Factors Leading to Oro-Facial Herpetic Eruptions in Patients Undergoing Surgery for Vestibular Schwannoma

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■ OBJECTIVE: **To study factors influencing oro-facial herpetic eruptions (HEs) in patients undergoing retromastoid suboccipital craniectomy for vestibular schwannomas (VS).**

■ METHODS: **A retrospective analysis of the prospectively collected database (from July 2014 to December 2015). A total of 87 patients underwent retromastoid suboccipital craniectomy for VS at our center. For the purpose of analysis the patient subset was divided into 2 groups, HE and non-HE. Pearson χ^2 test or Fisher exact test were used to identify the factors.**

■ RESULTS: **The overall incidence of postoperative HE was less than 1% (0.89%, 26 patients of 2916 cases); whereas after VS surgery, it was 20.69% (18 of 87). Demographic profiles of patients in the 2 groups were comparable. Average tumor size (with HE 3.19 $\pm$ 2 $\times$ 0.67 cm, non-HE 3.38 $\pm$ 2 $\times$ 1.07 cm), consistency, and laterality also were comparable between the 2 groups. Factors favoring development of postoperative HEs were large size (12 vs. 22, $P = 0.013$) and preoperative trigeminal nerve (CN V) involvement (9 of 18, 50%, $P = 0.046$). All patients developed HE in maxillary division of trigeminal nerve (V2), whereas involvement of ophthalmic (V1) and mandibular (V3) divisions were involved less commonly in combination with V2 (V2, 72.2%; V2 + V3, 22.2%; V1 + V2 + V3, 5.6%). The majority of the patients (55.56%) developed HE on postoperative day 3 and none beyond postoperative day 5. All patients responded to empirical oral acyclovir.**

■ CONCLUSIONS: **The study highlights the relatively high incidence and factors associated with this rare but benign complication.**

INTRODUCTION

Reactivation of latent herpes simplex virus (HSV) is not uncommon after microvascular decompression (MVD) of trigeminal neuralgia (TN), with an incidence of cutaneous herpetic eruptions (HEs) reported from 38% to 94%.[1-4] A similar observation in patients undergoing retromastoid suboccipital craniectomy (RMSO) for vestibular schwannoma (VS) is infrequent, however; reactivation of herpes leading to oro-facial HE and herpetic encephalopathy rarely has been reported.[5-7] Herpetic reactivation (leading to oro-facial eruption and rarely encephalopathy) can be triggered by a variety of stimuli, such as fever, ultraviolet radiation, menstrual cycle, or emotional stress. Another important factor is direct surgical manipulation of the trigeminal nerve during posterior fossa surgeries, with a majority of cases seen in patients undergoing trigeminal rhizotomy and MVD for TN[2,4,8-10] and few case reports after RMSO for VS.[6,7] Our study is an attempt to describe the clinicoradiologic features of patients who develop oro-facial HE after RMSO for VS and identify factors, if any, that predict such occurrence.

MATERIALS AND METHODS

A retrospective analysis of a prospectively maintained database during a period of 18 months from July 2014 to December 2015 was

Key words
- Oro-facial herpetic eruption
- Retromastoid suboccipital craniectomy
- Vestibular schwannoma

Abbreviations and Acronyms
CN: Cranial nerve
HE: Herpetic eruption
HSV: Herpes simplex virus
MVD: Microvascular decompression
NHE: Nonherpetic eruption
POD: Postoperative day
RMSO: Retromastoid suboccipital craniectomy
RT: Ryle's tube
VS: Vestibular schwannomas

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performed. A total of 87 patients (consecutive patients with VS who underwent RMSO for VS) with radiologically and histopathologically confirmed VS were included in the study.

Patients' demographic data and clinical presentation were recorded from the indoor files (patient's record while the patient was admitted at our center). Cranial nerve (CN) deficits and other symptoms caused by VS were recorded in detail in the preoperative as well as in the postoperative period (on the first postoperative day [POD], the patient was assessed for any change in the neurologic findings including cranial nerves compared with the preoperative status). Trigeminal nerve (CN V) involvement due to compression of nerve by mass lesion (VS) was assessed as graded facial hypoesthesia in facial distribution of CN V compared with the contralateral normal side, reddening of eyes/decreased lacrimation and impaired corneal reflex (for sensory root), and difficulty in mastication or wasting of temporal/masseter muscle (for motor root). A specific note of comorbidities such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, tuberculosis, etc., or any history suggestive of immunosuppression (steroid intake, human immunodeficiency virus infection, solid organ transplantation, etc.) and history of HEs were recorded. A need for preoperative cerebrospinal fluid diversion (external ventricular drain or shunt placement) for increased intracranial pressure, Ryle's tube (RT) feeding, and tracheostomy placement was noted.

All patients underwent preoperative evaluation comprising a neuro-otological evaluation with pure tone audiometry and radiologic evaluation with contrast-enhanced magnetic resonance imaging. Tumor size was recorded as the largest extent in axial, coronal, and sagittal planes; based on the size (largest diameter in any axis), the tumor was graded as intracanalicular (less than 1 cm), small (1–2 cm), medium (2–3 cm), large (3–4 cm), and giant (larger than 4 cm). Vertical distance between superior margin of tumor and tentorium cerebelli was measured in a sagittal cut.

All patients with VS underwent RMSO and tumor excision (microscopic or endoscopic). None of the patients in our study underwent middle fossa or translabyrinthine approach for the excision of VS. Intraoperative events (relationship with VII–VIII nerve complex, involvement of CN V by tumor thereby requiring operative manipulation, and lower cranial nerves involvement by tumor and operative handling) and postoperative course were recorded. Intraoperative facial nerve monitoring was used in all cases. Endotracheal tube fixation was done on side opposite to the tumor so that it did not interfere with facial nerve monitoring.

Patients were evaluated postoperatively to assess for new-onset hearing loss/deterioration, worsening of facial asymmetry, and new-onset/worsening facial hypoesthesia. Postoperative contrast-enhanced computed tomography was performed within 6–24 hours of surgery in all patients to look for the extent of surgical resection and postoperative complications, if any, such as operative cavity hematoma, peumocephalus, brainstem edema, and change in ventricle size.

Postoperative oro-facial eruption was defined as "occurrence of oro-facial eruptions within 30 days of surgery for VS." HE was defined as "a prodrome of pain, burning and tingling at the site followed by the development of erythematous papules that rapidly developed into tiny, thin-walled intraepidermal vesicles that become pustular and ulcerate."[11] The day of oro-facial HE, pattern of eruption (vesicular, nodular, ulcerative), and involved CN V dermatome along with duration of eruption were noted.

The diagnosis of oro-facial HE was based on clinical findings mentioned previously. All the patients who developed facial eruptions were referred to dermatologist affiliated with our institute. Patients who developed oro-facial HEs (based on clinical findings and diagnosis made by dermatologist) were treated with acyclovir tablets (200 mg) 5 times day for 1 week. Response to treatment was evaluated with clinical parameters (reduction/resolution of fever, malaise, and facial pain), loss of lesion crust, and reduction of the size of the area of the lesion between days 1 and 5.[12] If patients did not show any improvement or had the appearance of new lesions even after 5 days of antiviral therapy, serological examination of scrapings from the lesion was planned.

For the purpose of analysis, patients were divided into 2 groups: a HE and nonherpetic eruption (NHE) group based on whether they developed oro-facial HE in the postoperative period. The 2 groups were compared to identify factors associated with development of postoperative oro-facial HEs. This study was approved by our institutional ethics committee.

Statistical Analysis

To test the association between variables, Pearson χ^2 test or the Fisher exact test were used. The risk (odds ratio) was calculated with univariate logistic regression model, and P values less than 0.05 were considered to be statistically significant. Statistical analysis was done with SPSS, version 20 (IBM Corp., Armonk, New York, USA). In our study, test for normalcy was not applied because our study population comprised consecutive cases.

RESULTS

A total of 2916 (1986 cranial and 930 spinal) patients underwent different neurosurgical procedures at our institute during the study period. Incidence of postoperative HE was less than 1% (0.89%; 26 patients of 2916 cases). After RMSO, however, the incidence was 16.55% (23 of 139 cases); of these, 20.69% (18 of 87) patients were operated for VS and 25% (4 of 16) underwent MVD for TN. One patient (2.78%, 1 of 36 cases) developed HE after RMSO for CPA epidermoid. One patient developed HE after craniotomy for supratentorial glioma (0.05%, 1 of 1847 craniotomy procedures). Two patients developed HE after spinal surgery (0.22%; 2 of 930 spinal surgeries).

Eighty-seven patients underwent surgery for VS during our study period. Oro-facial HE was seen in 20.69% (18 of 87) of patients. The demographic profile of patients in the 2 groups (HE vs. NHE) was comparable without any statistically significant differences, although the majority of patients with oro-facial HE were women (61.1% of HE vs. 39% of NHE, $P = 0.114$). The mean age of patients in HE group was 37.17 years compared with 42.56 years in NHE group (**Table 1**).

Twenty patients had type 2 diabetes mellitus (3 HE and 17 NHE, $P = 0.513$), and 7 patients received steroids preoperatively (1 HE vs. 6 NHE, $P = 0.804$). There was no significant difference observed between the 2 groups as per these factors were concerned. History of HE (3 HE vs. 1 NHE, $P = 0.027$) was significantly more common in HE group. The majority of the patients in the 2 groups