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Ramsay hunt syndrome with multiple cranial nerve involvement: A rare case

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***Abstract*---**Ramsay Hunt Syndrome (RHS) is characterized by vesicles in external auditory canal, ear discomfort, and facial nerve palsy in the periphery. RHS which affects multiple cranial nerve involvement has rarely happened. This study is about RHS case that affect right multiple cranial nerves VI, VIII, IX, X. A 46-year old male patient complaint of crust and pain from right ear lobe. There were complaints of decreased hearing ability, tinnitus, difficulty to swallow, double vision, incapability of closing the right eyelid, and a facial slight *palsy* to the right. Multiple yellowish crusts and erosions were identified. Tzanck and Polymerase Chain Reaction test were not performed. Patient was diagnosed RHS with right multiple cranial nerves VI, VIII, IX, X, received Acyclovir and Prednisone tablets for 7 days. Patient improved. This finding showed that a detailed history taking, physical and additional examinations are required for accurate diagnosis for RHS multiple cranial nerve involvement.

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Introduction

Ramsay Hunt Syndrome (RHS) is a rare disorder. It manifests a complication of the Varicella Zoster Virus (VZV). Varicella zoster virus arises in the geniculate ganglion of VII cranial nerve (Crouch et al., 2020). Nerves communicate with the facial nerves, such as CNs V, VI, VIII, IX, X, XI, XII are also could be involved (Kanerya et al., 2020). Ramsay Hunt Syndrome has three features, those are otalgia, vesicles in the auditory canal, and ipsilateral facial palsy. These could be identified through the affected side of the face, hard palate, and tongue (Crouch et al., 2020).

Ramsay Hunt Syndrome affects 5 per 100.000 individuals in the United States. However, it is rare that RHS associates multiple cranial nerve involvement. It has been reported to be 1.8-3.2%. Females are affected 20% more frequently than males, but in some cases, there are no differences (Saho et al., 2016; Wijaya et al., 2019). There is no specific data in Indonesia for incidence rate of RHS. However, the Dermatology and Venereology Department, Dr. Soetomo General Academic Hospital, Surabaya had conducted a retrospective study in 2010-2013 that had found the incidence rate of RHS was about 3.9% (Ayuningati et al., 2015).

Ramsay Hunt Syndrome is responsible for 12% of facial nerve palsy cases. Also, could affect anyone, ranging from 3 months old to 82 years old individuals.[1] Ramsay Hunt Syndrome has some complications, such as bacterial secondary infection, postherpetic neuralgia, exposure keratitis and ulcers. Exposure keratitis and ulcers are caused by impairment of eyelid closure due to paresis CN VII. In addition, Paresis of CN VIII effects permanent facial palsy, long term ipsilateral hearing loss, and tinnitus (Worme, et al., 2013).

Ramsay Hunt Syndrome, especially with cranial nerve involvement, has some symptoms that do not occur simultaneously. It leads to misdiagnoses to other similar diseases, such as Bell's palsy, middle ear infections, Lyme disease, stroke or tumor. Early diagnosis is needed to start adequate treatment as soon as possible. Whenever adequate therapy is initiated within 72 hours of the beginning of facial paresis, full recovery might range from 27.3% to 70%. However, if treatment were not initiated within 72 hours, full recovery could drop to 50% (Crouch et al., 2020).

We would like to report a RHS case with the involvement of CN VI, VIII, IX and X. This report discusses accurate anamnesis and physical examination to enable diagnosing RHS with cranial nerve involvement and prescribe proper therapy to minimize complications.

Case Report

A 46-year old male hospitalized on December 25th 2020 in Otorhinolaryngology Department Dr. Soetomo General Academic Hospital, Surabaya with the diagnosis of right Chronic Suppurative Otitis Media (CSOM) malignant type, right paresis of nerves VI and VII suspected Gradenigo's Syndrome, House Brackmann (HB) IV, Paresis of CN IX, X. A day after, patient consulted to Dermatology and Venereology Department with complaints of crusts and pain on the right ear lobe.

On December 5th 2020, patient complained of pain, itchiness and burning sensation on his right ear and neck. A week after, patient complained of blisters on the right ear that grew and spread. Blisters burst out and crusted. Patient also coughed and suffered common cold with clear, unsmelled and discolored fluid discharge on his right ear. In mid December 2020, gradual hearing problems, difficulty to swallow, and face pointed rightward without weakness on his extremities existed. Patient could not raise his right eyebrow, right forehead was not able to wrinkle, and had difficulty to smile. There was double vision and the right eye could not close perfectly. No history of seizure, diabetes mellitus, hypertension, tumor, trauma, nor varicella vaccine and no varicella nor the same disease before.

Physical examination identified face pointed rightward with no lingual palsy. There was restriction to lateral right eye movement, indicated peresis of CN VI. Patient could not raise right eyebrow, and right forehead was not able to wrinkle. He had difficulty to smile, grimace nor whistle. His eyelid could not close perfectly. It indicated of paresis CN VII. Patient was attached to nasogastric tube (NGT) because of dysphagia, which indicated paresis of CN IX, X. No edema nor weakness on his extremities. Also, no enlargement of cervical, axillar, inguinal, even genital lymph nodes.

From dermatological examination on his right ear, multiple yellowish crusts and erosion were noted. No signs of new vesicles, bullae, nor pus. On his lips, mouth and tongue no blisters were found.

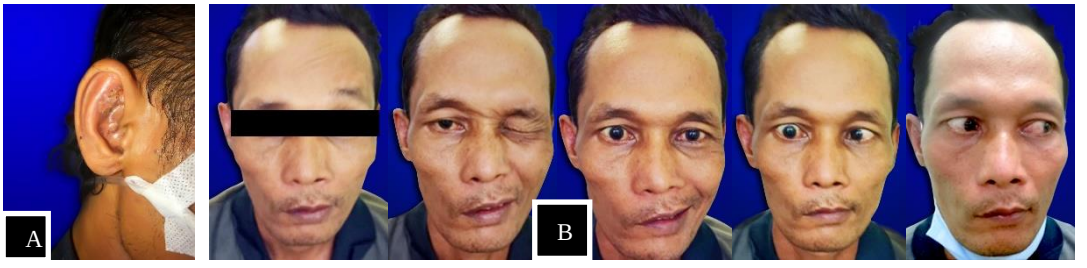

Figure 1. Patient's condition before treatment. (A) On the right ear, there were multiple yellowish crusts and erosion. There were no new vesicles, bullae, nor pus. (B) Patient's motoric test, it indicates that right CN VI and VII suffer from paresis

Otorhinolaryngology examination revealed purulent secrets without perforation in tympanic membrane, while hearing ability decreased. It could indicate paresis CN

VIII. Indirect laryngoscope examination notified hypersalivation. Schirmer's test result was abnormal, indicating paresis of CN VII. Neurological examination of CN III, IV, VI proved that there was abnormality on right eyeball movement, revealing the presence of the paresis of CN VI. Patient could not raise his right eyebrow, and right forehead was not able to wrinkle. He had difficulty smiling, grimacing and whistling. This condition showed there was right facial palsy peripheral type in CN VII. Pharyngeal reflex was negative on CN IX, X examination.

Ophthalmology examination proved there was lagophtalmus. Fluorescence test in the right cornea was positive. It indicated keratitis that might due to lagophthalmos. It could be because of paresis of CN VII. There was diplopia caused by lateral restriction of the ocular motility on the right eye. It meant that there was paresis of CN VI.

The Tzanck and Polymerase Chain Reaction (PCR) test were not performed because the lesions were crusts. Furthermore, no new vesicles were found. Result of Computerized Tomography Scan (CT-Scan) on December 25th 2020, might represent acute mastoiditis overlying right intra mastoid facial nerve. There was no abnormality of os petrous temporal, visible infarction, bleeding, mass nor infectious process on visualized brain parenchyma.

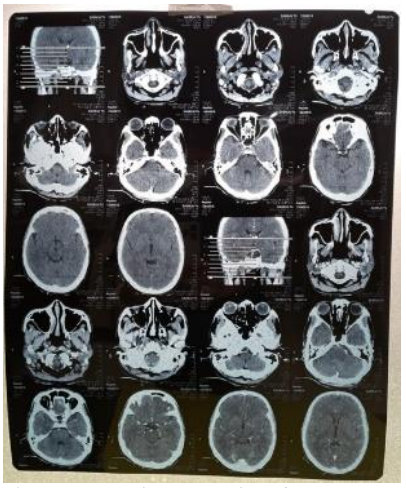

Figure 2. The result of CT-Scan

Patient was diagnosed with Herpes Zoster Oticus crust stage (RHS) and was prescribed Acyclovir tablet 5x800 mg for 7 days, Prednisone tablet 5mg 3x2 tablet for 7 days, Fucidic Acid cream 2x daily on the erosion lesions, and wet dressing with NaCl 0.9% 2x daily on the crusted lesions. Further, Otorhinolaryngology Department diagnosed of RHS with right multiple cranial palsy CN VI, VIII, IX, X, HB IV due to CT-Scan result. Patient was prescribed Ceftriaxone injection 2x1 gram, Metamizole injection 3x1 gram, Vitamin B complex 1x1 tablet. In addition, Ophthalmology Department diagnosed of lagophthalmos with exposure keratitis complication et causa paresis of CN VII, right binocular diplopia et causa paresis of CN VI et causa suspect RHS dd Gradenigo's Syndrome. Patient was prescribed Chloramphenicol eye ointment every 8 hours on right eye and tapping with plaster on right eye. Neurology Department assessed patient with compos mentis

condition without meningeal sign, but there was focal neurological deficit as right abducens palsy and right facial palsy peripheral type. These conditions might be caused by right Bell's palsy with right abducens palsy due to mastoiditis and right CSOM malignant type. Patient was prescribed Vitamin B tablets 2x50mg, Vitamin B6 tablets 2x10mg, Vitamin B12 tablets 2x50mg and undergone physiotherapy. Based on history taking, physical and additional examination from all of Department, patient was diagnosed RHS with right multiple cranial palsy CN VI, VIII, IX, X.

Figure 3. Condition of patient after 8 days of treatments - facialis region was slight palsy. The dermatology state after treatment - on right ear region, there were erosions but improved. There were no signs of new vesicles, bullae, nor pus. There were no blisters found on mouth and tongue.

On February 25th 2021, reported there were no erosions, crust, nor new vesicles on his right ear. There was no pain on his right ear nor neck. No more complaint of tinnitus and double vision. Hearing loss still persisted and facial palsy improved. Last results of FEES examination that patient was able to swallow some food and no coughing. Patient had taken off NGT. Since there was no complaint related to skin problems, the Dermatology and Venereology Department did not prescribe any therapies.

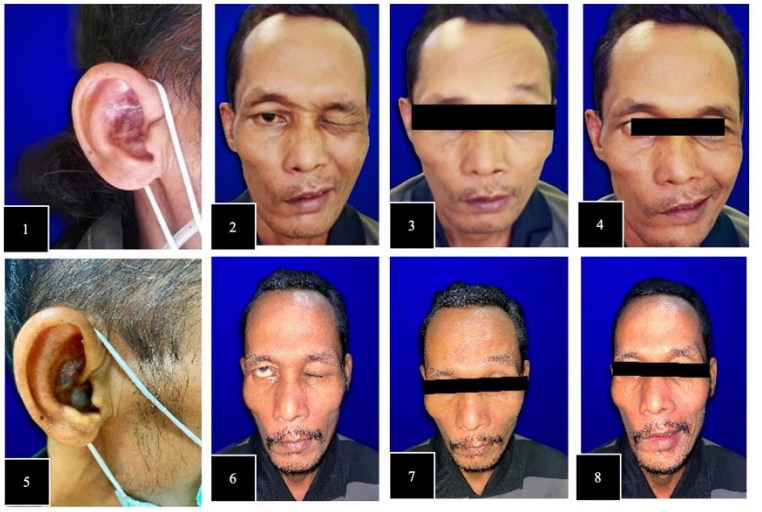

Figure 4. The above are eight pictures of patient. Pictures 1 to 4 were taken on the first hospitalization, December 24th 2020. Pictures 5-8 After 2 months of therapies in outpatient clinic.

Discussion

Ramsay Hunt Syndrome (RHS) is a rare condition that manifests a complication of the *Varicella Zoster Virus* (VZV). It associates with acute peripheral paresis of CN VII. While paresis of CN VI rarely occurs, other cranial nerves, such as CN V, IX, X, XI, and XII may involve. Ramsay Hunt Syndrome is characterized by otalgia, peripheral facial nerve paresis, and herpes zoster lesions on the external auditory tract, also in the concha of the ear, oral mucosa, and its environs (Wagner *et al.*, 2012; Crouch *et al.*, 2020).

In varicella, the VZV spreads from lesions on the skin and mucosal surfaces to sensory nerve ends. From the sensory fibers to the sensory ganglia, VZV spreads. Viruses persist latent infections in neurons ganglia. Density of latent VZV is greatest in ganglia innervating skin regions with the highest incidence of varicella lesions (Levin *et al.*, 2019).

In RHS, the VZV reactivation on the CN VII through the geniculate ganglion. It was reactivated with pressure and subsequent neural inflammation. Any possible destruction of facial nerve in the temporal bone could cause facial palsy. A viral prodrome or an upper respiratory tract infection might be the first symptoms. Viral prodrome evolves severe pain in the pinna, acute facial hypotonia, also a herpetiform vesicular eruption on the pinna, and external acoustic meatus. It could also evolve face, tongue, hard palate, neck, larynx, and oral mucosa. Cochleovestibular impairment, such as hypoacusis, tinnitus, and vertigo might occur (Ametati *et al.*, 2019). Concurrent involvement of CN V, IX, X, XI, XII rarely happens. The involvement leads to various symptoms of neurological deficits. Although the mechanism is unclear, vasculitis in the carotid, middle meningeal, and ascending pharyngeal arteries which could be infected by the direct perineural spread of the VZV along anastomotic pathways, may participate in to the development of cranial polyneuropathy in RHS (Lee *et al.*, 2017)

RHS diagnosis is mainly based on patient's history, physical examination and additional examinations. RHS clinical symptoms are otalgia, nausea, vomiting, lack of hearing and tasting (Jeon *et al.*, 2018; Crouch *et al.*, 2020). In this case, patient complained of otalgia, itching and burning sensation in the right ear, a week before vesicle lesions appeared. Few days after, patient suffered from hearing loss.

From physical examination, there were lesions in the forms of vesicles involving the eardrum, external auditory canal and conchae (Shim *et al.*, 2011). Other examination revealed peripheral facial palsy. Also, cranial nerves could involve (Yang *et al.*, 2018). In this case, patient complained of blisters on the right ear then burst out. Upon examination, there were only crusts. The involvement of paresis of CN VI, VIII, IX and X was also identified.

Facial nerve palsy is identified by facial weakness on the afflicted side, such as diminished forehead wrinkling, difficulty to close eyes, drooping corner of the mouth, and loss of motor control of facial muscles, resulting in decreased tears and saliva on the affected side (Lee *et al.*, 2017). In this case, patient had paresis to the right side. He could not raise his right eyebrow. His right forehead was not

able to wrinkle. He had difficulty to smile. Schirmer's test showed that there was tear deficiency.

The symptoms of vestibular nucleus injury are nausea and vomiting. The cochlear component damage leads to tinnitus and hearing loss (Jeon *et al.*, 2018). In this case, there were complaints of tinnitus and hearing loss 2 weeks before being hospitalized. From audiogram examination, mixed hearing loss on his right ear was obtained.

Paresis of CN VI causes double vision and CN IX, X involvements are associated with swallowing difficulty or vasovagal reactions (Jeon *et al.*, 2018). In this case, paresis of CN VI was characterized by diplopia due to lateral restriction of the ocular motility on the right eye. Swallowing difficulty was identified and patient was attached to NGT. It was a sign of paresis CN IX and X.

Additional examination could be performed to diagnose RHS with microscopic evaluation using the Tzanck smear on the vesicles. During VZV infections, smear would be able to find multinucleated giant cells (Crouch *et al.*, 2020). The best diagnostic test for detection of VZV is Polymerase Chain Reaction (PCR) assay that has higher sensitivity and specificity. Exudates from the geniculate zone of the ear or vesicle fluid are the best specimen for PCR analysis (Levin *et al.*, 2019). In this case, Tzanck test and PCR analysis were not performed because upon examination, there were only crusts.

RHS symptoms are often misdiagnosed because they do not always occur simultaneously. It is the same with this case. At the beginning of the examination, patient was diagnosed with right CSOM malignant type, paresis of right nerves VI and VII. However, on physical examination, the tympanic membrane was found to be intact. Patient also diagnosed with Gradenigo's Syndrome, but the diagnosis could be ruled out because there was no facial pain in the distribution of CN V and based on CT-Scan no involvement of the apex of the petrous temporal bone was found (Taklalsingh *et al.*, 2017).

The combination of acyclovir and prednisone is the most recommended therapy for RHS. Acyclovir is an effective antimicrobial agent against active replicating herpes zoster viruses. Due to the increasing viral resistance to acyclovir, newer antiviral medications, such as valacyclovir, famciclovir, penciclovir, and brivudine are being prescribed (Yang *et al.*, 2018). Acyclovir 5x800 milligrams per day is typically the first choice, because of its most cost-effective solution. Patients may take valacyclovir 3x1000 mg, or famciclovir 3x250-500 mg a day. Antiviral treatment needs 7-10 days. Facial palsy of RHS needs adjunctive steroid therapy that could be helpful. The Indonesian Dermatologist Association, in its clinical practice guideline stated that the therapeutic dose of prednisone for RHS was 40-60mg/day for 1 week in all patients (Perdoski, 2017). In this case, patient was prescribed with Acyclovir tablet 5x800mg, Prednisone tablet 3x10 mg, Fucidic acid cream 2x/day for erosion lesions and wet dressing with NaCl 0.9% 2x/day for crusted lesion. After 7 days of therapy, facial palsy improved, otalgia decreased, erosion lesions on the ear diminished. Furthermore, crusted lesions disappeared.

Symptomatic management is essential. Analgesia is often needed for RHS. Acetaminophen or ibuprofen, long-acting opioids could also be prescribed. Artificial tears and eye patches must be used to prevent corneal abrasions and ulcers (Crouch *et al.*, 2020). In this case, patient was prescribed Metamizole injection to reduce the pain and Chloramphenicol ointment for exposure keratitis. Comparing RHS with multiple cranial nerve involvement to RHS without multiple cranial nerve involvement, a recent study demonstrated that RHS with multiple cranial nerve involvement had a poor recovery rate. Primarily influencing prognosis is the intensity of symptoms at the beginning (Kim *et al.*, 2018). In this case, there was improvement of paresis CN VI, VII, IX, X which were signed by the absence of diplopia and the improvement of facial palsy. Results of the FEES examination proved good results. However, paresis on CN VIII did not improve. Based on the audiogram results, patient had severe mixed hearing loss. This was similar to previous studies which stated that CN VIII damage had a poor prognosis (Psillas *et al.*, 2019).

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