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Slowly progressive facial paralysis: Intraneural squamous cell carcinoma of unknown primary

Michael Eggerstedt[a], Hannah N. Kuhar[b], Peter C. Revenaugh[a], Ritu Ghai[c], R. Mark Wiet[a,*]

[a] Department of Otorhinolaryngology, Head and Neck Surgery, Rush University Medical Center, 1611 W. Harrison St., Suite 550, Chicago, IL 60612, United States of America
[b] Rush University Medical Center – Rush Medical College, 600 S Paulina St, Chicago, IL 60612, United States of America
[c] Department of Pathology, Rush University Medical Center, 1750 W. Harrison St., Suite 570, Chicago, IL 60612, United States of America

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ABSTRACT

Background: In this report, we present a unique case of intraneural squamous cell carcinoma of unknown primary found within the facial nerve and the proposed algorithms for diagnosis and management of progressive idiopathic facial paralysis.

Case presentation: A 66-year-old female with a previous history of basal cell carcinoma presented with right-sided progressive facial paralysis. Repeated magnetic resonance imaging as well as targeted workup failed to reveal a diagnosis. 20 months following symptom onset, after the patient's facial function slowly progressed to a complete paralysis, repeat magnetic resonance imaging revealed enhancement at the stylomastoid foramen. The patient underwent superficial parotidectomy, transmastoid facial nerve decompression and resection of descending and proximal extratemporal facial nerve segments, as well as great auricular nerve interposition grafting. Intraoperatively, frozen sections from the surface of the facial nerve, and the proximal and distal segments of the facial nerve following resection, were negative for malignancy. The final pathology revealed infiltrating poorly differentiated squamous cell carcinoma of the facial nerve with negative margins.

Conclusion: In cases of slowly progressive facial paralysis the clinician needs to consider malignancy until proven otherwise. Without an identifiable primary malignancy, early algorithmic assessment of presenting characteristics may facilitate expedited clinical decision making and surgical management of malignancy involving the facial nerve. In cases of slowly progressive facial paralysis, when the time comes for surgical exploration and biopsy, head and neck surgeons must be aware that malignancy can exist entirely within the facial nerve, without pathologic changes on the surface of the nerve or in the surrounding tissue.

1. Introduction

While Bell's palsy remains the most common cause of peripheral facial nerve paralysis, neoplasms that invade the facial nerve may manifest similarly as acute or subacute paralysis [1]. In rare cases, normal clinical and imaging findings are found in patients with unilateral facial paresis secondary to occult malignancy affecting the facial nerve [2]. Here, we report an unusual case of intraneural squamous cell carcinoma of unknown primary causing progressive facial nerve palsy.

2. Materials and methods

Approval for this retrospective case report and review of the literature was granted by the appropriate Institutional Review Board. All protected health information was de-identified by the primary author (ME) up front and stored on encrypted hard drives behind a locked door.

3. Results

3.1. Case presentation

A 66-year-old white female with a previous history of multiple basal cell carcinomas presented with right-sided progressive facial paralysis. Her symptoms began 12 months prior to presentation with onset of numbness in the right malar distribution, asymmetry of the smile, and twitching of the right eye. Magnetic Resonance Imaging (MRI) at the time showed no brain, skull base, or extratemporal pathology. Her

* Corresponding author.
E-mail addresses: Michael_Eggerstedt@rush.edu (M. Eggerstedt), Hannah_Kuhar@rush.edu (H.N. Kuhar), Peter_Revenaugh@rush.edu (P.C. Revenaugh), Ritu_Ghai@rush.edu (R. Ghai), Richard_Wiet@rush.edu (R. Mark Wiet).

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symptoms remained stable on gabapentin, prescribed by her neurologist, until 3 months prior to presentation, when she began to experience subtle ectropion of the right lower eyelid, epiphora, and progression of right-sided hemifacial paresthesias.

On presentation to the otorhinolaryngology clinic, the patient demonstrated weakness of the right orbicularis oris and orbicularis oculi with intact eye-closure. Physical examination of the ears, head and neck was otherwise normal, with no additional cranial nerve deficits. There was no evidence of cutaneous pathology on examination of the skin of her head and neck. Repeat MRI of the internal auditory canals (IAC) showed no abnormal enhancing lesions along the course of the facial nerve.

The patient re-presented 3 months later, 15 months from the onset of her symptoms, with progressive weakness in all divisions of the facial nerve, and was unable to close her right eye. MRI of the temporal bone again showed no definite abnormality along the course of the facial nerve. Lyme titers were found to be within normal limits.

5 months later, 20 months following the onset of her symptoms, the patient had complete paralysis of the right face. Computed Tomography (CT) of the chest demonstrated pulmonary hilar nodules with non-necrotizing granulomas concerning for sarcoidosis. High-dose steroid immunosuppression provided no improvement of function. Electromyography (EMG) and electroneuronography (EnoG) demonstrated complete denervation of the right face. Her fourth repeat MRI IAC demonstrated subtle enhancement of the facial nerve at the stylomastoid foramen, extending into the parotid gland. The patient elected to undergo facial nerve exploration, consisting of superficial parotidectomy and transmastoid resection of the descending and proximal extratemporal facial nerve segments. She was offered hypoglossal-facial nerve anastomosis as well as other reconstructive options, and elected to undergo great auricular nerve interposition grafting at the time of resection. The intraoperative appearance of the facial nerve at the stylomastoid foramen appeared as normal fibrous tissue.

Intraoperatively, frozen sections from the surface of the facial nerve, and the proximal and distal segments of the facial nerve following resection, were negative for malignancy. Final pathology revealed entirely intraneural, infiltrating, poorly-differentiated squamous cell carcinoma (SCC) along the endoneurium of the stylomastoid segment of the facial nerve with bookends of normal facial nerve tissue and no evidence of extraneural invasion along its length (Figs. 1, 2). A suspicious lymph node was sampled intraoperatively from level IIb within the neck, which was benign.

Postoperatively, positron electron tomography (PET) imaging showed no suspicious avidity and comprehensive dermatologic evaluation revealed no cutaneous malignancy. The patient received carboplatin-paclitaxel chemotherapy and 64 Gy radiation to the postoperative bed. At her most recent follow-up and nearly four years after initial presentation, the patient has remained without evidence of disease.

4. Discussion

Past reports have described facial nerve palsy secondary to perineural spread most commonly in the context of primary head and neck squamous cell carcinoma [3,4]. Suggested algorithms for the management of suspected neoplasm-induced facial paralysis have called for imaging of the parotid gland and temporal bone after four months of symptoms, and facial nerve biopsy after seven months of symptoms, though an algorithm has not been agreed upon [5]. In cases of progressive unilateral facial nerve palsy without identified clinical or imaging pathology, a history of pain or regional skin cancer, involvement of other cranial nerves, and prolonged facial paralysis have been identified as indications for facial nerve exploration [2]. Other authors have identified the absence of hearing loss and presence of facial paresthesias as two factors suggestive of extra-temporal malignant lesions requiring early surgical management [4].

This patient had no history of primary squamous cell carcinoma of the head and neck and experienced progressive facial nerve paralysis with paresthesia and preservation of hearing. Differential diagnoses included infectious etiologies such as Lyme disease, autoimmune etiologies such as sarcoidosis, and malignant lesions such as parotid tumor or temporal bone carcinoma. Early imaging, blood work and biopsy assisted in ruling out infectious and autoimmune etiologies. In the absence of identifiable primary squamous cell carcinoma, early systematic assessment of presenting characteristics and a high index of suspicion may facilitate expedited imaging, clinical decision-making, and surgical management of malignancy as a cause for facial nerve palsy of unknown origin.

In 2004, Boahene and colleagues published their series of 15 patients with facial nerve paralysis secondary to occult malignancy [2]. Greater than 50% of their patients had no history of regional skin cancer, the time to total paralysis varied from 6 h to 21 months. The median time point at which patients underwent surgical exploration was 12 months, with the earliest being 2 months and the latest being 180 months. The group recommended nerve exploration at 6 months in patients that are at higher risk for occult malignancy. Preoperatively, these patients must be counseled that the exploration may yield no new diagnostic information, as was the case in 2 of their 15 patients. In turn, to reduce the incidence of false-negative exploration the surgeon should be prepared to explore the entire intratemporal and extratemporal segments of the facial nerve. Two of their patients had false negative initial explorations, but then had positive nerve biopsy specimens on repeat exploration [2].

A difficult intraoperative decision presents itself when considering whether or not to biopsy a nerve which appears grossly normal. Some have recommended that when there is no history of regional skin cancer, and the nerve appears normal, biopsy may be deferred, and the patient can be followed with repeat imaging and examination. In our case this may have allowed interval progression of the patient's disease.

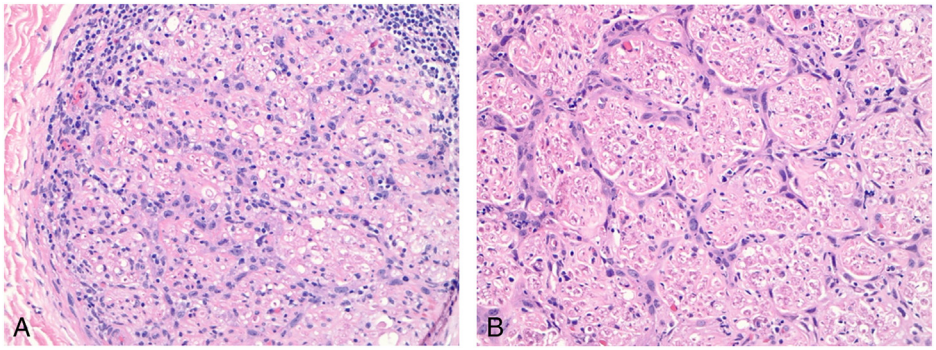

Fig. 1. Fig. 1 demonstrates hematoxylin and eosin-stained cross sections of the facial nerve at the stylomastoid foramen with preserved surrounding epineurium. Fig. 1A (left) is low magnification (10×) and the tumor cells are seen as cords with large atypical nuclei. Fig. 1B (right) is higher magnification (20×) and highlights the distinctly squamous cell differentiation infiltrating along the perineurium.

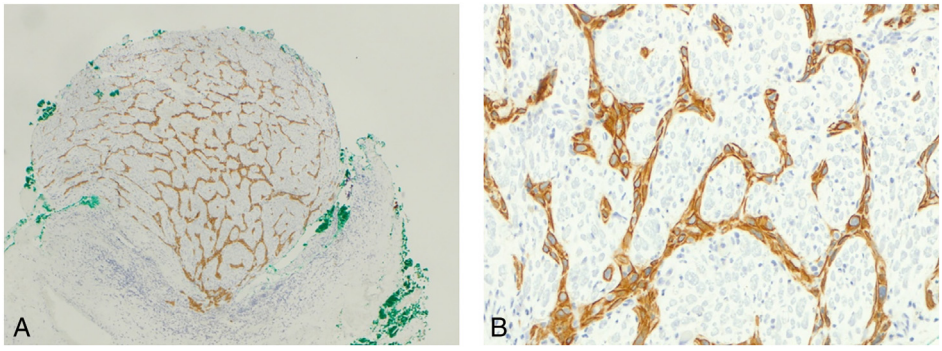

Fig. 2. Fig. 2 demonstrates cross-sections of the facial nerve with an immunostain against cytokeratin 5, highlighting the cytoplasm of tumor cells from squamous lineage. Fig. 2A (left; 10× magnification) demonstrates the squamous cell carcinoma cells confined to the axis of the facial nerve without violation of the epineurium. Fig. 2B (right; 20× magnification) demonstrates cytoplasmic staining of the tumor cells with cytokeratin 5, supporting squamous differentiation.

5. Conclusions

In cases of slowly progressive facial paralysis the clinician needs to consider malignancy until proven otherwise. Without an identifiable primary malignancy, early algorithmic assessment of presenting characteristics may facilitate expedited clinical decision making and surgical management of malignancy involving the facial nerve. Intraoperative anatomic appearance of our patient's facial nerve was normal, and frozen sections from the surface of the facial nerve, and the distal and proximal segments of the facial nerve, were negative for malignancy. In this particularly unusual case, only the final pathologic review revealed entirely intraneural infiltrating poorly differentiated squamous cell carcinoma of unknown origin involving the facial nerve at the stylomastoid foramen. Additionally, bookends of normal neural tissue lay on either side of the involved nerve. In cases of slowly progressive facial paralysis, when the time comes for surgical exploration and biopsy, head and neck surgeons need to be aware that malignancy can exist entirely within the facial nerve, without pathologic changes on the surface of the nerve or in the surrounding tissue.

Abbreviations

MRI	Magnetic Resonance Imaging
IAC	Internal auditory canals
CT	Computed tomography
EMG	Electromyography
EnoG	Electroneuronography
SCC	Squamous cell carcinoma
PET	Positron electron tomography

Declarations of interest

None.

Sources of funding

None.

Ethics approval and consent to participate

This project was approved by the IRB of Rush University Medical Center.

Consent for publication

Not applicable.

Availability of data and material

The data for this study are available through the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Michael Eggerstedt, conception of design, drafting of work, critical revision; Hannah N. Kuhar, drafting of work, acquisition of data, critical revision; Peter Revenaugh, critical revision and final overview; Ritu Ghai, acquisition of data and conception of design, R. Mark Wiet, critical revision, conception of design, final overview.

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