CASE REPORT

Perineural Spread of Cutaneous Squamous Cell Carcinoma Manifesting as Ophthalmoplegia

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ABSTRACT

An 89-year-old female presented with horizontal diplopia and was diagnosed with VI nerve palsy attributed to a microvascular event. She subsequently progressed to develop an orbital apex syndrome, with neuroimaging demonstrating tumour invasion. Eighteen months earlier, she had squamous cell carcinoma of the forehead excised with clear margins. Intraneural and perineural spread of squamous carcinoma from the face to the cranial cavity is an important cause of delayed cranial nerve palsies after local excision of the skin tumour.

Keywords: Orbital apex syndrome, perineural invasion, squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma (SCC) is the second most common tumour involving the periocular region, but its ability to cause neurological dysfunction is poorly recognised. This case report brings to attention the clinical presentation of cranial neuropathy caused by perineural invasion (PNI) of cutaneous SCC of the face.

CASE REPORT

An 89-year-old Caucasian female underwent excision of a left brow lesion. The histology was reported as a well-differentiated SCC of 6 mm thickness with evidence of PNI. The margins were clear, but the inferior margin was within 1 mm. The patient did not receive adjuvant radiotherapy. Eighteen months following surgery, and in the absence of any obvious signs of recurrence, the patient presented to her local eye department with diplopia. On ocular examination, she was noted to have impaired abduction on the left; the remainder of the examination was unremarkable. In view of her hypertension and age, the diplopia was

attributed to microvascular disease. The patient initially showed signs of improvement, but this was short-lived and she developed periocular pain. Over the following 3 months, this became severe, and she lost vision in her left eye.

On examination, right best-corrected visual acuity (BCVA) was 6/18 and left BCVA was hand movements. There was a left proptosis. A complete left ptosis was present, and the ipsilateral pupil was dilated, with no response to light or accommodation. She had impaired sensation in the left V₁ dermatome with an absent corneal reflex. Abducens nerve palsy was also present, but cranial nerves IV and VII were spared. Further, there was a left relative afferent pupillary defect associated with optic nerve head pallor. The clinical features were those of an orbital apex lesion on the left side.

Magnetic resonance imaging (MRI) showed an enhancing lesion in the orbital apex extending anteriorly along the superior aspect of the orbit and the track of V₁ and posteriorly to involve the cavernous sinus and in to Meckel's cave (Figure 1).

On closer inspection of the left brow area, there was a suspicious lesion, from where multiple biopsies were obtained. The histology was reported

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FIGURE 1 T1-weighted post-gadolinium (A and B) axial magnetic resonance images demonstrating an enhancing tissue within the left orbital wall arising from the brow area and extending back to the orbital apex along the path of a branch of the trigeminal nerve.

FIGURE 2 Histopathology (haematoxylin and eosin) demonstrating nests of moderately differentiated squamous cell carcinoma cells (dotted arrow) infiltrating between muscle fibres (solid arrow). (With thanks to Dr. Nigel Kirkham).

as moderately differentiated SCC (Figure 2). The patient was discussed at a multi-disciplinary team meeting, and in view of the extensive disease, palliative radiotherapy was offered.

DISCUSSION

SCC accounts for 5–10% of all periocular tumours.¹ Recognised predisposing risk factors are increasing age, prolonged sun exposure, fair complexion, male gender (due to occupational sunlight exposure), chronically injured skin (ulcers and scars), certain genetic skin disorders (xeroderma pigmentosa, albinism), and immunosuppression, especially following

renal transplant.¹ SCC causes local tissue destruction but may also metastasise via lymphatic, haematogenous, and perineural routes.² PNI in the periocular area may spread into the orbit and intracranial cavity, especially along the routes of cranial nerves V and VII as a result of their extensive subcutaneous distribution.¹ The frontal region is especially prone due to the rich supply provided by the supraorbital nerve.^{1,3} The incidence of PNI in periocular SCCs is estimated at 4–8% and is associated with recurrent disease, poorly differentiated histology, and lesions larger than 2 cm and deeper than 4 mm.^{1,4}

PNI is asymptomatic in its early stages in 60–70% of cases and is often not suspected until the orbit and cavernous sinus have been invaded.^{1,5} Inconsistency between clinical symptoms and the normal appearance of imaging studies, in addition to the assumed complete previous excision of the tumour, further contribute to delays in diagnosis.^{6,7} Just like in our patient, cranial neuropathy is not infrequently misdiagnosed as trigeminal neuralgia, Bell palsy, or attributed to a microvascular event.⁶

Perineural spread often cannot be visualised on neuroimaging, and sensitivities have been reported to be as low as 76%, for both MRI and computed tomography (CT).⁸ If a patient is suspected of PNI, then MRI with contrast enhancement is preferable to CT in detecting enlarged or asymmetric nerves. Typical radiological findings seen in PNI are nerve enlargement, foraminal enlargement, obliteration of fat planes, pseudocystic masses, and convexity of the lateral cavernous sinus wall.^{9–11}

Periorbital SCCs are treated with surgical resection, preferably Moh's micrographic surgery (MMS) or *en face* frozen section excision, as the primary modality.

Postoperative radiotherapy should be recommended in patients with evidence of PNI on histology as long as there are no other major comorbid risk factors.¹² At present there are no randomised control clinical trials addressing the efficacy of surgical excision alone versus surgical excision combined with radiotherapy in the treatment of cutaneous SCC with PNI, as a result adjuvant radiotherapy remains controversial.¹³ Nevertheless, several retrospective case series have demonstrated better local control and lower recurrence rate with adjuvant radiotherapy.¹⁴ Further, the National Comprehensive Cancer Network released a set of 2006 practice guidelines, which mention that postoperative radiotherapy should be considered when there is evidence of substantial PNI (*i.e.*, involvement of more than just a few small sensory nerve branches).¹⁵ If a specific cranial nerve is involved, then the entire course of the nerve should be treated with radiation, from the skin surface as far back as its origin.^{6,11} Once the tumour has spread to the orbital apex and beyond, treatment is often palliative.

McNabb *et al.* have published the largest series to date of periocular SCCs with PNI of the orbit.¹⁰ They reported on 21 cases of which impaired or altered sensation was the most common presentation; the majority were male, the forehead and brow were the most common primary sites for SCC with PNI, and the lesion was often larger than 2 cm. The average duration of 2 years from primary excision to clinical presentation with PNI was very similar to our case. The median duration from presentation of PNI to death secondary to their disease was 3 years.

Early recognition of PNI and better methods of detection are needed. As a result some advocate to routinely biopsy the supraorbital nerve in SCCs involving the forehead and brow area in order to identify the extent of tumour infiltration and to make staging more accurate.^{5,16,17} Furthermore, in all patients with suspected or known skin malignancy in the periocular area, the clinician should assess for the possibility of PNI by careful examination of cranial nerves V and VII, as well as ocular motility.¹¹

By presenting our case, we would like to alert clinicians that a cranial neuropathy in a patient with previous history of periocular SCC, even in the absence of any positive imaging, should raise the possibility of tumour progression.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Note: Figure 2 of this article is available in colour online at www.informahealthcare.com/oph.

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