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7 **Ramsay Hunt Syndrome Associated with Varicella-Zoster Virus Encephalitis**
8 **in a Child**

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15
16 **Abstract**

17 Ramsay Hunt Syndrome (RHS) is a triad of peri-auricular pain, ipsilateral facial nerve palsy and
18 vesicular rash around the ear pinna. It is caused by reactivation of varicella-zoster virus (VZV)
19 that lies dormant in the geniculate ganglia. It can be complicated by VZV encephalitis rarely. We
20 report the case of an 8-year-old previously healthy boy who presented to a tertiary care hospital
21 in Muscat, Oman in 2021 with fever, progressive left ear pain, vesicular rash around his ear
22 pinna and left-sided facial nerve palsy. His course was complicated by VZV encephalitis where
23 he was managed with IV acyclovir and IV corticosteroids. He improved significantly and was
24 asymptomatic with a normal neurology examination at the 6-months follow-up.

25 **Keywords:** Varicella Zoster Virus; Ramsay Hunt Syndrome; Encephalitis; Children.

26
27 **Introduction**

28 Ramsay Hunt syndrome (RHS), which is also known as geniculate neuralgia, is caused by
29 reactivation of varicella zoster virus (VZV) that lies dormant in the geniculate ganglion after the
30 primary infection with chickenpox.¹⁻³ It was described for the first time by James Ramsay Hunt,

31 an American neurologist in 1907.³ It tends to be less frequent and less severe in children
32 compared to adults but there is limited data on how to manage pediatric RHS.⁴ It is responsible
33 for about 16.7% of cases of facial paralysis in children and it can be complicated rarely with
34 encephalitis.^{1,3,5} RHS has a low incidence in children with a rate of 2.7/100.000 in younger than
35 10 years of age, and is more common in children 6 to 15 years of age.³

36

37 **Case Report**

38 An 8-year-old previously healthy boy presented to the emergency department of a tertiary care
39 hospital in Muscat, Oman, in 2020 with a 3-day history of fever, progressive left ear pain and
40 swelling and vesicular rash around the left ear pinna. In addition, he had poor oral intake but no
41 seizure or behavioral changes. There was no history of a previous chicken pox, recent travel or
42 any sick contacts. No history of recurrent ear infections, ear trauma or swimming in a pool was
43 given. His immunization was up-to-date and he got the varicella vaccine at 12 months of age as
44 per Oman's immunization schedule.

45

46 Upon initial examination, his left ear was swollen with redness extended to the pre-auricular and
47 postauricular area. He had vesicular lesions with red base on the outer ear canal, extending to the
48 left side maxillary dermatome, with yellowish discharge as well as tender enlarged left cervical
49 node (2 x 3 cm) Figure (1). His throat was clear and the examination of his right ear was
50 unremarkable.

51

52 Laboratory investigations showed normal full blood count, C-reactive protein, serum electrolytes
53 and random blood sugar. Based on the clinical findings, Ramsay Hunt syndrome diagnosis was
54 made and Acyclovir (450 mg orally every 6 hours) was started. Varicella zoster virus (VZV)
55 polymerase chain reaction (PCR) from the ear swab was reported positive while both bacterial
56 culture and Herpes simplex PCR were negative. The patient developed lower motor neuron facial
57 nerve palsy on day 2 of admission and later developed dizziness and he was noticed to be more
58 sleepy. On day 3 of admission, he developed vomiting, dysarthria and unsteady gait. No changes
59 in personality, seizures, meningeal signs or motor or sensory deficits were reported. At this stage,
60 Acyclovir was switched to intravenous formulation (15 mg/kg/dose 8 hourly) and prednisolone 1
61 mg/kg daily was added. He also underwent an urgent brain magnetic resonance imaging (MRI)

62 and magnetic resonance venography (MRV) and both were reported to be normal. Cerebrospinal
63 fluid was obtained and it showed 10 leukocytes (8 mononuclear cells and 2 polymorphonuclear
64 cells), and 2 red cells with normal protein and glucose. Bacterial culture was negative and VZV
65 PCR reported positive from the cerebrospinal fluid. In the following few days, his ear pain,
66 swelling, vomiting and the unsteady gait improved significantly and was asymptomatic on
67 discharge. He received 10 days of intravenous Acyclovir and 7 days of prednisolone of
68 1mg/kg/day. Eye care and physiotherapy was provided. He remained completely asymptomatic
69 and had a normal MRI with no evidence of cerebral arteritis vasculopathies on the 6 months
70 follow-up. Paternal consent was obtained for publication purposes.

71

72

73 **Discussion**

74 Ramsy hunt syndrome is uncommon in children. Our patient had a classic presentation on
75 admission. RHS is characterized by a triad of periauricular pain, ipsilateral peripheral facial
76 nerve palsy and erythematous vesicular rash around the ear pinna and outer ear canal or in the
77 oral mucosa.⁵ The clinical symptoms begin with otalgia which can last for 1 to 3 days.^{1,4,5} Facial
78 nerve palsy usually develops within 1–2 weeks after the rash appearance.³ RHS can affect both,
79 the facial and vestibulocochlear nerves.⁵ If the vestibulocochlear nerve gets affected, the patient
80 can develop nausea, vomiting, vertigo, tinnitus, and nystagmus.^{1,5} Hearing loss is reported in
81 24% of children with RHS.³ Our patient has normal hearing during his presentation and on
82 follow-up.

83

84 RHS is usually diagnosed clinically.³⁻⁵ Our patient presented with classic symptoms of RHS so
85 acyclovir was started from the beginning. Laboratory and imaging investigations are not
86 necessary to make the diagnosis most of the time and they do not affect the patient's outcomes.⁵
87 Confirming diagnosis can be done using molecular testing from skin lesions and this can be
88 considered when the diagnosis of RSH is doubtful. The use of serum anti-VZV IgG and IgM
89 antibody titers is recommended for the routine laboratory diagnosis of pediatric patients with
90 acute peripheral facial paralysis.^{3,5}

91

92 Childhood immunization with varicella vaccine can reduce the risk of getting RHS.⁴ Although
93 our patient had varicella vaccine at 12 months of age but he still developed RHS. He has no clear
94 history of chickenpox in the past, so RHS either resulted from a reactivation of subclinical
95 infection in the past or because of a vaccine-related strain.

96
97 RHS carry worse prognosis compared to Bell's palsy in children.⁵ Advanced facial paralysis at
98 presentation, audiovestibular findings and delayed treatment are unfavorable prognostic factors.¹
99 Early treatment with Acyclovir and high-dose corticosteroid therapy should be considered in all
100 patients with RHS.³ The combination of Acyclovir (for 7 -10 days) and corticosteroid therapy
101 has been found to be more effective than treatment with Acyclovir alone.^{1,3,5} Acyclovir inhibits
102 viral replication and help with rapid healing of lesions and corticosteroids help with reducing
103 edema and pain by reducing the inflammation in peripheral neurons.³ Hato et al. and his
104 colleagues examined the recovery of facial nerve function after initiating treatment in the first
105 three days, at 3–7 days, or later than seven-days and found that the recovery was better when
106 Acyclovir was started within 3-days of presentation. The recovery rates were 75, 48, and 30%,
107 respectively.⁶ Full recovery from RHS-related facial paralysis has been reported to vary between
108 27 and 70% even with early treatment.⁵ Our patient improved significantly and he was
109 asymptomatic with normal neurology examination at the 6-months follow-up after using the
110 combination of Acyclovir and corticosteroids.

111
112 Our patient's course was complicated by VZV encephalitis. He was sleepy, lethargic, and
113 complaining of headache and vomiting. His physical examination showed signs of cerebellar
114 involvement manifested as a wide-base gait with unsteadiness and dysarthria. Although some of
115 these symptoms can be explained by vestibular involvement, however, the headache, lethargy,
116 sleepiness, and wide base gait cannot be explained by vestibular involvement alone. The
117 constellation of these symptoms along with the isolation of VZV from cerebrospinal fluid
118 support the diagnosis of encephalitis. Although most of the reported patients with Ramsay Hunt
119 Syndrome associated with encephalitis, have abnormal MRI-brain, Ricigliano et al reported that
120 around 31% of patients with RHS-associated encephalitis have negative MRI-brain. Therefore,
121 normal MRI-brain in the context of RHS- associated varicella encephalitis does not exclude this
122 diagnosis.⁷

123
124 VZV can affect CNS disease through 3 mechanisms including acute VZV encephalitis, post-
125 VZV cerebellitis and VZV vasculopathy.^{2,5} Development of VZV encephalitis following RHS is
126 extremely rare in an immunocompetent patient, which is the case in our patient.^{2,3,5,8} The
127 available literature report only 6 adults with RHS complicated by VZV encephalitis and 2 of
128 them are immunocompetent.⁸⁻¹⁰ We could not find any pediatric cases of RHS complicated by
129 VZV encephalitis. Hematogenous spread of VZV to the central nervous system or dissemination
130 through the cerebrospinal fluid pathway has been hypothesized which could be the case in our
131 patient.⁸

132
133 Acyclovir-induced encephalopathy should be considered in the differential diagnosis of our
134 patient encephalopathy. Furthermore, this adverse effect is more common in patients with renal
135 insufficiency, which is not the case in our patient.¹¹ The main treatment of this entity is dialysis
136 along with cessation of acyclovir.¹¹ Our patient showed improvement of his clinical symptoms
137 without any dosing adjustment, and he improved before the end of the acyclovir course.
138 Therefore, it is unlikely for his presentation to be secondary to acyclovir-induced
139 encephalopathy.

140
141 There is limited data on how to manage VZV encephalitis. The Association of British
142 Neurologists and British Paediatric Allergy, Immunology and Infection Group recommend
143 giving intravenous Acyclovir (500 mg/m² if 3 months -12 years of age or 10 -15 mg/kg in > 12
144 years of age) for management of VZV encephalitis in children for total of 10 - 14 days.² In
145 immunocompromised patients with VZV encephalitis, prolonged course of antivirals may be
146 required.² If vasculopathy present, then it is recommended to use corticosteroids with or without
147 Acyclovir.² The limitation of this report is that we could not prove that our patient has RHS-
148 associated encephalitis because he has a normal MRI. The CSF pleocytosis can accompany
149 nerve inflammation. The mild clinical syndrome and the normal MRI may be secondary to early
150 initiation of antiviral therapy and corticosteroids in our patient.

151
152 **Conclusion**

153 Careful examination and early trial of treatment with antiviral therapy and corticosteroids should

154 be considered in children with RHS. VZV encephalitis, although uncommon, can complicate
155 RHS in children.

156

157 **Authors' Contribution**

158 Dr Eman Ahmed wrote the first draft which was directly supervised by Dr Laila Al Yazidi. All
159 other co-authors helped with the literature review and the manuscript writing and revision.

160

161 **References**

- 162 1. Derin S, Derin H, Sahan M, Caksen H. A pediatric case of ramsay hunt syndrome. Case
163 Rep Otolaryngol. 2014;2014:469565. <https://doi.org/10.1155/2014/469565>
- 164 2. Kneen R, Michael BD, Menson E, Mehta B, Easton A, Hemingway C, et al.
165 Management of suspected viral encephalitis in children - Association of British
166 Neurologists and British Paediatric Allergy, Immunology and Infection Group national
167 guidelines. J Infect. 2012 May;64(5):449–77. <https://doi.org/10.1016/j.jinf.2011.11.013>
- 168 3. Aydoğdu İ, Ataç E, Saltürk Z, Atar Y, Özdemir E, Uyar Y, et al. Pediatric Ramsay Hunt
169 Syndrome: Analysis of Three Cases. Case Rep Otolaryngol. 2015;2015:1–4.
170 <https://doi.org/10.1155/2015/971249>
- 171 4. Masukume G, Chibwowa S, Ndlovu M. Full recovery of a 13-year-old boy with pediatric
172 Ramsay Hunt syndrome using a shorter course of aciclovir and steroid at lower doses: a
173 case report. J Med Case Reports. 2011;5:376. <https://doi.org/10.1186/1752-1947-5-376>
- 174 5. Çiçek M, Kılıç Z, Mercen Y, Karaoğlan E, Öztarhan K. A Rare Cause of Facial Paralysis
175 in Children: A Case of Ramsay Hunt Syndrome. J Pediatr Neurol. 2021;19(1):43–
176 5.<http://doi.org/10.1055/s-0040-1719052>.
- 177 6. Hato N, Matsumoto S, Kisaki H, Takahashi H, Wakisaka H, Honda N, et al. Efficacy of
178 Early Treatment of Bell's Palsy With Oral Acyclovir and Prednisolone: Otol Neurotol.
179 2003;24(6):948–51.
- 180 7. Ricigliano VAG, Saraceno L, Cavalli M, Rodegher M, Meola G. Slowly progressing
181 varicella zoster brainstem encephalitis complicating Ramsay Hunt syndrome in an
182 immunocompetent patient: case report and review of literature. J. Neurovirol.
183 2017;23(6):922-928. Doi: 10.1007/s13365-017-0575-3.

- 184 8. Chan TLH, Cartagena AM, Bombassaro AM, Hosseini-Moghaddam SM. Ramsay Hunt
185 Syndrome Associated with Central Nervous System Involvement in an Adult. *Can J*
186 *Infect Dis Med Microbiol* ;2016:1–4. <https://doi.org/10.1155/2016/9859816>
- 187 9. Elshereye A, Erdinc B, Sahni S. Disseminated Varicella-Zoster Virus Infection
188 Complicated by Encephalitis and Ramsay Hunt Syndrome in an HIV Patient. *Cureus*.
189 2020;12(7):e9235. <https://doi.org/10.7759/cureus.9235>
- 190 10. Shen YY, Dai TM, Liu HL, Wu W, Tu JL. Ramsay Hunt Syndrome Complicated by
191 Brainstem Encephalitis in Varicella-zoster Virus Infection. *Chin Med J (Engl)*.
192 2015.;128(23):3258–9. <https://doi.org/10.4103/0366-6999.170275>
- 193 11. Sakamoto H, Hirano M, Nose K, Ueno S, Oki T, Sugimoto K, et al. A case of severe
194 ganciclovir-induced encephalopathy. *Case Rep Neurol*. 2013;5(3):183-6. doi:
195 10.1159/000355638.

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198 **Figure 1:** Shows redness, swelling and crusting of the left ear associated with vesicular rash in
199 the maxillary dermatome.