CASE REPORT

Perineural Spread in Squamous Cell Carcinoma of the Face: An Overlooked Facet of Information on Imaging

Venkatraman Bhat¹ · Jenna Devere² · Athira Ramakrishnan² · Moni A. Kuriakose²

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Abstract A case of malignant cutaneous lesion of the face diagnosed initially as sebaceous carcinoma, subsequently proven to be squamous cell carcinoma is presented. Patient was initially evaluated at an outside institution by computed tomography, which indicated extension of lesion to the maxillary sinus. Patient underwent local resection. Further imaging by magnetic resonance imaging was done for recurrent tumour. Examination revealed extensive, large volume, perineural extension of the disease via infraorbital nerve to the cavernous sinus. Patient was managed with extensive lesion resection, including the skull base component followed up by radiation. Patient showed recurrence despite aggressive management. This case highlights the crucial role of performing an optimal MR imaging of the target region, including skull base, to exclude a perineural extension, as part of assessment of oro-facial malignancy.

Keywords Perineural spread · MRI · Squamous cell carcinoma · Imaging · Infraorbital nerve · Cavernous sinus

Case report

A 40-Year-old male patient presented with the history of a small swelling on left side of the cheek of 1 year duration. Progression of swelling and associated pain led to hospital

consultation. Patient initially underwent plain computed tomography (CT) examination of the face followed by surgical excision of the lesion and radiotherapy (RT). Neck dissection was not performed at initial surgery. Persistent swelling led to re-examination by contrast enhanced CT, which showed recurrent subcutaneous lesion with suspicion of maxillary bony extension. Repeat needle aspiration of the lesion and examination of resected surgical specimen at second surgery was reported as sebaceous cell carcinoma. Patient was asymptomatic for a month, subsequently presented with burning sensation on left side of the nasal region. On clinical examination skin over the cheek showed post RT changes with scar in naso-labial area (Figure 1). Neurological examination showed the loss of sensation in the distribution of infra-orbital nerve. Corneal sensation was intact. Vision was 6/6 with direct and consensual reflexes present. Examination of all other cranial nerves was normal. Ophthalmologic evaluation revealed total ophthalmoplegia on left side. MR examination revealed extensive, poorly marginated subcutaneous soft tissue mass showing intense contrast enhancement. There was confluent extension to the infraorbital nerve with gross enlargement of the nerve. Infraorbital nerve and canal was enlarged, measuring 7–8 mm in diameter (Figure 2). Extensive tumour spread was also demonstrated to pterygopalatine fossa and to left cavernous sinus via maxillary nerve (Figure 3). Lesion appeared to involve the confluence of trigeminal nerve and adjacent mandibular division at the level of foramina ovale. However Meckel's cave appeared spared. Additional branching enhancing areas were noted in the subcutaneous soft tissues of the cheek. Craniofacial resection comprising of excision of cutaneous lesion with maxillectomy, left temporo-zygomatic craniotomy and excision of the intracranial lesion was performed. Frozen section of orbital margin intra-operatively

✉ Venkatraman Bhat
bvenkatraman@gmail.com

¹ 309, Greenwoods Apt, Royal Gardenia, Bommasandra, Bangalore 560099, India

² Department of Radiology, Head and Neck Surgery, Narayana Multispeciality Hospital and Mazumdar Shaw Cancer Centre, Bommasandra, Bangalore, India

Fig. 1 Clinical photograph of the patient demonstrates a scar at left infraorbital region. Focal areas of pigmentation, possibly induced by earlier radiation therapy are noted

did not reveal extension, hence orbital exenteration was not performed. Maxillary nerve was followed up to foramen rotundum. Selective Neck Dissection 1 through 3 was done as a part of craniofacial resection. Final staging of the tumour was T4b. Post operative concurrent chemo-radiation with focused boost radiation to skull base was done. Second pathology opinion on the resected specimen indicated moderately differentiated squamous cell carcinoma with perineural spread of the lesion. Evaluation of the specimen confirmed perineural extension around main lesion extending centrally to infraorbital nerve and

peripherally into the adjacent cutaneous nerves, which were demonstrated as enhancing branching structures around the lesion on imaging. Lymph nodes were negative for metastases. Also resected part of the orbit did not show tumour extension into the periorbital region. In view of intracranial spread with possible residual intracranial margin, patient was followed with RT. After 5 months post operative follow up revealed extension of lesion at skull base (Figure 4). Pattern of failure—intracranial extension of the tumour. Status of the patient at last follow up—Alive with the disease receiving palliative treatment.

Discussion

Many facial malignancies including squamous carcinoma and basal cell carcinoma show tendency to spread along the divisions of trigeminal nerve. [1, 2]. Reported incidence of perineural tumour spread in malignant cutaneous lesions of head ranges from 2.5 to 5.0 %, adenoid cystic carcinoma and squamous cell carcinoma, contributing to the majority [3, 4]. Trigeminal and facial nerves within the head and neck region are the nerves most commonly affected in perineural extension, in view of their extensive, intricate network and interconnectivity. Nearly half of the patients show imaging evidence of perineural spread on MR imaging [5]. Imaging evidence of perineural spread indicates poor prognosis. Especially large volume disease is known to have unfavourable outcome [4, 5]. Hence imaging with contrast-enhanced MRI is essential, while planning for management of patients with facial malignancy, to identify

Fig. 2 (A) Contrast-enhanced fat sat T1 weighted image in axial plane demonstrating a subcutaneous enhancing lesion (*arrow head*) in the left cheek. Enhancing the thick band of tissue extending to the cavernous sinus (the *open arrows*) is noted representing a perineural

spread to intracranial via infraorbital nerve. Meckel's cave appears intact (*black arrow*). (B) Coronal image showing the enlarged infraorbital nerve (*white arrow*)

Fig. 3 (A) Axial contrast-enhanced fat sat T1 image showing branching enhancing structures adjacent to the cutaneous lesion (*Long arrow*). Additionally lesion is seen along the infraorbital nerve, extending to pterygopalatine fossa (*open arrow*). (B) Coronal image

showing the component of the lesion in the cavernous sinus (*black arrow*) inferior extension to the region of foramen ovale and mandibular nerve (*white arrow*)

those needing aggressive RT. In the imaging techniques targeted MRI examination is the most optimal examination for evaluation of perineural spread. High resolution, contrast enhanced, multiplanar T1 weighted images with fat suppression techniques yield best information [4, 6, 7]. Imaging findings of significance in cases of perineural invasion include enlargement of involved nerve, obliteration of fat with and outside the nerve, obliteration of fat in the compartment where the nerve is situated and contrast enhancement of the nerve [5]. These observations are equally valid for interpretation of CT and MRI images. In a retrospective study MRI examinations had 100 % sensitivity with nearly 95 % specificity for perineural spread [6]. It should be noted that the MR examination may be negative in assessing perineural spread or examination may underestimate the extent of perineural spread. Thus an element of caution is necessary in accepting negative MR examination as a sole criterion for exclusion of perineural spread when clinical suspicion is very high.

Perineural spread of tumour has been extensively studied by imaging methods in large series [4, 7, 8]. Common tumours associated with perineural spread include squamous cell carcinoma, adenoid cystic carcinoma, mucosal epidermoid carcinoma, melanoma with desmoplastic response and lymphoma. Squamous cell carcinoma tends to have a larger number in view of a higher incidence [3]. Mechanism of perineural spread is well explained in many studies [8]. It is suggested that certain tumours play a more active role in perineural invasion. Wide variety of neurotrophic growth factors and matrix metalloproteinase's are

shown in association of cancers that exhibit perineural spread. NCAM is expressed in a large percentage of patients with adenoid cystic carcinoma, an immunoglobulin that has several functions (including adhesion, proliferation, and migration of neural cells) and is thought to play a role in perineural invasion. Role of NCAM is not well defined in squamous cell carcinoma (SCCa) [9].

Vicinity of the primary lesion to the major regional nerve dictates the likely pattern of spread and final intracranial extension. Understanding of this anatomical concept is essential for interpretation of the image. Failure to consider this possibility in the initial management, can lead to inadequate treatment with undesirable recurrence. Complete network of the nerve should be critically evaluated in imaging studies. Another important observation in our case is the perineural extension of the disease proximally as well as the distally. Cranial (or central) extension is easily evaluated with radiological technique, while extension more peripherally (distally), is not clearly detectable on imaging. Underestimating perineural extension and inadequate surgical measures in achieving total extirpation of the lesion invariably leads to lesion recurrence. Our case highlights this gap of disease under staging, in the initial evaluation, leading to improper management and unfavourable outcome. CT imaging, though useful in the evaluation of bony and lymph-nodal involvement, but fails to delineate perineural tumour spread optimally. Role of PET/CT in the imaging of perineural spread is highlighted recently [8]. However higher special resolution and superior sensitivity of MRI

Fig. 4 Coronal (A) and sagittal (B) contrast enhanced T1 W post operative MRI images after 5 month follow up show significantly increased enhancing tumour (*open arrows*) at para-sellar region and at infra-temporal fossa (*star*)

technique, is likely to favour MR techniques over others, in the imaging perineural tumour spread.

Conclusion

A case of squamous cell carcinoma of the facial region with perineural spread is presented. Conflicting pathology report and inappropriate choice of imaging methods of evaluation, lead to unsatisfactory management of the patient at initial presentation. Followup examination demonstrated the local tumour recurrence and extensive perineural spread of tumour to the cavernous sinus via the branches of trigeminal nerve. Imaging appearance of tumour spread is highlighted by MR techniques. Importance of choosing proper imaging technique, appreciating subtle, early changes of nerve involvement and awareness of region specific pathways of the tumour dissemination is highlighted.

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