

# Symptomatic perineural and intraneural invasion of the trigeminal nerve and subsequent abducens nerve palsy by cutaneous squamous cell carcinoma

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## Abstract

A 74-year-old woman who presented initially with trigeminal neuralgia of the left forehead and scalp was later found to have a poorly differentiated squamous cell carcinoma (SCC) with large-nerve perineural and intraneural invasion of the left supraorbital nerve. Negative histopathologic margins were achieved in three stages of permanent fixed tissue en face processing and the final defect was repaired with a large rotation flap. Approximately one month after repair, the patient presented with new-onset diplopia and was found to have a complete left cranial nerve VI palsy suspicious for continued disease spread. MRI confirmed perineural spread along the ophthalmic branch of the trigeminal nerve through the superior orbital fissure into the cavernous sinus. She was subsequently treated with radiation therapy (66Gy in 33 fractions). The involvement of two distinct cranial nerves by perineural invasion is uncommon and has mostly been described involving branches of the trigeminal and facial nerves. This case highlights the rare presentation of perineural invasion involving both the trigeminal nerve and the abducens nerve. Anatomically, this clinical presentation can be explained by the retrograde perineural spread along the ophthalmic branch of the trigeminal nerve through the supraorbital fossa into the cavernous sinus where these two nerves are in close proximity.

*Keywords: abducens nerve, carcinoma, perineural invasion, spread, squamous cell, trigeminal*

## Introduction

Perineural invasion (PNI) describes the spread of tumor cells into the perineural space that surrounds a peripheral nerve. The presence of PNI in cutaneous squamous cell carcinoma portends a worse prognosis with increased risk of local recurrence and metastasis [1]. Involvement and dysfunction of two cranial nerves by PNI is rare. We present a unique case of trigeminal nerve dysfunction and abducens nerve palsy caused by perineural spread of a primary cutaneous squamous cell carcinoma arising on the forehead.

## Case Synopsis

A 74-year-old woman presented to dermatology clinic with a 2.4cm×1.9cm ulcerated plaque of the left forehead that had been present and growing for the past two years (**Figure 1**). Prior to presentation she had been diagnosed with trigeminal neuralgia due to a 6-month history of numbness of the left forehead and frontal scalp with intermittent sharp shooting pain that did not improve with gabapentin.

A punch biopsy of the ulcerated lesion was performed, which revealed a poorly differentiated squamous cell carcinoma. The patient was referred for Mohs surgery. Following stage I of Mohs surgery, histopathologic examination of the margins revealed small nests of atypical squamous cells infiltrating the dermis, subcutaneous fat, and muscle with extensive PNI of multiple nerves with the largest



**Figure 1.** Erythematous 2.4cm x 1.9cm scar-like plaque with focal ulceration on the left forehead seen at initial presentation.

measuring 0.21 mm in diameter. Due to the extensive PNI and difficulty in interpreting the extent of tumor spread on frozen section, a second stage was taken and submitted for permanent fixed tissue en face processing.



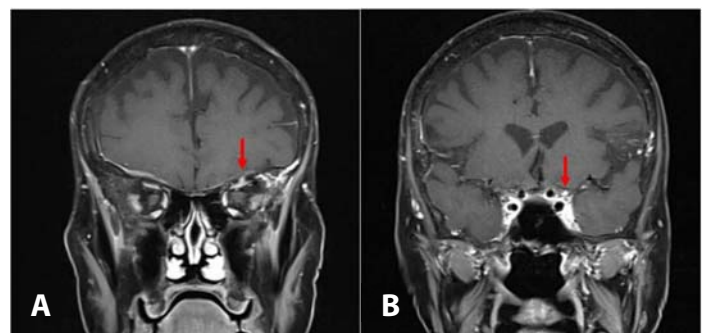
**Figure 2.** H&E histopathology showing perineural (black arrows) and intraneural (red arrows) invasion of squamous cell carcinoma involving a large-caliber nerve within subcutaneous adipose, 100x.

Histopathologic examination of the margins revealed residual perineural and intraneural invasion along with tumor invasion of fat and muscle (Brigham and Women's Hospital Tumor Staging System T3), (**Figure 2**). Given the extent of PNI on histopathology, computed tomography (CT) and magnetic resonance imaging (MRI) of the head and neck were obtained. No adenopathy or persistent PNI were appreciated on imaging.

A third stage was taken which achieved negative histopathologic margins and the final defect was repaired with a bilateral forehead rotation flap. Despite negative histologic margins, the patient's paresthesia and pain persisted postoperatively.

Approximately one month after repair, the patient presented with new-onset diplopia and was found to have a complete left abducens nerve (CNVI) palsy suspicious for continued perineural spread. Repeat MRI showed progression of perineural spread along the ophthalmic branch of the trigeminal nerve through the superior orbital fissure into the cavernous sinus (**Figure 3**). The patient was subsequently treated with radiation therapy (66Gy split into 33 fractions) with the goal of complete locoregional control.

At most recent follow up, approximately 6-months after completing radiation therapy, the patient's disease appeared clinically and radiologically controlled. However, she has not regained function of her left abducens nerve and requires full time occlusion of her left eye to control her diplopia. Return of function of the abducens nerve is not



**Figure 3. A)** Abnormal enhancement of the ophthalmic branch of the trigeminal nerve (red arrows) as it passes through the orbit, and **B)** asymmetric fullness within the cavernous sinus seen on MRI.

expected and her left lateral rectus muscle appears atrophied on examination.

## Case Discussion

Perineural invasion that becomes symptomatic or detectable on imaging is considered clinical PNI. The presence of clinical PNI carries a much worse prognosis compared to incidental PNI and necessitates more aggressive treatment often including adjuvant radiotherapy that incorporates the involved nerve territory [1]. The most commonly affected nerves in clinical PNI are the trigeminal (CNV) and facial (CNVII) nerves due to their widespread distribution over the head and neck [2,3]. Clinical PNI typically presents with sensory deficits; specifically, numbness/anesthesia, paresthesia, formication, and neuropathic pain such as allodynia or hyperalgesia [4]. When motor nerves are involved, it typically manifests as weakness or paresis. Sensory deficits typically precede motor deficits [4]. Early in the disease course these signs and symptoms are often misinterpreted as benign conditions such as trigeminal neuralgia and Bell palsy [2,4]. Perineural invasion, even when symptomatic, is often difficult to detect radiologically until it has spread beyond cranial foramina [2].

## References

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The majority of clinical PNI presentations involve a single cranial nerve. However, when more than one cranial nerve is involved the most common nerves are CNV and CNVII, due to their widespread distribution and frequent anastomoses [2-4]. Abdul-Hussein et al. described a case of adenoid cystic carcinoma with PNI leading to cranial nerve palsies of both CNV and CNVI [5]. There are scant reports of cutaneous squamous cell carcinoma with clinical PNI affecting cranial nerves controlling extraocular muscles [4].

## Conclusion

To our knowledge, this is the first described case of cutaneous squamous cell carcinoma with PNI involving both the trigeminal and abducens nerves. Anatomically, this clinical presentation with involvement of both the ophthalmic distribution of CNV and CNVI can be explained by the retrograde perineural spread through the superior orbital fissure into the cavernous sinus where these two nerves are in close proximity [3,5].

## Potential conflicts of interest

The authors declare no conflicts of interest.