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Case Report

Ramsay Hunt Syndrome with Multiple Cranial Neuropathies: Role of Pulse Steroid Therapy with Newer Antiviral Agent in Nonresponding Hiccoughs and Laryngeal Palsy

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Ramsay hunt syndrome (RHS) is characterised by herpetic blisters (small vesicles) of the skin of the external canal, pinna and/or the oral mucosa and severe otalgia (ear pain) along with acute peripheral facial paralysis and/or vestibulocochlear dysfunction (e.g., vertigo, hearing loss, hyperacusis, tinnitus). RHS with multiple cranial neuropathies is rare, more severe, and usually intractable. A combination therapy of antiviral agents and steroids is the preferred treatment. We present a case of 30-year-old man suffering from RHS with multiple cranial neuropathies treated effectively with combination therapy of intravenous pulse steroid therapy and newer antiviral agent for intractable hiccoughs and laryngeal palsy.

Key words: *cranial nerve palsy, herpes zoster oticus, herpes zoster, pulse steroid therapy, ramsay hunt syndrome*

Introduction

Herpes zoster of outer ear, combined with lesions of either seventh or eighth cranial nerve or both, is generally called Hunts syndrome.[1] Ramsay hunt syndrome (RHS) typically is characterised by zoster oticus, facial nerve palsy and cochleovestibular symptoms.[2] RHS accompanied by multiple cranial neuropathies is rare, more severe, and usually intractable compared with RHS without such an involvement.[3] Definitive treatment consist of antiviral therapy and steroids.[4] Only 1 case series is available on use of injectable methylprednisolone in nonresponding RHS.[5] No literature is available on use injectable steroid pulse therapy with newer antiviral drug in laryngeal palsy with RHS in best of our knowledge. This case report describes the case of herpes zoster oticus with intractable hiccoughs and laryngeal paralysis treated effectively with combination therapy of antiviral and IV pulse steroid therapy supported by rehabilitation program.

Case Report

A 30-year-old male with previous healthy condition presented with complaints of left ear pain for 2 days. After 2-3 days of onset of otalgia, patient develop left side facial weakness along with change in voice. Patient also complaint of dysphagia for solid and liquids. Patient had vomiting with hiccoughs. On examination, there was lower motor neuron facial palsy on left side with bells phenomenon. Movement of left sided soft palate was reduced. There were painful vesicles on conchae and external auditory meatus.

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Audiometry proved conductive hearing loss. Laryngoscopy examination revealed left vocal cord palsy. He was put on ryle's tube feeding because of bulbar weakness.

Diagnosis of herpes zoster oticus with left facial palsy and left vocal cord palsy was confirmed. The patient was given valacyclovir (1,000 mg/8 hourly for 7 days) and oral steroid (1 mg/kg/day in tapering doses). Facial palsy was improved over 7 days but laryngeal palsy remained persistent. Vesicular rashes converted into adherent crusts. He remained on ryle' tube feeding. After 10 days of onset of herpes zoster oticus, he developed intractable hiccoughs interfering in respiration, not responding to IV metoclopramide and oral baclofen. In view of intractability and severity of hiccoughs, decision of injectable steroid was taken. He was started on injectable steroid (IV methylprednisolone 1,000 mg/day for 5 days) along with antiviral (Famciclovir 500 mg/8 hourly for 7 days). His hiccoughs dramatically improved on days 2 of injectable steroid. With completion of injectable steroid course, his bulbar weakness and voice improved significantly. He was discharged with rehabilitation program for bulbar weakness and speech therapy.

Discussion

RHS was first described by Johns Ramsay Hunt in 1907.[1] It is characterized by acute facial nerve palsy with vesicular eruption of the skin of pinna and external auditory canal caused by varicella zoster virus. Simultaneous involvement of multiple cranial nerve ganglia (geniculate ganglion and peripheral ganglia of cranial nerves VIII, IX and X) by VZV may lead to multiple cranial neuropathies associated with RHS.[2] Pathophysiology of multiple cranial nerve involvement associated with RHS remains unclear though several theories have been postulated. Hunt suggested that adjacent gasserian, petrous, accessory, jugular, plexiform and second, third cervical dorsal root ganglia may form chain allowing the extension of the ganglionitis.[4] Other theories of multiple cranial nerves involvement include perineural spread of the VZV along the anastomotic pathways or from a vasculitis in which virus spreads through the small branches of the infected carotid artery, middle meningeal artery, and ascending pharyngeal artery that supply blood to cranial nerves V, VII, IX, X, XI and XII cranial nerves.[6,7] Our case had gradual progressive involvement of lower cranial nerves VII, VIII, IX and X associated with herpetic eruptions on the outer aspect of the ear. The vocal cord palsy was indicative of involvement of the left recurrent laryngeal nerve which is a branch of the vagus nerve.

RHS being a rare condition, only few studies are available on the treatment part of RHS.[4,8-16] Most of these studies are in favour of use of antiviral drugs. The effect of antiviral therapy particularly on cranial nerve paresis is controversial. According to a Cochrane review, only one randomized controlled trial was performed including 15 patients; and no significant conclusions could be drawn as the study was deemed of low quality.[11] Other studies comprising small study populations have shown increased effects of acyclovir combined with corticosteroids compared to corticosteroids alone.[10,15] A meta-analysis of 12 RHS articles concluded that antiviral therapy plus steroids compared to steroids alone significantly improved facial nerve function recovery [odds ratio of 2.8, 95% Confidence Interval (CI)].[4] In one case series of 2 patients with RHS unsuccessfully treated with antiviral drugs and oral corticosteroids, showing an almost complete recovery after late administration of intravenous (i.v.) high dose methylprednisolone.[5] Both patients had all poor prognostic predictors. Author suggests use of intravenous high dose methylprednisolone, even as a late treatment option, in patients with RHS non recovering after standard antiviral and oral steroid therapy as well as presenting clinical features suggestive of a poor prognosis. Studies on treatment of RHS have been summarized in Table 1. The effectiveness of corticosteroid therapy can be explained by their pharmacological effects on inflammatory edema and the resulting decompression of neurogenic structures within the facial nerve canal in the petrosal bone.

A main prognostic factor on outcome, with regard to medication, seems to be the time from debut of symptoms to initiation of treatment, whether consisting of combined acyclovir and corticosteroids or corticosteroids alone.[17] Our case was initially treated with oral steroid and antiviral (Valacyclovir) drug. With this, he had significant improvement in facial palsy but without significant recovery of laryngeal palsy. Decision of injectable steroid (1,000 mg of methylprednisolone) pulse therapy was taken in view of intractable hiccoughs interfering in respiration. Antiviral (famiciclovir) was added to injectable steroid pulse therapy to avoid reactivation of VZV secondary

Table 1. Summary of studies of treatment of Ramsay Hunt syndrome

Study/year	No. of patients	Combination therapy	Antiviral treatment	Route	Corticosteroid treatment	Route	Initiation of treatment (d = days)	Comments / strong points of study
Pinar 2014[8]	12	Yes	Acyclovir 800 mg × 5/days, 7 days	Oral	1 mg/kg/day, tapering dose regimen	Oral	< 5 days	Recovery rate 75%
Zainine 2012[9]	15	Yes	Acyclovir 800 mg × 5/days, mean 8 days	Oral	Hydrocortisone 100 mg × 3/day, mean 8 days	Intravenous	Not Commented	Better recovery in 10 patients, favours combination therapy
Coulson 2011[10]	101	Yes	Before 1998, Acyclovir 200 mg × 5, 21 days; From 1998, famciclovir 250 mg × 3, 21days		1 mg/kg/day, 14 days, decreased by 10 mg/ day until 0		Early: < 5 days, Late: > 5 days	Statistically significantly better in combination treatment of early Acyclovir + late Corticosteroid
de Ru 2011[4]	Not available	Yes	Not available	Not available	Not available	Not available	Not commented	Meta-analysis of reviews 1985-2010 -- strongly recommend combination therapy
Uscategui 2008 (Oct)[11]	Not available	No evidence	Not available	Not available	Not available	Not available	< 3 days	Cochrane Review; finds no quality randomized controlled trial to support the use of antiviral compared to the use of Corticosteroid alone
Uscategui 2008 (June)[12]	Not available	No evidence	Not available	Not available	Not available	Not available	< 3 days	Cochrane Review; finds no randomized controlled trial at all to address use of Corticosteroid to support antivirals

Table 1. Summary of studies of treatment of Ramsay Hunt syndrome (continued)

Study/year	No. of patients	Combination therapy	Antiviral treatment	Route	Corticosteroid treatment	Route	Initiation of treatment (d = days)	Comments / strong points of study
Yeo 2007[13]	26	Yes	Acyclovir 5 mg/kg/8 hr, 5 days Famciclovir 500 mg × 3, 7 days	Intravenous, Oral	Prednisolone 1 mg/kg/day	Oral	Not commented	-
Uri 2003[14]	31	Yes	Acyclovir 5 mg/kg/8 hr for 7 days	Intravenous	Hydrocortisone 100 mg × 3 for 7 days	Intravenous	Early 1-3 days, Late 4-7 days	Recommends Intravenous Acyclovir over oral administration
Kinishi 2001[15]	91	Yes	Acyclovir 800 mg × 5/day	Oral	Methylprednisolone 500 mg/day 1st day, then 250 mg/day 2nd and 3rd days, and 100 mg/day for last 4 days	Intravenous	< 7 days	Assess Acyclovir + Corticosteroid on facial nerve recovery compared to Corticosteroid alone
Murakami 1997[16]	80	Yes	Acyclovir either 250 mg × 3 Intravenous or 800 mg × 5 orally for 7 days		1 mg/kg/day for 5 days, decreased 10 mg/day until 0, over 10 days		Early 1-3 days, Late > 7 days	75% recovered in 1-3 days group; 30% recovered in > 7 days group; Argues that onset of treatment is essential

to steroid. This led to dramatic reduction of hiccoughs followed by recovery of laryngeal palsy. This is the first case of RHS with multiple cranial nerves involvement treated with pulse steroid therapy along with newer antiviral agent in the literature in best of our knowledge. The prognosis of Ramsay Hunt Syndrome is not as good as that of Bell's palsy. The rate of full recovery was found to be 67.7% in RHS, but as low as 27.3% in patients with multiple cranial nerve involvement.[3] The main prognostic factor seems to be the severity of the initial symptoms.[10] Our case had complete neurological recovery following antiviral and pulse steroid therapy.

Conclusion

RHS with multiple cranial neuropathies is a rare disease that can present with variable manifestations. A high index of suspicion and close follow up are essential in patients with RHS. Early intervention with antivirals and corticosteroids improve outcomes significantly in these patients. Newer antivirals may be considered instead of acyclovir in view of easy dosing schedule and superiority in herpes zoster compared to acyclovir. Intravenous pulse steroid therapy can be chosen as a viable option for treatment of RHS with multiple cranial neuropathies in case of intractable or nonresponding symptoms even in late phase of the disease.

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