Ramsay Hunt syndrome
Otologic Seminar

R3 陳建成
James Ramsay Hunt (1872–1937)

- Hunt received his MD from the University of Pennsylvania School of Medicine in 1893.
- Hunt became a full professor at Columbia University School of Medicine in 1924.
- Deep palmar neuropathy attributed to median nerve compression, sciatica, Parkinson’s disease and the structure and function of the basal ganglia.
- Hunt has been described as “Olympian” for his contributions to our understanding of the nervous system.
Ramsay Hunt syndrome

Hunt described three discrete syndromes

• 1: First zoster oticus with peripheral facial palsy
• 2: Second Ramsay Hunt syndrome encompasses the clinical features produced by carotid artery occlusion.
• 3: Third Ramsay Hunt syndrome is dyssynergia cerebellaris progressiva
Ramsay Hunt syndrome

• The strict definition of the Ramsay Hunt syndrome:
  • 1: Peripheral facial nerve palsy
  • 2: An erythematous vesicular rash on the ear (zoster oticus) or in the mouth.
Figure 1  Clinical features of Ramsay Hunt syndrome. Note peripheral facial weakness characterised by a widened palpebral fissure and decreased forehead wrinkling and smile on the right, often associated with vesicles in the ipsilateral ear, on the hard palate, or on the anterior two thirds of the tongue.
Ramsay Hunt syndrome

- Ramsay Hunt syndrome & Bell’s palsy
- More severe paralysis at onset & less
- More severe paralysis at onset & less
- Less likely to recover completely & likely
- Varicella zoster virus (VZV) & HSV
- Steroid + anti-viral agent & steroid
Ramsay Hunt syndrome

• Unilateral facial palsy accompanied by contiguous cranial neuropathies associated with vesicles in the mouth—usually on the tongue or hard palate—or ear.

• Other regular symptoms and signs such as tinnitus, hearing loss, nausea, vomiting, vertigo, and nystagmus.
Ramsay Hunt syndrome

* These eighth nerve features by the close proximity of the geniculate ganglion to the vestibulocochlear nerve within the bony facial canal.

* Hunt surmised that the gasserian, geniculate, petrous, accessory, jugular, plexiform, and second and third cervical dorsal root ganglia comprised a chain in which inflammation of a single ganglion could extend to nearby ganglia.
Ramsay Hunt syndrome

*Selective vulnerability of blood vessels to varicella zoster virus (VZV)
  --Ascending pharyngeal artery supplies the glossopharyngeal, vagal, accessory, and hypoglossal nerves.

*Transaxonal spread of VZV from one or more cranial nerve ganglionic afferent fibres.
Epidemiology

- Ramsay Hunt syndrome is the second most common cause of atraumatic peripheral facial paralysis.

- 2076 patients presenting with unilateral facial palsy, in Japan. It was diagnosed in 16.7% of children and 18.1% of adults with facial palsy.

- Reactivation of VZV is thought to occur in 2–25% of patients with ‘Bell’s palsy’ (zoster sine herpete).
Zoster sine herpete

• Normally defined as localised radicular pain with virological evidence of VZV infection.
• Ramsay Hunt syndrome zoster sine herpete is characterised by peripheral facial paralysis without ear or mouth rash, and the presence of either a fourfold rise in antibody to VZV or the detection of VZV DNA in skin, blood mononuclear cells, or middle ear fluid.
Zoster sine herpete

- Hato *et al*, 1705 patients with ipsilateral facial palsy without vesicles, the data imply that 42 patients (2.4%) had zoster sine herpete.

- Morgan *et al* found that 9.3% of patients with Bell’s palsy seroconverted to VZV.

- Thus, a small proportion of patients with” Bell’s palsy” have zoster sine herpete.
Virology

- Primary VZV infection usually produces chickenpox after which the virus becomes latent in neurons of cranial nerve ganglia and dorsal root ganglia along the entire neuraxis.
- Latent VZV DNA is extra-chromosomal (nonintegrated), probably in a circular or concatameric (end to end) configuration.
Virology

- At least five VZV genes, corresponding to open reading frames 4, 21, 29, 62, and 63, are transcribed.

- One VZV protein corresponding to gene 63 is expressed in latently infected ganglia.
Natural history

- A retrospective study of 102 untreated patients with Ramsay Hunt syndrome:
  - Partial clinical or electrical function at onset
    - 66% recovered completely.
  - Complete loss of clinical and electrical function
    - 10% recovered completely, (all with residual synkinesis).
Natural history

* In patients with complete facial paralysis and a partial electrical response: oral synkinesis in 70%, eyelid synkinesis in 60%.

* In patients with incomplete paralysis both electrically and clinically, oral synkinesis in 10% and eyelids synkinesis in 15%.
Natural history

• HIROSHI AIZAWA et al:
• In patients with oropharyngeal zoster lesions, the VZV load in saliva is extremely high and the recovery from facial paralysis is worse than in patients who have zoster lesions only on the skin.
• These results suggest that the VZV DNA level in saliva reflects the kinetics of viral reactivation in the facial nerve.
Natural history

Fig. 1. The distribution of times of appearance of zoster relative to the onset of facial paralysis. Day 0 is the day of appearance of facial paralysis.
Natural history

**TABLE I. Patterns of Salivary VZV DNA Positivity and Load**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of VZV DNA-positive patients at the onset of facial paralysis</th>
<th>Patterns of VZV load in saliva</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gradually decrease</td>
<td>Increase after the initial visit</td>
</tr>
<tr>
<td>I (n = 13)</td>
<td>4 (31%)</td>
<td>4</td>
</tr>
<tr>
<td>II (n = 22)</td>
<td>16 (73%)</td>
<td>9</td>
</tr>
<tr>
<td>III (n = 7)</td>
<td>5 (71%)</td>
<td>1</td>
</tr>
<tr>
<td>Total (n = 42)</td>
<td>25 (60%)</td>
<td>14</td>
</tr>
</tbody>
</table>

**TABLE II. Antibody Responses to VZV**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients with high IgG or positive IgM antibodies at the onset of facial paralysis</th>
<th>No. of patients with fluctuations of antibody titers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High IgG antibody</td>
<td>Positive IgM antibody</td>
</tr>
<tr>
<td>I (n = 11*)</td>
<td>10 (91%)</td>
<td>8 (73%)</td>
</tr>
<tr>
<td>II (n = 21*)</td>
<td>11 (52%)</td>
<td>9 (43%)</td>
</tr>
<tr>
<td>III (n = 7)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total (n = 39)</td>
<td>21</td>
<td>16</td>
</tr>
</tbody>
</table>

*Paired sera were not obtained from two patients in group I and from 1 patient in group II. Anti-VZV IgG antibodies were considered to be high if the ELISA value was $50 \times 10^2$ mIU/ml or more.
Natural history
Natural history

- Time of onset of facial paralysis may differ in different patients:
  1: Differences in the causes of neuritis,
     --- direct damage of the nerve by VZV
     --- an immune-mediated post-infection process
  2: The anatomical variation in the facial nerve and the fallopian canal
Natural history
In children

Table 1. Frequency of Ramsay Hunt Syndrome in Children

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Preschool children</td>
<td>5/86 a (5.8%)</td>
<td>13/85 a (15.3%)</td>
<td>18/171 a (10.5%)</td>
</tr>
<tr>
<td>Elder children</td>
<td>14/59 (23.7%)</td>
<td>20/81 (24.7%)</td>
<td>34/140 (24.3%)</td>
</tr>
<tr>
<td>Adults</td>
<td>111/778 (14.3%)</td>
<td>208/987 (21.1%)</td>
<td>319/1765 (18.1%)</td>
</tr>
</tbody>
</table>

*a p < 0.05.

RHS is not a major cause of facial palsy in preschool children.
Natural history
In children

Fig 1. Timing of herpetic vesicle appearance on the auricle in children and adults. The simultaneous palsy means the vesicle appearance within 2 days before and after the onset of the facial palsy.

Children
n=32

- 11 (34.4%)
- 16 (50.0%)
- 5 (15.6%)

Adults
n=213

- 42 (19.7%)
- 103 (48.4%)
- 68 (31.9%)

■ before palsy ■ simultaneous ■ after palsy

Fig 2. Prognosis of facial palsy in children and adults. The ratio of complete recovery to grade I in House-Brackmann grading system (H-B grade) was significantly different between children and adults; children showed better prognosis than adults (p < 0.05).

Children
n=42

- 33 (78.6%)
- 7 (16.6%)
- 2 (4.8%)

Adults
n=173

- 85 (49.1%)
- 55 (31.8%)
- 29 (16.8%)
- 4 (2.3%)

■ H-B grade I ■ grade II ■ grade III ■ grade IV

Table 2. VIII, IX, and X Cranial Nerve Dysfunction

<table>
<thead>
<tr>
<th>VIII Nerve Symptoms</th>
<th>IX and/or X Nerve Symptoms</th>
</tr>
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<tbody>
<tr>
<td>Hearing Loss</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Children</td>
<td>11/45 (24.4%)</td>
</tr>
<tr>
<td>Adults</td>
<td>125/237 (52.7%)</td>
</tr>
</tbody>
</table>
Natural history
In children

• 1: The facial palsy was milder and complete recovery of the function was achieved in 78% in children. (49% in adults)
• 2: Cranial neuropathies were less common in children than in adults.
• 3: The timing of vesicle appearance tended to be delayed in children
• 4: Serial audiograms showed complete recovery in 37.7% of adults, and 66% of children with complete recovery.
Diagnosis

- The history and neurological examination remain the bases for diagnosing Ramsay Hunt syndrome. (Facial paralysis, ear pain, and herpetic eruptions).

- Seroconversion of VZV immunoglobulin IgG antibody: In the acute phase & convalescent phases---more than fourfold.

- IgM or IgA antibody titers: diagnostic value remains obscure.
Diagnosis

• However, the vesicles of this disease are sometimes absent (zoster sine herpete) or may appear several days after the onset of facial palsy.

• A study: 325 patients with Ramsay Hunt syndrome, one-third developed herpetic eruption 2 to 14 days after the onset of facial palsy.
Figure 1. Collection of exudate of auricular skin. After scratching the interior surface of the geniculate zone on the auricle with a needle, exudate of auricular skin was absorbed with a sterilized Schirmer’s strip.
Diagnosis

• In all 12 patients with typical Ramsay Hunt syndrome patients. (Specific VZV DNA)
  Vesicle specimens (100%)
  PBMC specimens (50%),
  Tear fluid specimens (75%)
• In 7 patients with Ramsay Hunt patients without vesicles at the initial visit
  Auricular skin exudate (71%)
  PBMC specimens (29%)
  Tear fluid specimens (29%).
Diagnosis

- PCR analysis of VZV DNA in exudate of the auricular skin can be a rapid and useful diagnostic tool for identification of VZV infection in acute peripheral facial palsy without herpetic eruption.

- PCR to detect VZV in exudates from the geniculate zone of the ear is more sensitive than VZV PCR performed on tears or blood mononuclear cells.
Diagnosis

- Gadolinium enhanced MRIs have had no diagnostic or prognostic value.

- A case report: High concentrations of protein in the inner ear are associated with hearing deterioration in some patients with Ramsay Hunt syndrome- 3D-FLAIR MRI shows high signal which were not detected by T1- and T2-weighted MRI.
Treatment

• Acyclovir (800 mg five times daily) shortened the duration of viral shedding, halted the formation of new lesions more quickly, accelerated the rate of healing, and reduced the severity of acute pain.

• Corticosteroids in combination with acyclovir resulted in an improved prognosis.
Treatment

• Corticosteroid therapy should not be used in patients at risk for corticosteroid-induced toxicity (e.g., patients with diabetes mellitus or gastritis).

• The use of corticosteroids for herpes zoster without concomitant antiviral therapy is not recommended.
Treatment

- Three drugs — acyclovir (Zovirax), valacyclovir (Valtrex), and famciclovir (Famvir) — are approved in the United States for the treatment of herpes zoster.

<table>
<thead>
<tr>
<th>TABLE 1. RECOMMENDED ORAL ANTIVIRAL THERAPY FOR HERPES ZOSTER IN IMMUNOCOMPETENT ADULTS WITH NORMAL RENAL FUNCTION.</th>
</tr>
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<tbody>
<tr>
<td>Acyclovir, 800 mg every 4 hours (5 times daily) for 7 to 10 days</td>
</tr>
<tr>
<td>Famciclovir, 500 mg every 8 hours (3 times daily) for 7 days</td>
</tr>
<tr>
<td>Valacyclovir, 1000 mg every 8 hours (3 times daily) for 7 days</td>
</tr>
</tbody>
</table>
Treatment

- Valacyclovir, a prodrug of acyclovir, produces serum acyclovir levels that are three to five times as those achieved with oral acyclovir therapy.
- Valacyclovir (1000 mg every eight hours) and acyclovir (800 mg five times daily) resulted in equivalent rates of cutaneous healing.
- Valacyclovir and famciclovir were compared for the treatment of herpes zoster in immunocompetent patients and were shown to be therapeutically equivalent.
- Combination therapy using valacyclovir or famciclovir with corticosteroids is assumed to be equally effective.
Treatment

- Murakami S, et al 1997, 80 patients
- Less than 3 days, 3–7 days, and after 7 days.
- Oral prednisone (1 mg/kg/day for 5 days followed by a 10 day taper), as well as with intravenous acyclovir (250 mg three times daily), or oral acyclovir (800 mg five times daily).
- Complete recovery
  75% : first 3 days (p<0.05)
  48% : 4–7 days
  30% : after 7 days
Treatment

- The retrospective Ramsay Hunt syndrome treatment study showed a statistically significant improvement in patients treated with prednisone and acyclovir within 3 days of onset.
- No statistically significant differences were noted among patients treated with intravenous or oral acyclovir.
Reference