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Review article

Combined isolated trigeminal and facial neuropathies from perineural invasion by squamous cell carcinoma: A case series and review of the literature

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ABSTRACT

Perineural invasion is a targeted cellular proliferation guided by neurotrophins, rather than a simple diffusion of tumor in a path of least resistance. Invasion of cranial nerves by squamous cell carcinoma can represent an important diagnostic dilemma. It commonly presents as a distinct clinical neurological syndrome of combined isolated trigeminal and facial neuropathies. The focal cancer source may have been overlooked or remain occult. This case series illustrates diverse clinical presentations and neuroimaging challenges in four patients with squamous cell carcinoma of the cranial nerves. Anatomical pathways linking the trigeminal and facial nerves are reviewed, with emphasis on the auriculotemporal and pterygopalatine nerves. A successful neuroimaging strategy requires a targeted multimodality analysis of specific anatomical loci at the base of the skull. Attention must be directed to subtle radiological findings, such as obliteration of fat planes and linear enhancement along nerve branches, rather than bulky tumor tissue or bony invasion. Despite advances in microsurgical dissection and targeted radiotherapy, recovery of established neuropathic deficits is not expected. The prognosis remains poor in cases of advanced disease, emphasizing the importance early diagnosis by clinical acumen and focused neuroimaging.

1. Introduction

Distant perineural invasion (PNI) by tumor at the level of cranial and facial structures is an uncommon but worrisome clinical syndrome. Trigeminal (CNV) and facial (CNVII) nerves are by far the most frequently affected cranial nerves, alone or in combination. The predilection for these two specific nerves is explained by their wide anatomic distribution in the craniofacial territory and their rich anastomotic connections. The diagnostic dilemma in many cases of PNI is exacerbated by frequently negative or equivocal neuroimaging studies, at least in early stages of the disease.

The tumors most likely to present with PNI of CNV or VII are squamous cell carcinoma (SCC) arising from facial skin or mucosal surfaces of the nasopharynx and sinuses [1,2], cutaneous basal cell carcinoma, adenoid cystic carcinoma of the parotid gland [3], sarcoma [4], melanoma [5,6] and lymphoma [7]. In many patients, clinical neuropathic deficits predate the discovery of malignancy.

The present case series demonstrates varied presentations of PNI from SCC with combined isolated involvement of facial and trigeminal nerves. It highlights differences in clinical symptoms, sequence of neuropathic involvement, peripheral spread, imaging features as well as treatment challenges in advanced disease. We provide a discussion of relevant neuroanatomic pathways and review the literature on the pathophysiology and neuroimaging criteria of PNI for this particular syndrome.

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2. Case series

2.1. Case 1

This previously healthy woman presented with burning facial pain over the right zygomatic region at age 74. She was first diagnosed with trigeminal neuralgia, and sequentially prescribed carbamazepine and gabapentin. Both medications were poorly tolerated and ineffective. The first two MRI studies of the brain with contrast were felt to be unrevealing. Four months later, the patient noticed formication over her right cheek, and by the end of the same year she had developed mild right facial droop. By age 75, deficits had progressed to complete right maxillary (V2) and facial neuropathies. Concurrently with these disabling deficits the patient noticed a small skin lesion over the base of her nose, 1 cm below the inner canthus. Punch biopsy revealed squamous cell carcinoma extending into the underlying dermis (Fig. 1). There was no microscopic PNI in this specimen.

A third MRI at age 75, detected enlargement of the right V2 segment extending through the right cavernous sinus, pterygopalatine fossa and distal infraorbital course (Fig. 2). The patient underwent surgical exploration through an expanded endonasal approach.

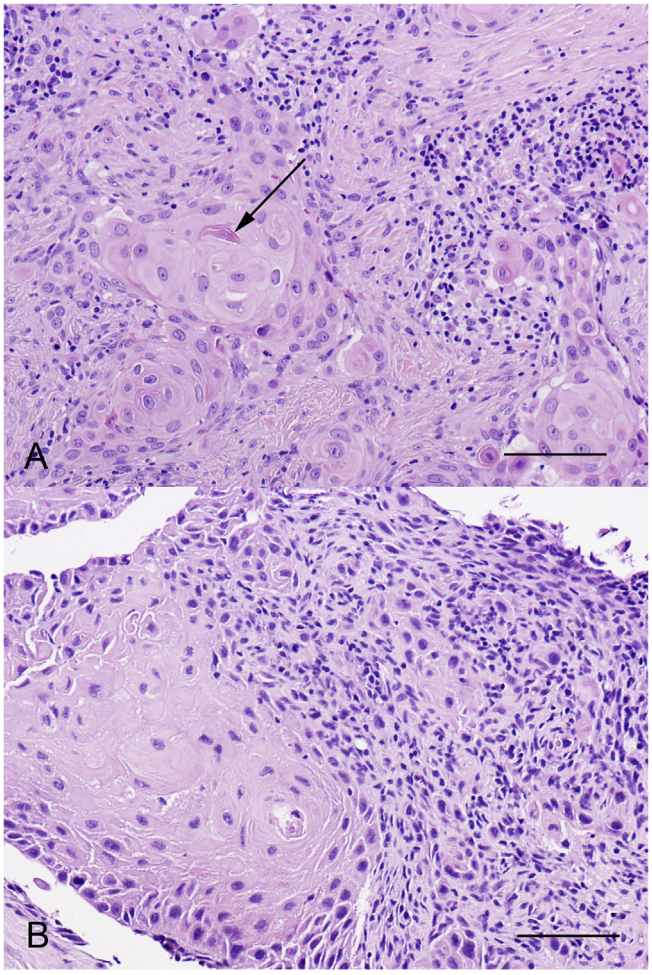

Fig. 1. Squamous cell carcinoma pathology (Case 1). Very similar pathology is demonstrated in the specimen obtained from the nasal skin punch biopsy at the level of the dermis (A) and the transcranial biopsy obtained from the region of the foramen ovale (B). There are cords and nests of well-differentiated cells with pale cytoplasm. Concentric layers of abnormal squamous cells and some dyskeratotic cells are noted (arrow in A). Despite a careful search, neither specimen demonstrated definite peripheral nerve elements. Hematoxylin and Eosin stain, bar = 100 μM.

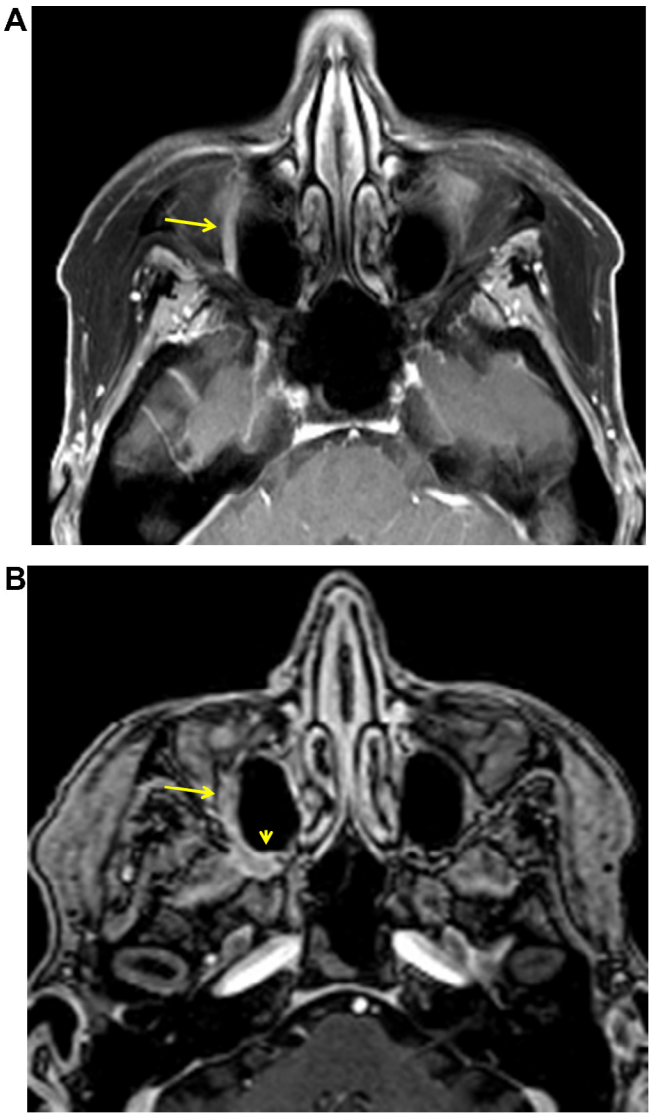

Fig. 2. PNI along the infraorbital nerve and the pterygopalatine fossa (Case 1). Axial T1 post-contrast fat-saturated MRI imaging on two parallel slices demonstrates thickened, enhancing right infra-orbital nerve (yellow arrow) with tumor enhancement in the right pterygopalatine fossa (arrowhead).

Tumor was seen in the maxillary sinus, and infiltrating the pterygopalatine fossa. Tumor around the trigeminal maxillary branch was carefully dissected, up to the level of the foramen rotundum. Pathological analysis was again consistent with squamous cell carcinoma (Fig. 1).

Postoperatively, the patient was treated with adjuvant radiation consisting of a total dose of 66 Gy in 33 fractions. Though facial pain resolved, there was only minimal improvement in trigeminal sensory loss and no recovery of facial paralysis.

2.2. Case 2

This 69 year-old man presented with recurrent brief right-sided otalgia. He was initially treated with carbamazepine with good results. By the end of the first year, he reported formication and spreading hypoesthesia in the mandibular (V3) territory. His past medical history was notable for arrhythmogenic right ventricular cardiomyopathy, requiring an implantable cardioverter defibrillator (ICD).

Neurologic examination demonstrated only slight hypoesthesia limited to the right mandibular cutaneous distribution. Because of