CASE REPORT

Herpetic cranial polyneuritis mimicking brain stem infarction—an atypical presentation of Ramsay Hunt syndrome

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SUMMARY

An elderly man presented with severe right ear pain and discharge, hoarseness and dysphagia causing significant involuntary weight loss. Extensive investigations by varied specialties only highlighted right vocal cord palsy and right parotid lymphadenitis. Reassessment on transfer to a rehabilitation ward noted clinically subtle right Ramsay Hunt syndrome with multiple lower cranial nerve involvement. We illustrate a case of varicella zoster virus cranial polyneuritis with bulbar symptoms mimicking bulbar stroke, requiring percutaneous endoscopic gastrostomy feeds, with significant clinical and radiological recovery over 1 year.

BACKGROUND

Delayed diagnosis of a viral cause of unilateral vocal cord palsy (UVCP) is associated with significant morbidity and prolonged hospital stay. Temporal evolution of sensory and motor symptoms in herpetic cranial polyneuritis is not uncommon. Herpetic vesicles, when present, can precede and resolve prior to motor symptoms, and be easily missed when assessment is delayed. Empirical antiviral therapy should be initiated early to reduce symptom severity and duration, and close follow-up is necessary to ensure adequate recovery and address residual symptoms. Cranial polyneuritis in the elderly has several differential diagnoses requiring exclusion.

CASE PRESENTATION

A 90-year-old previously independent man presented to a metropolitan hospital, with syncope, resulting in a fall, in the context of 3 weeks of general ill health and significant involuntary weight loss of 10 kg over this period. He reported a temporal evolution of symptoms beginning with severe right ear pain and discharge interfering with sleep, followed by hoarseness of voice, nasal speech, difficulty swallowing food and drinks, shortness of breath and productive cough unresponsive to antibiotics prescribed by his primary care physician. He had a background of ischaemic heart disease, coronary artery bypass grafts, paroxysmal atrial fibrillation, bovine aortic valve replacement, hypertension, hypercholesterolaemia and an episode of vasovagal syncope 8 years earlier.

He was admitted under a medical team and extensively investigated. Ear, nose and throat (ENT) review with flexible nasendoscopy revealed right UVCP, compensated with a glottic gap and

persistent pooling of secretions around the pyriform fossae, despite multiple swallows. No mucosal lesions were noted and the patient denied prior history of chicken pox. A diagnosis of idiopathic UVCP was provided. The patient was then referred to a dietician and speech pathologist, for dietary modification and manoeuvres to prevent aspiration, with a plan for ENT review 3 months later to monitor his progress. Ten days later, he was transferred to a rehabilitation ward.

Reassessment following transfer revealed eczematization of the right external auditory canal associated with serous discharge (figure 1) and inflammation of the tympanic membrane. The right parotid region was noted to be swollen and tender. The patient had a hoarse voice, with dysphonia and inspiratory stridor. He was dehydrated and dysphagic, neither able to swallow his own saliva nor to tolerate level 150 thickened fluids, with nasal regurgitation of oral contents.

Figure 1 Eczematization of the right external auditory canal.

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Figure 2 Subtle right hemifacial weakness without sparing of the forehead, indicating right seventh cranial nerve lower motor neuron involvement.

Cranial nerve examination demonstrated involvement of right-sided cranial nerves VII (subtle lower motor neuron (LMN) facial weakness, House-Brackmann grade II (figure 2)), VIII (impaired hearing and vestibular ataxia), IX and X (reduced gag reflex and dysphonia and dysphagia secondary to hemilaryngeal and palatal paresis) and XII (ipsilateral tongue deviation (figure 3)). Transmitted upper airway sounds were noted on auscultation.

INVESTIGATIONS

Bloods showed iron deficiency anaemia with haemoglobin 129 g/L, ferritin 169 µg/L, iron 4 µmol/L, transferrin 24 g/L

Figure 3 Tongue deviation to the right, indicating 12th cranial nerve involvement.

and transferrin saturation 8%, faecal occult blood being negative. Inflammatory markers were raised with white cell count $14.80 \times 10^9/L$, neutrophils $13.08 \times 10^9/L$, C reactive protein (CRP) 140 and erythrocyte sedimentation rate (ESR) 72 mm/hour. Both CRP and ESR later reverted to normal without intervention. Renal function was impaired with serum creatinine $107 \mu\text{mol/L}$. The patient was acidotic, with bicarbonate being 19 mmol/L, and hypokalaemic, with potassium of 2.4 mmol/L. Phosphate was low at 0.70 mmol/L. Calcium, magnesium, vitamin B₁₂, vitamin D and folate were normal.

ECG noted sinus rhythm with first-degree atrioventricular block, and evidence of a past inferior and anterior myocardial infarction. Twenty-four-hour ambulatory ECG monitoring excluded transient arrhythmia.

Extensive imaging organised by the medical team included chest X-ray, which showed a long-standing left midzone opacity. CT of the neck showed mild asymmetry of the right hypopharynx and prominent cervical spine osteophytes indenting the posterior oesophagus, likely resulting in a compressive effect, with no other definitive cause for dysphagia. CT of the chest showed a normal mediastinal oesophagus and no mass lesion. Ultrasound of the neck revealed a reactive lymph node over the right parotid duct. CT of the head showed age-related involution and widespread periventricular chronic small vessel disease. The patient underwent gastroscopy, which showed patchy oesophagitis with neither dysplasia nor malignancy, consistent with gastro-oesophageal reflux disease. No swabs were collected for varicella zoster virus (VZV) PCR at this stage.

On transfer to the rehabilitation ward, having noted the pattern of cranial nerve involvement, swabs were taken for VZV PCR of eczematized skin (right external auditory canal) and were found to be positive. Bloods collected for viral serology were positive for VZV IgM and IgG, consistent with an acute VZV infection. Herpes simplex virus 1 IgG was positive, indicating prior infection.

Figure 4 Axial T2-weighted image on brain MRI showing linear T2 signal abnormality in the right posterolateral medulla and inferior cerebellar peduncle.

MRI of the brain was requested 34 days into the admission, to further investigate the dysphonia and dysphagia. The MRI showed widespread white matter changes of small vessel ischaemic disease. Postcontrast imaging included postgadolinium fat saturated high-resolution T1 volume sequences magnetisation-prepared rapid gradient-echo (MPRAGE), with axial and coronal reformatted images. A linear T2 signal abnormality was noted in the right posterolateral medulla and inferior cerebellar peduncle (figure 4), interpreted as an ischaemic infarct in the region of the vagal nuclei. The diffusion weighted sequence was positive (figure 5), although the apparent diffusion coefficient was indeterminate due to the small size of the lesion (figure 6). There was also bilateral pathological enhancement within the internal auditory canals, involving the vestibulocochlear nerves, as well as the tympanic portions of the right facial nerve (figure 7). There was asymmetrical enhancement of the right external acoustic meatus, suggestive of Ramsay Hunt syndrome (RHS). There was no convincing pathological enhancement of the 9th, 10th, 11th or 12th cranial nerves.

Repeat video fluoroscopy (VFS) identified reduced lingual control, delayed swallow trigger, incomplete epiglottic deflection, reduced right pharyngeal wall contraction and persistent food residue towards the right pharynx, along with active aspiration.

Audiometry performed 6 months prior to initial presentation noted bilateral sensorineural hearing loss, more severe at higher frequencies.

Lumbar puncture with cerebrospinal fluid (CSF) analysis was not performed due to the absence of encephalopathy and delays in arranging gadolinium-enhanced MRI.

Figure 5 Positive diffusion weighted sequence on brain MRI demonstrating a lesion in the right posterolateral medulla.

Figure 6 Apparent diffusion coefficient image with indeterminate ADC due to the small size of the lesion in the posterolateral medulla.

DIFFERENTIAL DIAGNOSIS

- ▶ RHS with associated embolic medullary infarct
- ▶ Herpes cranial polyneuritis
- ▶ Autoimmune cranial polyneuritis
- ▶ Malignant cranial polyneuritis

TREATMENT

As the bulbar symptoms were prominent, the patient was started on level 400 thickened fluids with education on strategies to avoid aspiration. However, poor compliance with thickened fluids and dehydration prompted placement of a nasogastric tube (NGT). Valaciclovir was started (1 g three times per day via

Figure 7 Axial fat-saturated postgadolinium T1-weighted image showing abnormal enhancement of the tympanic portion of the right facial nerve.

NGT for 2 weeks), along with paracetamol to address the right ear pain. Corticosteroids were not administered due to concurrent aspiration pneumonia requiring antibiotic therapy. The MRI finding of medullary ischaemic stroke, and poor recovery of swallow over the next 6 weeks, necessitated a percutaneous endoscopic gastrostomy (PEG) for enteral feeding. The patient was provided stroke-specific speech and swallow rehabilitation at a dedicated stroke unit.

OUTCOME AND FOLLOW-UP

Three months later, the patient was discharged home with support from a rehabilitation in the home service and subsequent referral to an outpatient day therapy unit, for regular follow-up with a dietician, speech pathologist and geriatrician. He experienced recurrent episodes of dizziness. A Reveal cardiac monitor was arranged to capture symptomatic arrhythmias, however none were noted.

The dysphonia resolved 6 months following discharge with return of normal speech. The patient recovered ability to swallow over 12 months and was able to tolerate a soft diet. The PEG was removed and there was gradual weight gain. Follow-up audiometry showed normal progression of hearing loss, with no unilateral predominance. Repeat brain MRI, at 18 months, with comparable postgadolinium high-resolution MPRAGE sequences and reformat images, noted persistent bilateral enhancement of vestibulocochlear nerves (figure 8) and resolution of the right posterolateral medullary lesion (figure 9). Discussion with the neuroradiologist highlighted the possibility of persistent dizziness being secondary to vestibular neuropathy. It was also noted that resolution of the posterolateral medullary T2 signal abnormality was more characteristic of recovery of localised oedema of VZV neuritis, involving cranial nerves IX and X, rather than vasculitis or the previously reported

Figure 8 Axial T1-weighted image magnetisation-prepared rapid gradient-echo fat-saturated postgadolinium image on repeat brain MRI at 18 months, showing persistent bilateral enhancement of vestibulocochlear nerves.

Figure 9 Corresponding axial T2-weighted image on repeat brain MRI showing resolution of the right posterolateral medullary lesion demonstrated in figure 4.

ischaemic infarct, both of which would demonstrate persistent signal abnormality on subsequent imaging.

DISCUSSION

The word ‘herpes’ originates from the Greek word ‘herpein’ (‘to creep’) and has been used to illustrate permanent infection caused by VZV (belonging to herpes virus group).¹ Following primary infection, VZV typically remains dormant in the dorsal root ganglia of sensory nerves, with secondary reactivation causing the well-known dermatomal vesicular eruption of shingles.² VZV can also remain quiescent in autonomic ganglia and cranial nerves, commonly affecting the fifth and seventh nerves, resulting in herpes zoster ophthalmicus and oticus, respectively.² Common triggers for reactivation of latent VZV include emotional stress, physical trauma, smoking, recent viral infection and decreased cell-mediated immunity, either as a feature of advancing age or immunocompromised states.³ The severity and duration of symptoms is often greater in the elderly.^{4 5}

RHS results from reactivation of VZV in the geniculate ganglion. Vesicles in the external auditory canal are due to involvement of the auricular branch (sensory) of the seventh cranial nerve while involvement of motor branches causes ipsilateral LMN facial palsy.⁶ The classic temporal pattern of symptoms begins with severe ear pain, followed by redness and swelling of the external ear, fever and malaise, vesicles in the external auditory canal and ipsilateral LMN paralysis, usually evolving over 1 week.^{7 8} Cases without vesicles are termed zoster sine herpete and are clinically similar to Bell’s palsy.⁶

Coinvolvement of the eighth cranial nerve in RHS is common, presenting as dizziness, vertigo, nystagmus, tinnitus and sensorineural hearing loss.⁷ Facial nerve paralysis (FNP) usually recovers well; however, high-frequency hearing loss often persists despite vestibular recovery, likely due to vestibular compensation.^{9 10} RHS with extensive cranial polyneuropathy is rare, and other rare associations include aseptic meningitis and syndrome of inappropriate antidiuretic hormone secretion.⁴

Severe VZV cranial polyneuropathy commonly involves the pharynx and larynx,² following infection of the recurrent laryngeal nerve, which is most vulnerable to injury due to its long length.³ The subsequent ipsilateral paralysis of several intrinsic laryngeal muscles and vocal cord causes severe dysphagia and

dysphonia.³ Dysphagia is an uncommon presenting feature of RHS, and VFS assists in diagnosis and serial assessment of motor recovery of pharyngeal muscles, following antiviral therapy.¹¹ VFS in UVCP typically shows abnormal contraction of one side of the pharyngeal wall, delayed laryngeal elevation of a half-vertebra width, large amounts of laryngeal residue and pooling of dye in both pyriform fossae causing aspiration.^{11 12}

VZV affects both, neurons and glial cells,¹³ and intracranial vasculopathy by transmural spread of VZV is known to occur.¹ Cerebral thrombotic infarctions and haemorrhages due to VZV vasculitis are rare.¹³ Herpetic basal ganglia and subcortical infarcts have been attributed to involvement of small penetrating vessels (eg, lenticulostriate arteries),¹ with age above 80 years increasing VZV-associated stroke risk in the first year by 30%.¹³ Cranial angiography can identify areas of stenosis in affected vessels.¹ VZV vasculopathy may present weeks to months following resolution of vesicular eruption (when present).¹ In immunodeficient individuals, small vessel multifocal herpetic vasculitis may present as subacute encephalitis.¹³

VZV cranial polyneuropathy has several postulated mechanisms, including direct perineural spread along anastomotic pathways and VZV vasculitis with contralateral spread via inflamed meninges.¹⁰ Other postulated mechanisms of neuronal damage include direct viral cytopathogenic effect on surrounding neural tissue, allergic response of tissues to VZV and occlusive vasculitis.¹⁴

In RHS, T1-weighted postgadolinium MRI may show abnormal enhancement of the internal auditory canal, membranous labyrinth and intratemporal facial nerve.¹³ T2-weighted imaging may show abnormal thickening of affected nerves.¹⁵ In our patient, brainstem changes were caused by involvement of the ganglia of cranial nerves VII (geniculate ganglion) and IX (superior and inferior ganglia located at the jugular foramen). Reactivated VZV tracked proximally towards the brainstem resulting in cranial nerve radiculitis and inflammatory demyelination, supporting the theory of retrograde transaxonal or perineural spread of VZV.^{16 17} The linear T2 signal abnormality in the posterolateral medulla most likely represented demyelination of intra-axial cranial nerve IX.

Treatment with antiviral agents helps decrease discomfort and may improve prognosis by limiting viral spread to other cranial nerves and stabilising or improving VZV vasculopathy.^{11 18} Ideally, antivirals should be started within 72 hours of symptom onset.¹¹ A short course of oral corticosteroids has also been advocated as it reduces inflammation in affected arteries.^{13 18} Although convalescent VZV serology is useful to confirm infection, serum IgM antibodies are only detectable 8–10 days after vesicles appear¹⁹ and may be negative in a minority of cases,⁸ emphasising the need for empirical antiviral therapy based on clinical suspicion, and the need for repeat serology.⁹ Onset of neurological motor symptoms is often delayed and VZV DNA is often undetectable in CSF 2–6 weeks following infection.¹³ Injection laryngoplasty or medialisation of paralysed vocal cords can be considered for severe symptoms, to provide airway protection.⁴

RHS with cranial polyneuritis is more severe and has a more protracted course.⁹ Despite treatment, recovery of UVCP can be delayed beyond 8 months and persistent bulbar symptoms, residual hearing loss, incomplete recovery of FNP and postherpetic neuralgia are not uncommon.²⁰ RHS in patients under the age of 50 years should prompt further investigation to exclude causes of immunodeficiency.²⁰

In our case, diagnosis of VZV cranial polyneuritis causing bulbar symptoms was delayed due to atypical eczematous of

skin in the right external auditory canal and absence of laryngeal mucosal vesicles. This resulted in recurrent episodes of aspiration pneumonia, prolonged hospital stay and extensive investigations prior to initiation of antiviral therapy. Detailed clinical reassessment, recognition of motor symptoms involving multiple cranial nerves and correlation with sensory symptoms allowed appropriate investigations, initiation of antiviral treatment and a nutrition management plan. The unusual resolution of the posterolateral medullary T2 signal abnormality facilitated a revision of diagnosis from ischaemic stroke to resolved VZV neuritis mimicking an infarct. We believe this is the first case to report improvement in brainstem changes on MRI correlating with clinical recovery of swallow and ipsilateral UVCP, indicating resolution of herpetic demyelination. The patient's residual dizziness has now been attributed to the persistent vestibular neuritis demonstrated on MRI.

Our case illustrates the importance of careful clinical assessment. VZV pathology should be suspected in all cases of UVCP with ipsilateral bulbar symptoms, particularly when associated with otalgia and atypical ipsilateral auditory canal skin lesions. This should prompt rapid initiation of antiviral and steroid therapy to reduce symptom severity and chronicity.

Learning points

- Ramsay Hunt syndrome with cranial polyneuropathy is uncommon.
- Varicella zoster virus (VZV) intracranial vasculopathy or neuritis can present as subcortical, basal ganglia or brainstem infarction.
- Bulbar recovery in herpetic cranial neuropathy distinguishes it from medullary stroke.
- The temporal pattern of presentation and disease severity correlates with time to recovery and chronicity of symptoms.
- Based on clinical suspicion, antiviral therapy should be initiated within 72 hours, regardless of VZV PCR or serology.

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REFERENCES

- 1 Soares BP, Provenzale JM. Imaging of herpesvirus infections of the CNS. *AJR Am J Roentgenol* 2016;206:39–48.
- 2 Nisa L, Landis BN, Giger R, et al. Pharyngolaryngeal involvement by varicella-zoster virus. *J Voice* 2013;27:636–41.
- 3 Hosseini S, Zawawi F, Young J. Atypical presentation of a common disease: shingles of the larynx. *J Voice* 2015;29:600–2.

- 4 Coleman C, Fozo M, Rubin A. Ramsay hunt syndrome with severe dysphagia. *J Voice* 2012;26:e27–e8.
- 5 Van Den Bossche P, Van Den Bossche K, Vanpoucke H. Laryngeal zoster with multiple cranial nerve palsies. *Eur Arch Otorhinolaryngol* 2008;265:365–7.
- 6 Shinha T, Krishna P. Ramsay Hunt syndrome and zoster laryngitis with multiple cranial nerve involvement. *IDCases* 2015;2:47–8.
- 7 Ozel L, Toros SZ, Unal E, *et al.* Ramsay Hunt syndrome with atypical progress in a renal transplant recipient: a case report. *Exp Clin Transplant* 2011;9:413–16.
- 8 Lin YY, Kao CH, Wang CH. Varicella zoster virus infection of the pharynx and larynx with multiple cranial neuropathies. *Laryngoscope* 2011;121:1627–30.
- 9 Shim HJ, Jung H, Park DC, *et al.* Ramsay Hunt syndrome with multicranial nerve involvement. *Acta Otolaryngol* 2011;131:210–15.
- 10 Kim YH, Chang MY, Jung HH, *et al.* Prognosis of Ramsay Hunt syndrome presenting as cranial polyneuropathy. *Laryngoscope* 2010;120:2270–6.
- 11 Kim TU, Kim SY, Kim JI, *et al.* Ramsay-Hunt syndrome accompanied by dysphagia: a videofluoroscopic swallowing study. *Am J Phys Med Rehabil* 2013;92:547–50.
- 12 Chitose SI, Umeno H, Hamakawa S, *et al.* Unilateral associated laryngeal paralysis due to varicella-zoster virus: virus antibody testing and videofluoroscopic findings. *J Laryngol Otol* 2008;122:170–6.
- 13 Chiang F, Panyaping T, Tedesqui G, *et al.* Varicella zoster CNS vascular complications. A report of four cases and literature review. *Neuroradiol J* 2014;27:327–33.
- 14 Babu K, Kini R, Murthy KR. Unique presentation of 3rd and 6th cranial nerve palsies, nodular scleritis and nummular keratouveitis in an immunocompetent patient following an attack of herpes zoster ophthalmicus. *Ocul Immunol Inflamm* 2012;20:365–7.
- 15 Reichel MA, Meltzer DE. Herpes zoster ophthalmicus affecting the spinal trigeminal nucleus and tract. *Neurographics* 2012;2:144–7.
- 16 Fabian VA, Wood B, Crowley P, *et al.* Herpes zoster brachial plexus neuritis. *Clin Neuropathol* 1997;16:61–4.
- 17 Hu S, Walker M, Czartoski T, *et al.* Acyclovir responsive brain stem disease after the Ramsay Hunt syndrome. *J Neurol Sci* 2004;217:111–13.
- 18 Amlie-Lefond C, Jubelt B. Neurologic manifestations of varicella zoster virus infections. *Curr Neurol Neurosci Rep* 2009;9:430–4.
- 19 Choi JH. Two cases of pharyngolaryngeal zoster advanced to multiple cranial neuropathy. *Am J Otolaryngol* 2013;34:369–72.
- 20 Shihada R, Brodsky A, Luntz M. Laryngeal mass with multiple cranial neuropathies as a presenting sign for varicella zoster infection. *Dysphagia* 2010;25:153–5.

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