

**LETTERS TO THE EDITOR****TO THE EDITOR****Endoscopic Associated Iatrogenic Terson's Syndrome**

Terson's syndrome has traditionally been associated with subarachnoid hemorrhage. Litten first described it in 1881, noting intra-retinal hemorrhage associated with subarachnoid hemorrhage. Later, in 1900, Terson described vitreous hemorrhage following subarachnoid hemorrhage. His name subsequently became associated with this syndrome. Case reports of the association of raised intracranial pressure with intra-ocular hemorrhages in the absence of subarachnoid hemorrhage have more recently emerged<sup>1-3</sup>. We describe the case of a 46-year-old with a colloid cyst who developed intra-ocular hemorrhages following an acute episode of raised intracranial pressure intra-operatively during a neuro-endoscopic attempt at surgical resection.

**CASE REPORT****Clinical presentation**

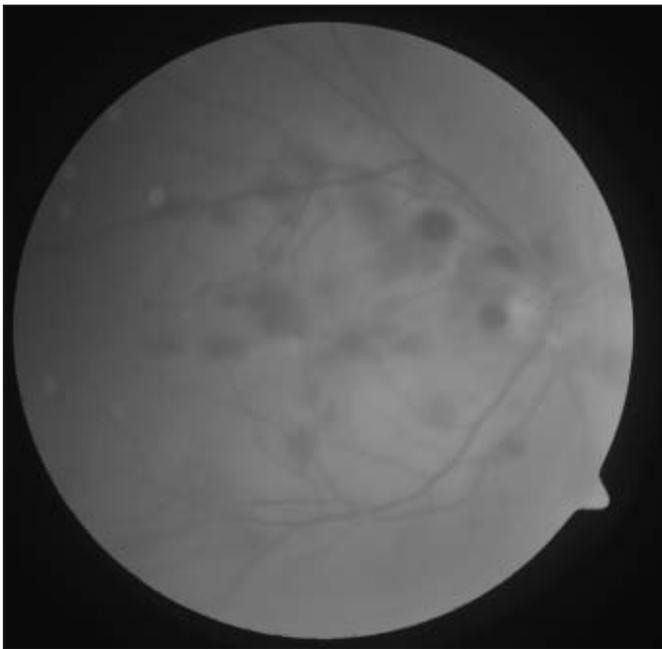
A 46-year-old male, previously healthy, presented to a community hospital with a history of headaches and diplopia. Neurological examination was normal. Magnetic resonance imaging revealed an intraventricular cyst in the region of the anterior roof of the third ventricle. Neurosurgical consultation was sought and a decision was made to proceed with endoscopic surgical resection. Pre-operative anesthesia assessment noted a 30-pack year smoking history, symptoms consistent with obstructive sleep apnea and an exercise tolerance of greater than

4 metabolic equivalents. Surgical history included previous L4-5 discectomy, appendectomy and tonsillectomy with no reported difficulties with anesthesia.

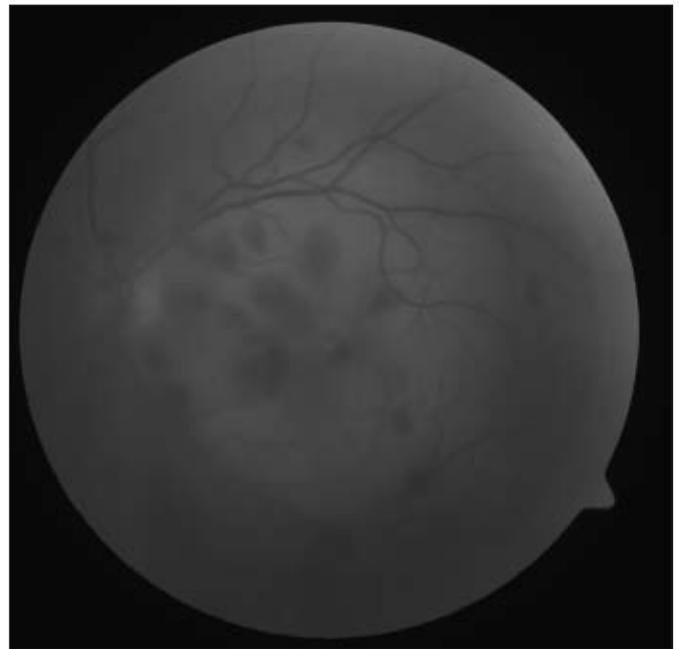
**Surgery**

The surgical procedure, an image-guided left frontal ventriculoscopy proceeded. Standard monitors were applied including a radial arterial line. Initial recorded blood pressure was 140/75. General anesthesia was induced with midazolam, remifentanyl, propofol and rocuronium. He was intubated with an 8.0-cuffed endotracheal tube under direct laryngoscopy on first attempt with a grade 3 view of the larynx. The patient was positioned supine with his head fixed in a Mayfield. Mayfield pinning was tolerated with minimal hemodynamic response. Monitoring parameters remained stable with blood pressure averaging 120/60, heart rate range 65-75/minute, central venous pressure 5-7 mm Hg and oxygen saturation 98-99%. Unfortunately, the usual endoscopic equipment that the surgeon preferred was contaminated just prior to use and after a short delay another endoscope (different model) was brought in.

The endoscope was introduced with image guidance. The ventricles were noted to be extremely narrow and collapsing around the endoscope. Irrigation was initiated and shortly thereafter a precipitous rise in blood pressure and bradycardia was noted. Peak systolic blood pressure was 260/120 with the heart rate dropping to the low 50's. Anesthesia immediately notified the neurosurgical team of this significant hemodynamic change, clearly a Cushing response to acutely elevated



**Figure 1:** Digital Fundoscopy demonstrating vitreous and retinal hemorrhages (Right eye)



**Figure 2:** Left eye

intracranial pressure. Irrigation ceased and the endoscope was removed, as the outflow of fluid was exceptionally slow. A ventriculostomy catheter was promptly inserted with backflow of cerebrospinal fluid under high pressure and hemodynamic parameters quickly normalized. The surgical procedure was aborted. The patient was awakened, extubated and transferred to the recovery room. He remained hemodynamically stable in the immediate post-operative period.

### Postoperative course

The patient complained of a red haze in bilateral visual fields and his wife noted him to have some difficulty with his memory on the first post-operative day. He was found to have reduced visual acuity and impaired short-term memory (mini mental state exam 24/30) on clinical assessment. Ophthalmology was consulted and he was diagnosed with Terson's syndrome [Figure 1 and 2]. Bilateral retinal and left vitreous hemorrhages were noted. Corrected visual acuity was 20/50(right) and 20/70(left). Intraocular pressures were 12 mmHg in both eyes. His visual acuity and short-term memory improved at a one-month follow-up visit (right eye 20/30, left eye 20/40, mini mental state exam 30/30). Three months later, the patient underwent an open surgical procedure (a right interhemispheric, transcallosal approach), with successful resection of the colloid cyst.

### DISCUSSION

This case report highlights a potentially serious complication of neuro-endoscopy. We describe an acute elevation in intracranial pressure resulting in a case of iatrogenic Terson syndrome. This patient also developed transient short-term memory impairment, likely from distension of the fornices.

The pathophysiology of Terson's syndrome has been controversial since its first description. It is currently accepted that intraocular hemorrhages are attributed to the sudden increase of intracranial pressure that is transmitted to the optic nerves due to the communication of the subarachnoid space within the optic nerve sheath. It results in compression and obstruction of the retinal vein and retinohoroidal anastomoses causing a precipitous rise in intraocular venous pressure with subsequent distension and rupture of retinal capillaries<sup>4,5</sup>.

Several factors contributed to increased intracranial pressure in this particular case. Patient factors included small and relatively non-compliant ventricles. Less than optimal or familiar equipment also played a role with apparent malfunctioning or obstruction of the outflow tract. This was likely the most significant factor rendering an imbalance in inflow and outflow of irrigation fluid and resulting in a near-catastrophic elevation in intracranial pressure.

Early recognition, effective team communication and appropriate intervention limited the damage, though was not adequate to prevent the subsequent complications of intraocular hemorrhage and transient memory impairment.

A few case reports of iatrogenic Terson's syndrome have appeared in the literature in recent years. We present our experience to increase the awareness of this risk specific to neuro-endoscopy. Hoving et al reported bilateral retinal hemorrhage after endoscopic third ventriculostomy<sup>2</sup>. Boogaarts reported Terson's syndrome after endoscopic colloid cyst removal<sup>1</sup>. Elevated intracranial pressure related to intra-

operative technical issues is identified as the causative factor in all of these cases.

### CONCLUSION

We report a case of iatrogenic Terson's syndrome and transient short-term memory impairment following a neuro-endoscopic attempt at resection of an intra-ventricular colloid cyst. Patient and equipment factors were key contributors to an acute elevation of intracranial pressure. We hope that highlighting these factors raises awareness of this potentially significant complication, and reduces the likelihood of it occurring by careful patient selection, early recognition, and intervention when it does arise.

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## TO THE EDITOR

**Clinically Silent Posterior Reversible Encephalopathy in Guillain-Barré Syndrome**

Posterior reversible cerebral vasoconstriction syndrome (PRES) is a clinicoradiologic syndrome characterized by headache, encephalopathy, visual disturbances and seizures, associated with a transient vasogenic oedema predominantly located in the posterior circulation system on brain imaging.<sup>1</sup> The most frequent aetiologies include hypertension, eclampsia, cytotoxic or immunosuppressive drugs, and sepsis.<sup>2</sup> Some cases of PRES have been described in association with Guillain-Barré syndrome (GBS).<sup>3</sup> Here we report the case of a woman who presented with a GBS, dysautonomia, and an asymptomatic incidental finding on brain magnetic resonance imaging (MRI) suggestive of PRES, but without any encephalic symptom suggestive of that syndrome.

## CASE REPORT

A 67-year-old woman with a one week history of limb paresthesia was admitted with moderate neck pain followed by sudden tetraparesis. Neurological examination revealed flaccid weakness in all four limbs and no cranial nerve involvement. Cervical spinal cord MRI revealed no spinal cord abnormalities but led to the incidental discovery of clinically silent PRES (Figure).

The patient's cerebrospinal fluid revealed albuminocytologic dissociation with a protein level of 67 mg/dl and a normal cell count and normal glucose. Nerve conduction studies and electromyography were also consistent with the diagnosis of GBS and she was treated with intravenous immunoglobulin. Serology was negative for HIV, hepatitis B and C, *Mycoplasma pneumoniae*, *Borrelia*, *Chlamydia*, syphilis, Epstein-Barr virus and Cytomegalovirus. Wide fluctuations of blood pressure occurred over the following days despite continuing antihypertensive medication and a transient episode of altered mental functions was observed. However, she did not develop headache, seizure or visual disturbance and brain MRI abnormalities rapidly resolved.

## DISCUSSION

This case description focuses on the MRI features of PRES, but yet not fulfilling the clinical definition of this syndrome. Indeed, a transient alteration of mental function does not qualify. One could argue that the term "clinically silent PRES" to describe this case is a misnomer without the appropriate clinical symptoms to accompany the MRI findings, and a more appropriate radiological description might include transient bilateral occipital edema rather

than "PRES" for this case. Nevertheless, almost ten cases of PRES in association with GBS have been previously reported in the literature, although most of them were symptomatic.<sup>3</sup> Parmentier et al recently reported similar findings in a 28-year-old woman with GBS and moderately elevated blood pressure.<sup>4</sup> One likely explanation is that brain imaging is rarely performed in GBS, reducing the likelihood that a diagnosis of associated PRES will be made.

Although the underlying physiopathology supporting the association between PRES and GBS remains unclear, the most accepted mechanism is dysautonomia induced by GBS.<sup>5</sup> It is the presumably mechanism in our case, with wide fluctuations of blood pressure leading to failed cerebral autoregulation and vasogenic edema. Alternative hypotheses may include endothelial dysfunction in keeping with elevated cytokines levels in plasma and cerebrospinal fluid, leading to altered integrity of the blood-brain barrier.<sup>6</sup>

In conclusion, this case emphasizes the fact that PRES may be clinically silent, and may therefore be more common than previously reported.

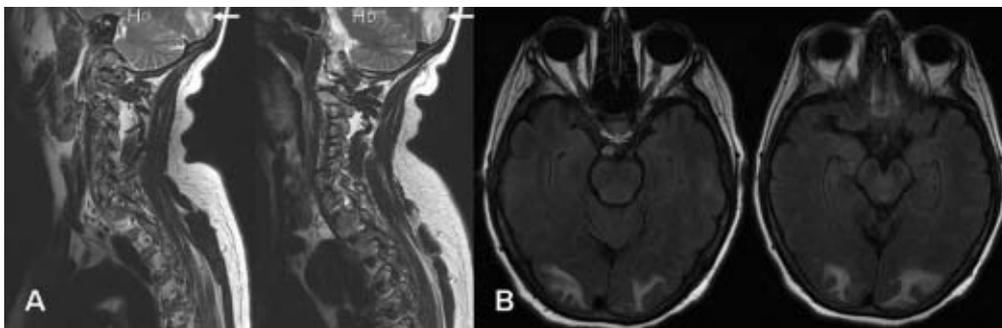
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**Figure:** Cervical spinal cord (A) and brain (B) neuroimaging. A) Sagittal T2-weighted MR sequence showing "incidental" high signal intensity of occipital lobes (arrow); B) Axial FLAIR sequence showing bilateral occipital high signal intensities, suggestive of PRES.

## TO THE EDITOR

**IL6-Gene Variation in Parkinson's Disease**

I have read with interest the recent report on the putative impact of chemokine polymorphisms in Parkinson's Disease<sup>1</sup>. Based on a meta-analysis of case-control investigations for *IL-6* and several other candidate genes, the authors concluded protective effects of an *IL-6* promoter variant, rs1800795 or IL-6 G[-174]C. However, key issues appear to have been overlooked. Firstly, the study by Infante et al<sup>2</sup> used a TaqMan genotyping procedure with unknown primers. It is therefore impossible to tell in retrospect whether the transcribed or the antiparallel DNA strand served for allele calling and whether the risk allele was "G", or "C". As rs1800795 stands for a canonical substitution that can be read as "G" or as "C" depending on the template, strand information is essential to define genetic exposure. A second study<sup>3</sup> used sequence-specific oligo probes that do not differentiate between "G" and "C" but rather call only the "C" allele on the transcribed strand. A third study<sup>4</sup> genotyped the non-transcribed strand as can be verified by consulting the original pyrosequencing protocol. Chu et al failed to correct for the alternate strand and have mistaken "G" for "C". In other words, two of the three studies in question are non-informative and the third gives results that were misinterpreted. Finally, the authors have muddled IL-6 studies in Table 2 and have omitted additional studies<sup>5</sup>.

The confusion of risk and protective alleles emphasizes further the need for strand-sensitive meta-analyses of G:C and A:T transversions. It is unfortunate that this procedure is not routinely implemented in PDGene (URL: <http://www.pdgene.org>), a database that was consulted by the authors and that also offers meta-analyses of case-control investigations. Having

reviewed all PDGene entries for rs1800795, I note that as of September 2012, data from multiple studies<sup>2-4</sup> have been misassigned to rs13447446, a G:T substitution 63bp downstream from rs1800795. Other studies that did not investigate rs1800795 are included in PDGene's meta-analysis of this variant. While Chu et al must be given credit for identifying these errors, the information available is insufficient to support a protective role of rs1800795 in Parkinson's disease.

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## TO THE EDITOR

**A Case of Collet-Sicard Syndrome Caused by Necrotizing Otitis Externa**

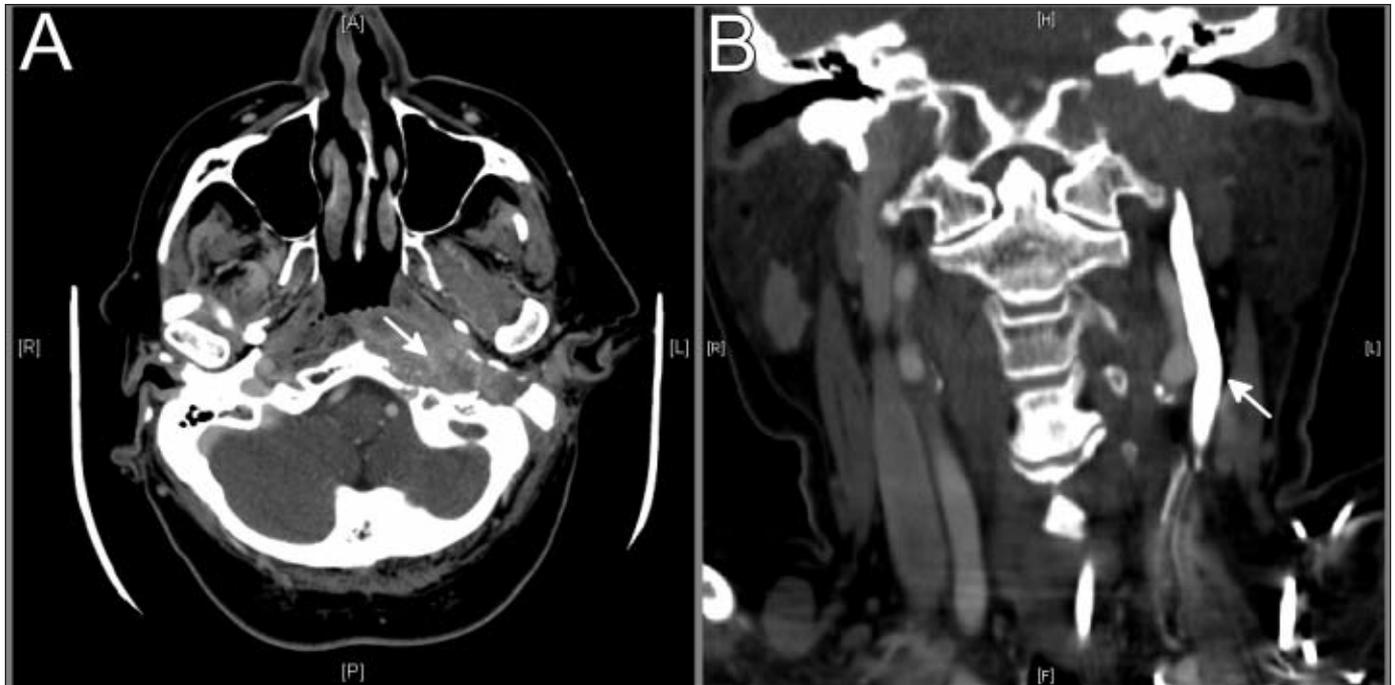
Collet-Sicard syndrome (CSS), palsy of cranial nerves nine, ten, eleven, and twelve, can be caused by a diverse set of disorders. Collet-Sicard syndrome is distinguished from Villaret syndrome by the lack of sympathetic nerve fibre involvement. The most common cause of CSS is otologic tumour<sup>1</sup>. Other causes include non-otologic neoplasia (primary or secondary): parotid tumours, skull base tumours, prostate metastases, kidney metastases, breast metastases, and melanoma metastases. Multiple myeloma and schwannomas of the hypoglossal nerve, and Hodgkin's disease have been reported as causes. Vascular lesions including carotid aneurysms and jugular vein phlebitis can cause CSS. Other rare causes of CSS have been reported<sup>1</sup>.

Herewith, we report a patient with Collet-Sicard syndrome resulting from malignant otitis externa (OE) and subsequent abscess formation. To the best of our knowledge, this is only the second reported case of infectious CSS.

## CASE REPORT

A 67-year-old man presented with a three week history of progressive dysphagia to solids and liquids accompanied by episodic regurgitation and emesis of partially digested food. His past history was significant for type 2 diabetes mellitus, hypertension, erectile dysfunction, obesity, osteoarthritis, and hypothyroidism. He had been diagnosed with left sensorineural hearing loss and left OE five months prior. Ear culture was positive for *Pseudomonas aeruginosa*. Despite an aggressive antibiotic regimen and frequent debridement and microcleaning, the OE had persisted.

A swallowing assessment prior to neurologic consultation suggested severely impaired oral and pharyngeal phases of swallowing with a high risk of aspiration on all textures. This necessitated a G-tube placement. The patient was admitted to hospital. Examination by a neurologist showed a deviated tongue to the left, failure of the left soft palate to rise, severe left sternocleidomastoid (SCM) and upper trapezius weakness and atrophy, and mild dysarthria. The initial differential diagnosis included bulbar-onset amyotrophic lateral sclerosis (ALS). Subsequent examination 3.5 months later revealed persistent



**Figure:** CT head with contrast taken shortly after the onset of cranial nerve IX, X, XI, and XII palsy. A) Contrast-enhanced axial CT shows ill-margined soft tissue (arrow) in the left carotid space that completely surrounds the distal cervical internal carotid artery. B) Contrast-enhanced coronal CT shows erosion of the left clivus and temporal styloid process with deep venous sinus thrombosis (arrow).

dysarthria, dysphagia, tongue deviation to left with mild atrophy, and significant atrophy and weakness of the left SCM and upper trapezius. Infrequent fasciculations were noted in the left hemi-tongue and left trapezius.

Magnetic resonance imaging suggested a left nasopharyngeal carotid space mass with osseous involvement of the left clivus. This mass impinged on cranial nerves IX, X, XI, and XII exiting the brainstem. Contrast computed tomogram (CT) of the neck revealed bony erosion of the left skull base including the left side of the clivus, bony walls of the foramen lacerum, the jugular foramen, and the inferomedial portion of the petrous temporal bone adjacent to the petrooccipital fissure. Additionally, there was a venous sinus thrombosis in the left transverse and sigmoid sinuses (Figure).

The patient was treated with heparin for the venous thrombosis. He subsequently developed a lower gastrointestinal bleed that necessitated discontinuation of anticoagulation. The infection was treated with intravenous meropenem and oral ciprofloxacin for four months. His symptoms gradually improved. Follow-up CT scans, two months after the initial presentation, showed a persistent skull-base mass, an unchanged venous sinus thrombosis, and slight improvement to the left mastoid air cells.

Four months after presentation, the patient's deficits had partially, but not fully, resolved. He was back on a normal diet and had had his G-tube removed. There was less weakness of the SCM, trapezius, and swallowing musculature. Further nerve conduction studies were performed. The left spinal accessory nerve compound motor action potential was 0.7 mV compared

with the right side at 2.3 mV. There was denervation with chronically-remodelled polyphasic motor unit potentials in the left SCM and trapezius muscles.

## DISCUSSION

Cranial nerves IX, X, and XI all pass through the jugular foramen. The jugular foramen pars nervosa contains the glossopharyngeal nerve and the jugular foramen pars vascularis contains the vagus and spinal accessory nerves. Cranial nerve twelve passes through the hypoglossal canal, and exits near the jugular foramen. An inflammatory process located in the posterior laceroccondylar space can cause CSS<sup>1</sup>.

This patient developed otitis externa (OE) likely as a result of his poorly-controlled type 2 diabetes mellitus. This OE was subsequently complicated by skull-base abscess, which caused CSS. *Pseudomonas aeruginosa* is a common cause of OE in diabetic patients. Despite local and systemic antibiotic therapy for the OE, the infection spread from the mastoid air cells to the skull base whence it caused cranial nerve palsies. In this patient's case, it is unlikely that the venous sinus thrombosis caused the cranial nerve palsies. The palsies improved when the infection was resolved despite the thrombosis remaining. There have been several reports of CSS caused by venous thrombosis<sup>1</sup>. In all of these cases, the thrombosis was in the jugular vein; in this patient's case, the thrombosis was in the transverse and sigmoid sinuses.

In a review of the literature, we found one case report in which there was an infectious cause of CSS<sup>2</sup>. A 56-year-old man

with a history of type 2 diabetes mellitus and prior cerebrovascular accident (CVA) developed skull-based osteomyelitis and subsequent CSS plus unilateral facial nerve palsy. In his case, the presenting symptoms included dysphagia to solids and liquids, hoarseness, facial palsy, and neck pain. These symptoms were mistaken for a CVA. Eventually, osteomyelitis was recognized, he underwent surgical debridement, and he had a course of intravenous antibiotics. His condition soon drastically improved.

There were several reports of syndromes similar to CSS caused by infection. In these cases, the syndromes involved palsies of some, but not all of cranial nerves IX, X, XI, and XII, with or without sympathetic nerve fibre involvement. Lee et al<sup>3</sup> described a case of osteomyelitis causing cranial nerves IX, X, and XII palsy. An infectious cause of Villaret's syndrome was reported by Huang and Lu<sup>4</sup> and by Goldstein et al<sup>5</sup>. The case reported by Goldstein et al<sup>5</sup> is very similar to the case reported herewith. In that case, a 72-year-old man with prior history of type 2 diabetes mellitus and treatment-resistant OE presented with generalized weakness, confusion, otorrhea, otalgia, progressive hoarseness, and weight loss. He soon developed all of the signs of Villaret's syndrome. He responded well to aggressive surgical debridement.

We conclude that infection is a rare cause of Collet-Sicard syndrome. Skull-base infection should be on the differential diagnosis of a patient presenting with swallowing difficulties and focal cranial nerve palsies. Index-of-suspicion should be especially high when a chronic, treatment-resistant course of OE precedes the nerve palsies.

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