Ramsay Hunt syndrome: Clinical analysis of 15 cases

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ABSTRACT: Introduction: The Ramsay Hunt syndrome (RHS) is characterized by acute facial nerve paresis and/or paralysis accompanied by a herpetic lesion on the external ear. Material and Methods: Fifteen patients were evaluated and treated for RHS. After a detailed history was obtained, clinical examination was performed, and treatment was initiated based on steroids and acyclovir. The House-Brackmann grading system (HB I-VI) was used to evaluate the facial nerve function; this was further electrophysiologically assessed with the nerve excitability test (NET) and electro-neurography. Results: In RHS cases, the most common accompanying findings were the cochleovestibular symptoms (73%) and in particular vertigo and balance disorder. The combined treatment of acyclovir with steroids resulted in satisfactory facial nerve function (HB I-II) in 75% of cases. The recovery was satisfactory in all the cases in which the NET was normal or diminished. In 4 cases in which the recovery was non-satisfactory (HB III-V) no response was initially obtained in NET. Conclusion: In RHS, the possible neuritis and the inflammatory process which occur into the internal auditory canal may result in facial nerve dysfunction and cochleovestibular symptoms. The combined therapy of the antiviral agent acyclovir with the anti-inflammatory effect of steroids is recommended for the treatment of RHS. The NET was proved as the most useful method in the prognostication of RHS.

Key Words: Ramsay-Hunt syndrome, Herpes zoster oticus, Facial paralysis, Acyclovir, Steroids.

INTRODUCTION
In 1907, the Ramsay Hunt syndrome (RHS) was first described by James Ramsay Hunt. It is characterized by acute facial nerve paresis or paralysis accompanied by the presence of herpetic lesions on the external ear (auricle and external auditory canal). In his original classification, Ramsay Hunt stated that the facial nerve was always the first to be affected in its sensory and/or motor portion; the cochleovestibular symptoms, such as hearing loss, tinnitus or vertigo could also occur. The RHS is caused by reactivation of latent varicella-zoster virus (VZV) in the geniculate ganglion and possibly in the vestibular and spiral ganglia.

The VZV is a member of human herpesviruses; it is the etiologic factor for varicella and herpes zoster appearance. Following the primary infection, VZV becomes latent in the cells of the dorsal root ganglia and may be reactivated after a period of several decades; it thus results in the characteristics painful dermatomal rash of herpes zoster. Reactivation is usually associated with depressed cell-mediated immunity, such as in immunosuppressive therapy or HIV infection cases. In herpes zoster, the majority of the morbidity occurs in the elderly and is accompanied by complications such as ophthalmic zoster and post-herpetic neuralgia. The VZV is a ubiquitous infection agent; in a recent publication it was shown that over 50% of young children had antibodies to VZV by their 5th of their age, and over 90% of adolescents were already seropositive for VZV.

VZV has been detected by means of DNA tests in the saliva, tears, cerebrospinal fluid, and peripheral blood mononuclear cells, as well as in vesicles of patients suffering RHS. In RHS, VZV was identified...
The treatment was initiated within the first 5 days after the onset of facial paralysis; this consisted of intravenous administration of steroids (prednisolone, 25mgX3/day, and then tapered over 10 days period), and/or oral administration of Acyclovir 800 mg (five times daily for one week). In only one case the antiviral agent Valaciclovir was orally administrated 500 mg two times daily for one week.

The facial nerve function was evaluated on the day of admission, and then 6 months later. The grading of the facial RHS palsy was performed according to the House-Brackmann grading system (I-VI) (Table 1). The recovery of the facial function was characterized as «satisfactory» with HB grade I and II or «non-satisfactory» with HB grade III to VI.

Within the first 10 days after the onset of the disease, the facial nerve function was electrophysiologically assessed with two tests: a) the nerve excitability test (NET) and b) the electroneurography (ENoG). The Myoton 2 Facial Nerve Stimulator was used for the NET examination. The test was initially performed on the healthy side and then on the affected. The current intensity level at which a barely visible muscle twitch was elicited was determined as the NET threshold respectively on both sides. A comparison of the NET threshold between the two sides was made. A difference of 3.5 mA was defined as «normal»; a difference of 3.5 mA or greater between the two sides was defined as «diminished»; whereas no facial reaction was produced the cases were characterized as «no response».

For ENoG, the surface stimulator (Amplaid MK12) was placed over the main trunk of the facial nerve with anode just outside the stylomastoid foramen and the cathode in front of the ear lobe. The applied current intensity was increased from zero to a maximal level sufficient to evoke the myogenic compound action potential. The percentage of degenerated nerve fibers was calculated by dividing the amplitude of the myogenic compound action potential of the affected side by that of the normal side. The prognosis for recovery to normal facial function was considered poor when the electroneurography showed greater than 90% neural degeneration.

Finally, an audiometric assessment was performed in all the patients and a pure tone audiometry was con-
ducted across the frequencies from 250 to 8000 Hz with the GSI-61 audiometer, which was calibrated according to ISO 389 (International Organization for Standardization, 1991).

**RESULTS**

According to the initial House-Brackmann facial nerve function grading, 9 (60%) patients were characterized as grade V, 1 as grade IV, and 5 as grade III. Four patients exhibited facial paresis (or paralysis) after the appearance of the vesicles, 3 patients developed the vesicles after the onset of facial paresis or paralysis, and in 8 cases the facial paresis (or paralysis) and the vesicles appeared simultaneously. The main localizations of vesicles are shown in Table 2.

The most common accompanying symptoms were cochleovestibular (73%) (Table 3). In particular, vertigo and balance disorder occurred in 9 (60%) patients. Tinnitus was reported in 5 patients. Four patients had sensorineural hearing loss (moderate to severe sensorineural hearing loss in 2 patients, one patient had high-frequency hearing loss; one patient had ipsilateral anacusis).

In 11 (73%) out of the 15 patients, the facial nerve recovered satisfactorily in 6 months after the treatment. However, in 4 patients the recovery was non-satisfactory (Figure 2). Twelve patients were treated with acyclovir in combination with steroids (Table 4); 9 (75%) out of these 12 patients recovered to grade I and II.

In 6 cases, the recovery was complete (grade I); one patient remained to grade V. It was noticed that the recovery was satisfactory in half of the cases in which the initial facial paralysis was complete (grade V). According to the history, the first signs of recovery were observed in the time span of 7 to 30 days after the onset of RHS. In the cases that recovered to grade III a certain form of synkinesis occurred in the long-term (after 6 months).

The recovery was satisfactory in all the cases in which the NET was normal or diminished (Table 5). In 4 cases in which the recovery was non-satisfactory no response was initially obtained in NET. In one case, although the ENOg showed less than 90% of degeneration the outcome was poor (grade III), and in 4

**Table 2.** Main localizations of the vesicles in RHS.

<table>
<thead>
<tr>
<th>Localization</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinna</td>
<td>8 (53%) (Figure 1)</td>
</tr>
<tr>
<td>External auditory canal</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Cervical region</td>
<td>2 (13%) (Figure 1)</td>
</tr>
<tr>
<td>Parotid region</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Mastoid area</td>
<td>1 (6%) (Figure 1)</td>
</tr>
<tr>
<td>Hard palate</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

**Table 3.** Distribution of accompanying symptoms of RHS among the patient sample (n = 15).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochleovestibular symptoms</td>
<td>11</td>
<td>73</td>
</tr>
<tr>
<td>- Vertigo, instability</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Tear flow</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Taste disorders</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Otalgia</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Headache</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Neck pain</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Numbness in the parotid region</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Vocal cord paresis</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>
cases although the degeneration exceeded the 90% the recovery was satisfactory (grade I and II).

**DISCUSSION**

In this study, 15 (10%) out of the 149 patients presenting with unilateral acute facial palsy suffered from RHS. This is consistent with the incidence reported in other studies\(^{12,16,17}\), in which RHS cases ranged from 3.3% to 18% of patients with unilateral acute facial palsy. In the present study, the RHS cases in relation to Bell’s (idiopathic) palsy cases were 9:1.

In 10 out of the 15 patients the vesicles were localized on the external ear. The first sign of RHS may initially be presented as erythema of the auricle\(^{18}\) or as vesicles on the external ear. When the vesicles become apparent after the facial paralysis then the facial paresis (or paralysis) may be misdiagnosed as Bell’s palsy. There is also a clinical condition not included in the present study called «zoster sine herpete», which is characterized by facial paralysis in the absence of vesicles; the condition is diagnosed based on a four-fold rise in serum antibody titre to VZV\(^{19}\).

The distribution of major symptoms of RHS is shown in Table 3. The vestibular symptoms dominated over all the other symptoms. In other studies, vertigo has been reported to be a more frequent symptom and occurs in a significant number of patients with RHS, from 72%\(^{20}\) to 85%\(^{21}\). It was shown that in RHS both the superior and the inferior division of the vestibular nerve are affected\(^{22}\). Although hearing loss incidence in RHS was reported to be high (85% of cases\(^{21}\)), in the present study it occurred in only 26% of the cases. The hearing loss is always of sensorineural type\(^{16}\).

Seventh and eighth cranial nerve dysfunction in RHS is considered to be caused primarily by VZV neuritis; secondarily by inflammatory oedema of these nerves in their course within the temporal bone\(^{16}\). The

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**Figure 1.** Vesicles in RHS a) on the pinna b) on the mastoid and cervical region.

**Table 4.** Facial nerve function (House-Brackmann grading system) before and after treatment in the 4 treatment regimens.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th></th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n    III IV V</td>
<td>I    II III V</td>
<td></td>
</tr>
<tr>
<td>Acyclovir + steroids</td>
<td>12   4 1 7</td>
<td>4    5 2 1</td>
<td></td>
</tr>
<tr>
<td>Acyclovir + valaciclovir</td>
<td>1 1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acyclovir</td>
<td>1    1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>1    1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15   5 1 9</td>
<td>6    5 3 1</td>
<td></td>
</tr>
</tbody>
</table>
nerve oedema in the confined space within the facial canal or internal auditory meatus induces nerve compression and hypoxia, leading to further degeneration of the nerves. Inflammation and oedema of the paralyzed facial nerve in the Fallopian canal have been demonstrated during decompression surgery in patients with RHS.

The antiviral agent acyclovir is a nucleotide analogue that interferes with herpes virus DNA polymerase and inhibits DNA replication, preventing further proliferation or spread of VZV. Moreover, the antiedematous effect of steroids is clinically well confirmed. Thus, the combined therapy with acyclovir-steroids is expected to eliminate the oedema, to avoid immunological reactions, and to reduce proliferative formations.

It has been shown that if RHS was not treated, the recovery rate to normal facial function was very low between 21% and 31% respectively, demonstrating the poor natural outcome of the disease. In our study, the therapeutical benefit of the treatment for RHS was proved as the recovery rate after treatment was 73%. In other studies, the recovery rate to grade I and II especially after the combined therapy of acyclovir with steroids was reported to range from 80 to 85%.

Murakami et al supported the effectiveness of early treatment in RHS in a sample of 80 patients; they found that if the treatment (prednisone and acyclovir) initiated within 3 days of the onset of the disease the patients significantly improved, compared to the cases in which the treatment was delayed for more than 3 days after the onset. In the same study, it was demonstrated that there was no significant difference in facial nerve outcome between intravenous and oral acyclovir treatment.

The beneficial effect of the combined treatment of acyclovir with steroids compared to steroids alone was shown in Kinishi et al’s study in which the former treatment resulted in complete recovery to grade I in 90% of cases and in the latter in 64% of cases. Inamura et al reported no beneficial effect on facial function when only acyclovir was administered in RHS.

According to our results (Table 5), it seems that the NET predicted better the final recovery than the ENoG. It is possible that the nerve degeneration was better determined after a minimal applied electrical stimulation (NET) compared to a maximal stimulation (ENoG). Thus, a normal or diminished response on NET was in favor of good prognosis and a lack of response on NET could predict a poor recovery. In a recent study, Ikeda et al advocated that in Bell’s
palsy, RHS and zoster sine herpete, the NET response was an especially important prognostic factor of facial paralysis; in the same study\textsuperscript{29}, it was also shown that the poor recovery rate was only 3\% in patients who were normal on NET, and the poor recovery rate increased to 83\% when the NET response was absent. In agreement with our results, it was concluded\textsuperscript{29} that an abnormal response on NET was considered to be a high risk factor for the poor prognosis of facial paralysis.

In conclusion, a significant number of RHS cases may accompanied by cochleovestibular symptoms and in particular vertigo and balance disorder. Instead of the low recovery rate reported for the natural course of RHS\textsuperscript{11,16}, the combined treatment of acyclovir with steroids resulted in satisfactory recovery in 75\% of patients. Among the electrophysiological tests, the NET was demonstrated to be the most useful method in the prognostication of RHS.

ΠΕΡΙΛΗΨΗ: Το σύνδρομο Ramsay Hunt (RHS) χαρακτηρίζεται από περιφερική πάρεση ή παράλυση του προσωπικού νεύρου σε συνδυασμό με την εμφάνιση φυσιαλιώδους εξανθήματος στο εξω αυτί.

Υλικό-Μέθοδοι: Αξιολογήθηκαν 15 ασθενείς που έπαιζαν από RHS. Σε όλους τους ασθενείς έγινε λήψη ιστορικού, κλινική εξέταση και στη συνέχεια υποβλήθηκαν σε αγωγή με στεροειδή και ακυκλοβίρη. Για την εκτίμηση της λειτουργίας του προσωπικού νεύρου χρησιμοποιήθηκε το σύστημα ταξινόμησης κατά House-Brackmann (HB I-VI) καθώς και οι ηλεκτροφυσιολογικές εξετάσεις της δοκιμασίας ερεθιστότητας (NET) και ηλεκτρονευρογραφία.

Αποτελέσματα: Στο RHS, τα πιο συχνά συμπτώματα ήταν από το αυτουσοκοχλιακό σύστημα (73\%) και κυρίως η εμφάνιση ύλιγκου και διαταραχής της ισορροπίας. Η συνδυασμένη θεραπεία της ακυκλοβίρης και των στεροειδών είχε ως αποτέλεσμα την μεγάλη βελτίωση της λειτουργίας του προσωπικού νεύρου στο 75\% των περιπτώσεων. Η ανάνηση ήταν σε όλες τις περιπτώσεις ανάλογη των αποτελεσμάτων του NET. Η εξέλιξη της παράλυσης δεν ήταν ικανοποιητική σε τέσσερις περιπτώσεις στις οποίες ο NET ήταν καταργημένο.

Συμπέρασμα: Στο RHS είναι πιθανόν να λαμβάνουν χώρα νευριτιδά και οίδημα μέσα στον έσω ακουστικό πόρο, τα οποία προκαλούν πάρεση ή παράλυση του προσωπικού νεύρου και συμπίπτουν από το αυτουσοκοχλιακό σύστημα. Γι’ αυτόν το λόγο, για την θεραπευτική αντιμετώπιση του RHS συνιστάται η συνδυασμένη αγωγή των αποδηματικών στεροειδών με την αγωγή ακυκλοβίρη. Η εξέλιξη με το NET είναι η πιο ενδεδειγμένη ως προγνωστική μέθοδος γι’ αυτό το σύνδρομο.

Λέξεις Κλειδιά: Σύνδρομο Ramsay Hunt, Ωτικός έρπης ζωστήρας, Παράλυση προσωπικού νεύρου, Ακυκλοβίρη, Στεροειδή.
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