CASE REPORT

Ramsay Hunt syndrome with cranial polyneuropathy with features of supraglottitis

Lloyd Steele, Reshma Ghedia, Hena Ahmad, Alasdair Mace

Imperial College Healthcare
NHS Trust, London, UK

Correspondence to

Dr Lloyd Steele,
lloyd.steele@imperial.nhs.uk

Accepted 25 July 2017

SUMMARY

A 67-year-old woman presented with a 1-week history of left otalgia and a 1-day history of odynophagia, pain extending into the face and neck, and a productive cough. Flexible nasendoscopy showed features of supraglottitis, with swollen arytenoids and pooling of saliva in the piriform fossae. Laboratory investigations revealed a mildly raised C reactive protein. A CT scan of the neck supported the diagnosis of supraglottitis and pharyngitis, with thickening of the mucosa of the left piriform fossae and left oropharynx. Standard supraglottitis treatment was instigated, but on day 4 of the admission, a vesicular rash and features of cranial nerve involvement (V, VII, VIII, X) developed. A revised diagnosis of Ramsay Hunt syndrome with cranial polyneuropathy was made and later confirmed by varicella zoster virus PCR. After 4 weeks, facial nerve function normalised, but features of other cranial nerve palsies were persistent.

BACKGROUND

This is the first reported case of Ramsay Hunt syndrome (RHS) with cranial polyneuropathy in which features of supraglottitis were a major part of the presentation. RHS describes varicella zoster virus (VZV) recrudescence in the geniculate ganglion of cranial nerve (CN) VII, which typically presents with the classic triad of a vesicular rash in the sensory distribution of the facial nerve, a prodromal neuralgia and a facial nerve palsy.¹ Our case illustrates the wide range of symptoms and signs possible with VZV reactivation, and the diagnostic and therefore therapeutic challenges that this can present. Cases of RHS with extensive cranial nerve involvement are often the most difficult to diagnose, but are those most at risk of complications and poor recovery.^{2,3}

CASE PRESENTATION

A 67-year-old Caucasian woman presented to the emergency department. Her medical history was significant for rheumatoid arthritis, well controlled with methotrexate and sulfasalazine, and previous herpes zoster (shingles) of the abdomen, which represents VZV reactivation. Her surgical history was significant for a previous splenectomy after trauma, requiring daily prophylactic penicillin V, and a carotid endarterectomy for symptomatic carotid artery stenosis, after which she had residual left cranial nerve (CN) XI palsy.

She presented with a 1-week history of left otalgia, which had earlier been diagnosed as otitis media by her primary care practitioner. For this, she had been prescribed oral amoxicillin and Sofradex ear drops (framycetin sulfate, gramicidin, dexamethasone). The patient later developed pain extending into the face and neck, odynophagia and a productive cough. There was no change in voice.

On otoscopy, the left tympanic membrane was only partially visualised but not thought to be abnormal, and the canal was mildly erythematous with minimal debris, not thought to be infective and therefore did not warrant topical antibiotic treatment. Flexible nasendoscopy (FNE) revealed swollen arytenoids and pooling of saliva in the piriform fossae, but a normal glottis and no airway compromise. The vocal cords were normal in appearance and function. Oral examination was unremarkable and cranial nerves I–XII were intact minus the known left CN XI palsy. There were palpable left cervical lymph nodes (levels II and III).

On admission, she was haemodynamically stable, afebrile, but had a mild degree of respiratory compromise (respiratory rate 21 breaths per minute, oxygen saturation 94% on room air). Examination of the chest suggested a possible left lower zone pneumonia.

Laboratory investigations revealed mildly raised C reactive protein (12.1 mg/L (0.5–5.0 mg/L)) but a normal white cell count (WCC) (9.4×10^9 cells/L (4.2 – 11.2×10^9 cells/L)). Renal and liver function tests were normal. Sputum and blood cultures were negative. A chest radiograph confirmed the left lower zone pneumonia. A CT scan was ordered to exclude a laryngeal or oesophageal malignancy due to the unimpressive blood results but supported a diagnosis of supraglottitis.

Standard supraglottitis treatment was instigated with intravenous antibiotics, intravenous dexamethasone, intravenous fluids and analgesia. Microbiology advised use of piperacillin with tazobactam to treat the supraglottitis and the concomitant aspiration pneumonia.

On day 4 of admission, the patient developed nasal regurgitation, hoarseness and reduced taste sensation. On subsequent examination, she was found to have uvula deviation to the right, indicating a left vagus nerve palsy, and left hemifacial weakness (House-Brackmann (HB) grade 3), confirming a facial nerve palsy. Repeat FNE showed that the previously seen supraglottic oedema had resolved, but there was a new complete left vocal cord palsy (left CN X). Review of her ear with microscopy

CrossMark

To cite: Steele L, Ghedia R, Ahmad H, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221135

Figure 1 CT imaging showing asymmetrical soft tissue within the left side of the distal larynx just inferior to the hyoid bone.

found copious vesicles, crusting, pus and debris in the external auditory canal. A revised diagnosis of RHS with cranial polyneuropathy with features of supraglottitis was made. The patient was commenced on aciclovir, and the steroid treatment and her regular immunotherapy medications were discontinued.

While on treatment for RHS, further features of cranial nerve involvement developed: tinnitus, reduced hearing, broken vestibulo-ocular reflex, impaired balance (all VIII), reduced facial sensation and reduced jaw opening (both V). The facial nerve palsy deteriorated to a HB grade 4.

INVESTIGATIONS

A CT scan of the neck supported the diagnosis of supraglottitis and pharyngitis, with thickening of the mucosa of the left piriform fossa and left oropharynx (figure 1). A chest X-ray confirmed a pneumonia, suspected to be secondary to aspiration, although this usually involves the right lower lobe.

On day 4, due to new symptoms and signs, a working diagnosis of RHS was made but required confirmation and exclusion of skull base pathology. VZV PCR was performed on an external auditory canal swab and on a cerebrospinal fluid (CSF) sample, which were both positive for VZV. CSF analysis also showed mildly raised protein (protein 0.57 g/L (0.15–0.45), WCC 3/mm³ (0–5), glucose 3.9 mmol/L (1.8–4.7), red cells <1 cell/mm³, acellular, no oligoclonal bands).

CT of the temporal bones showed no evidence of a skull base or intracranial space-occupying lesion or infection (namely necrotising external otitis). An MRI showed enhancement along the left facial nerve (figure 2), particularly at the geniculate ganglion and mastoid segment, which supported the diagnosis

Figure 2 T2-weighted axial MR images of the brain showing enhancement of cranial nerve VII at the geniculate ganglion (white arrow).

of VZV reactivation. No alternative aetiologies for the cranial nerve palsies were demonstrated.

Further bloods tests were performed to further investigate the polyneuropathy. Serological tests for HIV, *Borrelia*, syphilis, Epstein-Barr virus (EBV), cytomegalovirus (CMV), *Listeria* and *Cryptococcus* were negative. ELISpot for tuberculosis was negative. Angiotension-converting enzyme (ACE) was normal, and anti-neutrophil antibodies (ANA) and anti-neutrophil cytoplasmic autoantibodies (ANCA) were also negative. There was no serum paraprotein.

DIFFERENTIAL DIAGNOSIS

At the time of presentation to our department, the features were overwhelmingly of supraglottitis, which can be life threatening and which required treatment. *Haemophilus influenzae* type B has traditionally been thought to be the most common cause of supraglottitis. Our patient was predisposed to *H. influenzae* infection because of asplenia, although she had received a prophylaxis vaccine booster after the splenectomy in 2001. However, a recent series found the majority of supraglottitis cases were due to *Streptococcus* species.⁴

When our patient developed a cranial polyneuropathy, we considered that they had a standard supraglottitis, but that the treatment of high-dose steroids had caused further immunosuppression, predisposing to a new infection that had caused the cranial polyneuropathy. We also considered that the cranial polyneuropathy was due to the same pathogen as the supraglottitis, most likely VZV, and that the polyneuropathy manifested due to progressive infection or because high-dose steroids had exacerbated the infection. We also performed neuroimaging to exclude a skull base lesion.

The differential diagnosis for a cranial polyneuropathy is broad, and includes:

- ▶ intracranial space-occupying lesion
- ▶ infective disorders (eg, Lyme disease, tuberculous meningitis)
- ▶ inflammatory disorders (eg, acute inflammatory demyelinating polyneuropathy, chronic inflammatory demyelinating polyneuropathy)
- ▶ autoimmune disorders (eg, sarcoidosis)
- ▶ carcinomatous meningitis
- ▶ neurodegenerative disorders.

TREATMENT

Based on the progression of symptoms on day 4, a revised diagnosis of suspected RHS was made and treatment with intravenous aciclovir and oral prednisolone was initiated prior to VZV PCR results being obtained. Eye protection therapy was also commenced. The rheumatology team advised suspension of her immunosuppressant therapy (sulfasalazine and methotrexate). The prednisolone dose was also weaned down to prevent further immunosuppression. She was assessed by the speech and language therapy (SLT) team who deemed her swallow unsafe and enteral feeding was thus commenced via a nasogastric tube.

Due to a positive CSF VZV PCR, intravenous aciclovir was continued for 21 days, and a further week of oral valaciclovir was then given, as advised by microbiology. She also completed 10 days of antibiotics for aspiration pneumonia, which also required a short intensive care unit (ICU) admission for ventilatory support.

OUTCOME AND FOLLOW-UP

On commencement of aciclovir, there was a rapid improvement in the patient's pain. After 4 weeks, the facial palsy improved to a HB grade 1, although the unilateral vocal cord palsy failed to improve. A fat injection into the left cord was given for medialisation to improve the patient's voice and for symptomatic relief.⁵ Currently, she is still working with the SLT to improve her speech and swallow on an outpatient basis after managing a pureed diet and thickened liquids. She has completed all antimicrobial treatment. Voice dysfunction, left-sided hearing loss and impaired balance continue to be problematic sequelae for the patient, which is being addressed.

DISCUSSION

VZV is an exclusively human alpha-herpes virus which, after the primary infection (chickenpox), becomes latent in cranial nerve ganglia, dorsal root ganglia and autonomic ganglia along the entire neuraxis.⁶ The virus can later reactivate and replicate to cause herpes zoster if host immunity wanes. This can be due to a natural decline in VZV-specific cell-mediated immunity with age, with zoster being most common in those aged over 60 years, or due to an acquired immunodeficiency, such as the use of immunosuppressant therapies.⁶ Other factors can also contribute, including stress and trauma.^{1 7} Reactivation in our patient was predisposed to by age, use of immunosuppressants (methotrexate and sulfasalazine) and stress.

Dissemination of VZV may occur in immunosuppressed patients.⁶ In our case, the multiple cranial nerve involvement was predisposed to by the patient's use of regular immunosuppressants, as well as the immunosuppressive effects of the supraglottitis treatment with intravenous dexamethasone. Immunosuppression may also explain why the CSF sample in our case did not show evidence of a pleocytosis.

RHS describes herpes zoster in the geniculate ganglion of CN VII, which presents with the classic triad of a vesicular rash in the sensory distribution of the facial nerve, a prodromal neuralgia (which is the most common presentation of herpes zoster⁸) and a facial nerve palsy.¹ Although most clinicians would be able to diagnose the classic triad of RHS, parts of the triad can present at different times or not at all, causing diagnostic difficulty. For example, the prodromal pain stage can be prolonged from 7 to >100 days,⁹ and thus patients can present with a non-specific ear pain alone,¹⁰ as in the initial presentation of our case to their primary care practitioner. Patients can also present with an isolated facial nerve palsy without vesicles. This may be because the vesicular eruption has not yet occurred, as in 14%–33% of cases^{11 12}; has occurred and since disappeared¹³; or will never occur, a condition known as zoster sine herpete.^{9 11}

A further diagnostic dilemma in RHS can be created by the involvement of additional cranial nerves beyond VII. Vestibuloauditory symptoms representing CN VIII involvement—such as tinnitus, hearing loss and vertigo¹—are well recognised and common, occurring in 40%–50% of cases.¹⁴ However, in 1.8% of RHS cases, cranial nerves beyond VII and VIII are involved.¹⁵ Most commonly, these are (in descending order) IX, X/V and III/XII/IV.¹⁵ The spectrum of symptoms and signs of RHS is therefore wide.

Our case was initially diagnosed as supraglottitis. We did not identify any cases of RHS with pharyngolaryngeal involvement presenting as supraglottitis in the literature. Although supraglottic swelling has been reported in other RHS cases,^{16–22} most commonly on the left side (77%),²³ clues against a diagnosis of supraglottitis on initial presentation in these cases were vocal cord

palsy,^{16 17 19 21} pharyngolaryngeal vesicles or other rash,^{16 17 19 20} facial weakness,^{17 18} hearing loss,^{17 18} facial hypaesthesia¹⁷ or an appearance of granulation tissue in the supraglottis.²² One study reported that pharyngolaryngeal vesicles are absent in 34% of cases of RHS with pharyngolaryngeal involvement.²³ We identified three case reports of primary VZV infection (chickenpox) presenting as supraglottitis in children.^{24–26}

Diagnosis, treatment and prognosis

Although the history and examination remain the basis for diagnosing uncomplicated RHS, in complicated cases detection of VZV DNA by PCR can aid the diagnosis. We confirmed the clinical diagnosis of zoster by PCR of an ear swab and a CSF sample. VZV PCR of ear exudates is more sensitive than VZV PCR on blood samples and can be positive before the development of vesicles.¹¹

PCR results should not delay the initiation of treatment as early treatment of RHS is associated with a reduced risk of persisting facial nerve palsy. In one study recovery of facial nerve palsy to HB grade I occurred in 75% of patients treated (aciclovir and prednisolone) within the first 3 days (pretreatment HB grade IV–VI, n=28) compared with only 30% of those in whom treatment was started after 7 days (pretreatment HB grade IV–VI, n=21).²⁷ The rationale for early treatment with aciclovir seems biologically plausible as it works by interrupting viral DNA synthesis and thus is effective only when the virus is multiplying.²⁸ A Cochrane review could make no conclusions about the use of adjuvant corticosteroids because of an absence of randomised controlled trials,²⁹ but its use is generally recommended.^{8 27} In our case, corticosteroids were later avoided due to the possibility that it contributed to the patient's immunosuppression and fulminant of the virus.

Cranial polyneuropathy in RHS seems to portend a poorer prognosis than RHS alone. In one study, the complete recovery rates from facial nerve palsy in patients with and without multiple cranial neuropathy were 27.3% and 67.7%, respectively.² Cranial polyneuropathy can also be associated with life-threatening conditions,³ such as aspiration pneumonia and meningoencephalitis.^{22 23} This was evinced in our case by an ICU admission for aspiration pneumonia. It has thus been suggested that RHS associated with cranial polyneuropathy may need a

Patient's perspective

I am putting down my thoughts about my illness, as I can remember. I was under a lot of strain and stress prior to my illness. I am normally a strong person physically and mentally. I saw a doctor who gave me penicillin ear drops, but it didn't work. Before I was admitted to Charing Cross Hospital, I had terrible pain on the left side of my face and my neck swelled up terribly. It felt like a razor blade was going across my head. I had difficulty in swallowing all food and liquid. Eventually I called an ambulance and was admitted by the emergency doctor. Then my health spiralled out of control. I was scared and very frightened. I was caring, along with my sister, for our very elderly mother, who was bedridden with dementia, who we both loved. I was afraid I wouldn't survive. The nurses and doctors, I can never thank them enough, they treated me very very well.

My health is still not good. I am unable to speak properly, still deaf in my left ear and my balance is very bad. I have to walk with a crutch when I go out but I hope the balance will get much better with time.

more active and aggressive treatment compared with the treatment of uncomplicated RHS.³ However, paradoxically, treatment is often delayed when cranial polyneuropathy is present due to greater diagnostic difficulty.^{2,30}

A comprehensive work-up is needed when cranial polyneuropathy is present to exclude other causes, although this should not delay treatment. An MRI can show a space-occupying lesion or other diagnosis, such as neurosarcoidosis,^{3,15} and can also reveal enhancement of cranial nerves, which can aid the diagnosis of RHS.¹⁵ A videofluoroscopic swallow study can also be useful to assess for swallowing difficulty and to give guidance about further management, including surgical interventions such as vocal cord medialisation. Multidisciplinary management for RHS is recommended (Ear, Nose and Throat (ENT) surgery, SLT, infectious diseases/microbiology, neurology) to aid diagnosis and expedite recovery.

Learning points

- ▶ Varicella zoster virus infection is a rare cause of supraglottitis.
- ▶ In Ramsay Hunt syndrome (RHS), the symptoms of otalgia, facial nerve palsy and a vesicular eruption do not always present at the same time, may not all be present and may be accompanied by additional features suggesting extensive cranial nerve involvement. Zoster sine herpete describes zoster without a vesicular rash.
- ▶ RHS with cranial polyneuropathy portends a poorer prognosis for recovery than RHS alone. Intervention may be needed to minimise functional impairment, such as vocal cord medialisation.
- ▶ RHS with cranial polyneuropathy can be associated with a risk of life-threatening conditions, such as aspiration pneumonia and meningoencephalitis.
- ▶ Multidisciplinary management for RHS is recommended (Ear, Nose and Throat (ENT) surgery, speech and language therapy, infectious diseases/microbiology, neurology).

Contributors LS and RG drafted the manuscript. RG and HA critically revised the manuscript. RG, HA and AM were all involved in the clinical care of the patient during their admission. AM was the senior author.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Hunt JR. On herpetic inflammations of the geniculate ganglion. A new syndrome and its complications. *J Nerv Ment Dis* 1907;34:73–96.
- 2 Shim HJ, Jung H, Park DC, *et al*. Ramsay Hunt syndrome with multicranial nerve involvement. *Acta Otolaryngol* 2011;131:210–5.
- 3 Kim CH, Kang SI, Kim YH. A case of Ramsay Hunt syndrome with cranial polyneuropathy. *Korean J Audiol* 2012;16:80–2.
- 4 Chroboczek T, Cour M, Hernu R, *et al*. Long-term outcome of critically ill adult patients with acute epiglottitis. *PLoS One* 2015;10:e0125736.
- 5 Khadivi E, Akbarian M, Khazaeni K, *et al*. Outcomes of autologous fat injection laryngoplasty in unilateral vocal cord paralysis. *Iran J Otorhinolaryngol* 2016;28:215–9.
- 6 Mueller NH, Gilden DH, Cohrs RJ, *et al*. Varicella zoster virus infection: clinical features, molecular pathogenesis of disease, and latency. *Neurol Clin* 2008;26:675–97.
- 7 Choi HJ, Kim JH, Lee YM. Herpes zoster developing within recent subciliary incision scar. *J Craniofac Surg* 2012;23:930–1.
- 8 Coulson S, Croxson GR, Adams R, *et al*. Prognostic factors in herpes zoster oticus (Ramsay Hunt syndrome). *Otol Neurotol* 2011;32:1025–30.
- 9 Gilden DH, Dueland AN, Devlin ME, *et al*. Varicella-zoster virus reactivation without rash. *J Infect Dis* 1992;166 Suppl 1:S30–S34.
- 10 Kim D, Bhimani M. Ramsay Hunt syndrome presenting as simple otitis externa. *CJEM* 2008;10:247–50.
- 11 Murakami S, Honda N, Mizobuchi M, *et al*. Rapid diagnosis of varicella zoster virus infection in acute facial palsy. *Neurology* 1998;51:1202–5.
- 12 Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. *Acta Otolaryngol Suppl* 2002;549:4–30.
- 13 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.
- 14 Wagner G, Klinge H, Sachse MM. Ramsay Hunt syndrome. *J Dtsch Dermatol Ges* 2012;10:238–43.
- 15 Kim YH, Chang MY, Jung HH, *et al*. Prognosis of Ramsay Hunt syndrome presenting as cranial polyneuropathy. *Laryngoscope* 2010;120:2270–6.
- 16 Hosseini S, Zawawi F, Young J. Atypical presentation of a common disease: shingles of the larynx. *J Voice* 2015;29:600–2.
- 17 Pahor AL. Herpes zoster of the larynx—how common? *J Laryngol Otol* 1979;93:93–8.
- 18 Lin YY, Kao CH, Wang CH. Varicella zoster virus infection of the pharynx and larynx with multiple cranial neuropathies. *Laryngoscope* 2011;121:1627–30.
- 19 Wu CL, Linne OC, Chiang CW. Herpes zoster laryngitis with prelaryngeal skin erythema. *Ann Otol Rhinol Laryngol* 2004;113:113–4.
- 20 Morinaka S. Herpes zoster laryngitis with intractable hiccups. *Auris Nasus Larynx* 2009;36:606–8.
- 21 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.
- 22 Pinto JA, Pinto HC, Ramalho JR. Laryngeal herpes: a case report. *J Voice* 2002;16:560–3.
- 23 Nisa L, Landis BN, Giger R, *et al*. Pharyngolaryngeal involvement by varicella-zoster virus. *J Voice* 2013;27:636–41.
- 24 Nozicka CA, Naidu SH, McFadden J. Varicella-associated acute supraglottitis. *Ann Emerg Med* 1994;23:888–90.
- 25 Narasimhan N, van Stralen DW, Perkin RM. Acute supraglottitis caused by varicella. *Pediatr Infect Dis J* 1993;12:619–20.
- 26 Slack CL, Allen GC, Morrison JE, *et al*. Post-varicella epiglottitis and necrotizing fasciitis. *Pediatrics* 2000;105:e13.
- 27 Murakami S, Hato N, Horiuchi J, *et al*. Treatment of Ramsay Hunt syndrome with acyclovir-prednisone: significance of early diagnosis and treatment. *Ann Neurol* 1997;41:353–7.
- 28 Dickens JR, Smith JT, Graham SS. Herpes zoster oticus: treatment with intravenous acyclovir. *Laryngoscope* 1988;98:776–9.
- 29 Uscategui T, Doree C, Chamberlain IJ, *et al*. Corticosteroids as adjuvant to antiviral treatment in Ramsay Hunt syndrome (herpes zoster oticus with facial palsy) in adults. *Cochrane Database Syst Rev* 2008;3:CD006852.
- 30 Rasmussen ER, Mey K. Vocal cord paralysis associated with Ramsay Hunt syndrome: looking back 50 years. *BMJ Case Rep* 2014;2014:bcr2013201038.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow