PNS can be subtle and missed on initial pathology but, because of the propensity for local recurrence, most specialist multidisciplinary units that deal with skin cancer will recommend adjuvant radiotherapy, particularly if the lesion is excised from the trigeminal nerve distribution. In Patients 1 and 4, no histology was available. Small skin lesions are often treated with cryotherapy or curettage, resulting in no pathological report. However, these lesions may still have a propensity for PNS, so their excision should be elicited in the history. In Patient 4, the skin lesions were excised from the side of the face contralateral to the cranial nerve palsies and were unlikely to represent the primary disease. Nevertheless, this case illustrates that patients with a history of cutaneous lesions from any site on the head and neck are at risk of developing PNS. These cases also illustrate that the interval between excision of a lesion and presentation of PNS can be long.¹¹ Clinicians should hold a high index of suspicion even if the interval is several years.

2 Contrast-enhanced T1-weighted MRI images of Patient 4



The images show perineural spread of melanoma with perineural thickening and enhancement along the left V2 (A), V3 (B), the trigeminal ganglion (C) and the trigeminal nerve as it exits the pons (D). MRI = magnetic resonance imaging. ♦

A further source of delay is that patients are seen by a variety of clinicians before diagnosis. Cross-referral for second opinions is common, resulting in further delay. Patients 1–3 illustrate how the unfamiliarity of clinicians with the disease process resulted in patients seeking opinions from several specialties before definitive diagnosis. In addition, investigations may be performed to exclude a different pathology or misinterpreted because the clinician is unaware of the phenomenon, resulting in further delay. In Patients 2 and 4, initial imaging revealed changes compatible with PNS, but these were not recognised, either because the radiologist was not familiar with the entity or because the referring clinician may not have raised the possibility of PNS. In Patient 2, the hyperintensity of the masseter muscle on magnetic resonance imaging (MRI) led the clinician to suspect a primary muscular disorder, instead of the correct interpretation of denervation changes from trigeminal nerve involvement. The patient underwent an unnecessary muscle biopsy. Earlier detection may have resulted in Patients 2 and 4 being treated with curative intent instead of palliative care.

High resolution MRI is the investigation of choice, and may identify the earliest changes of PNS. However, disease may not be radiologically apparent until it has reached the orbit, cranial fossa or the skull base foramina. Computed tomography (CT) identifies the disease at a late stage when the tumour has eroded adjacent bony margins. MRI has the added advantage of defining the relationship of the perineural tumour to important anatomical landmarks such as the cavernous internal carotid artery; this is important when planning a resection or biopsy. However, subtle changes on MRI may be missed even by experienced radiologists and, given a strong clinical suspicion with normal imaging, nerve biopsies should be performed. Presently, positron emission tomograph (PET) scanning has no role to play in the staging of PNS.

Delayed diagnosis of major cranial nerve PNS may result in devastating outcomes for patients, so early detection is crucial. Patients who present with slowly progressive cranial nerve palsies with a history of head and neck cutaneous malignancies should be investigated for PNS with a high index of suspicion. We recommend that all patients who undergo excision of high risk skin malignancies should be advised to seek a medical opinion if they develop facial numbness or weakness in subsequent years.

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Competing interests

None identified.

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DIAGNOSTIC DILEMMA

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