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Ramsay Hunt Syndrome type II and meningoencephalitis — complications of Varicella zoster virus

Zespół Ramsaya Hunta oraz zapalenie opon mózgowo-rdzeniowych i mózgu — powikłania wirusa ospy wietrznej i półpaśca

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Streszczenie

Wstęp: Wirus ospy wietrznej-półpaśca (**VZV**) jest powszechnie kojarzony z wywoływaniem ospy wietrznej oraz półpaśca. Niestety, może również spowodować szereg komplikacji, włącznie z zajęciem ośrodkowego układu nerwowego.

Opis przypadku: Opisany w artykule przypadek, dotyczy dwóch rzadkich, lecz poważnych powikłań, które mogą wystąpić podczas reaktywacji **VZV**. Zapalenie opon mózgowo-rdzeniowych i mózgu — kiedy zajęte są opony mózgowo-rdzeniowe oraz tkanka nerwowa mózgowia, a także Zespół Ramsaya Hunta II, opisywany jako półpasiec uszny z towarzyszącym porażeniem nerwu twarzowego.

Wnioski: Objawy widoczne podczas komplikacji infekcji **VZV** leżą w zakresie kilku specjalizacji lekarskich, dlatego dla lekarza bardzo przydatna jest świadomość istnienia tego rzadkiego obrazu choroby.
Biorąc pod uwagę fakt, że nasze społeczeństwo starzeje się, a choroba ta częściej dotyka ludzi w podeszłym wieku, wydaje się istotne branie jej pod uwagę podczas procesu terapeutycznego. Powinno się także pamiętać, że choroba ta nie dotyczy jedynie pacjentów w immunosupresji – co pokazuje ten artykuł.

Słowa kluczowe: herpesvirus 3, human, zapalenie opon mózgowo-rdzeniowych i mózgu, półpasiec uszny, zespół Ramsaya Hunta II

Abstract

Background: Varicella zoster virus (**VZV**) is commonly associated with causing chickenpox (varicella) and shingles (zoster). Unfortunately, it can add several complications, also affecting central nervous system.

Case report: The case of study described in this article, concerns two rarely met, but severe complications, which can appear during **VZV** reactivation. Meningoencephalitis, when the meninges and cerebral parenchyma are involved, and Ramsay Hunt syndrome, described as Herpes Zoster Oticus accompanied by facial nerve palsy.

Conclusions: As the symptoms visible during the complications of infection cover a few medical specialties, it is very useful for physicians to be aware of this uncommon VZV's clinical presentation.
Furthermore, our society is getting older and as those manifestations of illness can be more often connected with the elderly people, it appears to be crucial to take this disease into consideration during therapeutic proceeding. We should also remember, that this infection does not only occur among immunosuppressed patients, which is shown in this article.

key words: herpesvirus 3, human, meningoencephalitis, herpes zoster oticus, Ramsay Hunt Syndrome II

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Introduction

Varicella zoster virus (**VZV**) is a solely human neurothropic DNA virus, which belongs to the family Herpesviridae. Primary infection results in varicella (chickenpox), mostly seen in children, after which the virus presumably becomes latent in ganglionic neurons (the mechanism of reactivation is still uncertain) [1, 2]. In several situations, when the host's immune system is suppressed, the dormant virus can reactivate causing herpes zoster (shingles). Taking into consideration the incidence of involved localization, the sequence is: thorax, neck, face and lumbosacral region. The most frequently distinguished facial forms are herpes zoster ophthalmicus and oticus [3]. The latter one results from the reactivation of the latent infection in the geniculate ganglion. Ramsay Hunt Syndrome (RHS), also called Herpes zoster oticus (HZO), is a rare acute complication. It is defined as an ipsilateral, peripheral facial nerve palsy accompanied by otalgia and erythematous vesicular rash.

VZV can also cause meningoencephalitis and it is said to be one of the most frequent causal viral agents, together with enterovirus, herpes simplex virus type 2 and tick-born encephalitis virus [4].

The case in question illustrates the situation when the above mentioned relatively rare complications of VZV's reactivation were found. Undoubtedly, it can confirm the importance of considering the etiology of **VZV** in the central nervous system (CNS) infections, especially among the immunocompetent elderly patients.

Case report

A 72-year-old male was admitted to the neurological department due to severe headache, vertigo lasting for 10 days, rash situated in the area of the left ear and bloody outflow from the left ear canal. Additionally, the mobility of the left facial side and hearing in the left ear had significantly worsened for a few days before the admission. Deterioration of the sense of taste had been noticed – everything tasted bitter. He had already visited an otolaryngologist, who prescribed him penicillin, which was badly tolerated (vertigo) and had to be stopped. A few days before the onset of symptoms, the patient had his tooth extracted (the right side). There were no other potentially risky situations. The patient suffered from paroxysmal atrial fibrillation (on unfractionated heparin), polyneuropathy, lumbalgy, dyspepsia. He was operated on inguinal hernia, perianal abcess in the remote past. He had undergone childhood diseases without any problems. His family medical history did not contribute to the case. He used to work as an office worker, but now he has been a pensioner for more than ten years. He was a non-smoker. The patient was on low molecular weight heparin (Fraxiparin 1,0 ml), nebiwolol (Nebilet 5 mg),gabapentin (Neurontin 100 mg) chronic therapy.

The CT scan of the brain did not show any signs of acute pathology or cerebellar atrophy. Only old post-ischemic changes, lacunar infarct in the frontal right area, were detected.

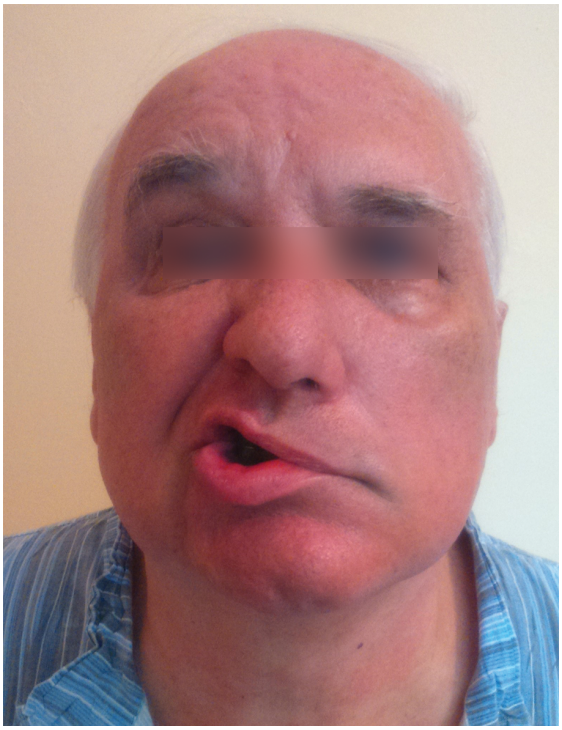

Fig. 1: Patient photography 1

On neurological examination, the patient was described as well-oriented in time and place, cooperative. The frontal area of the head was tactilely painful, the pupils were isochoric, fotoreaction preserved, no nystagmus, exit points of the trigeminal nerve (V) were not painful, the mimic was altered on the left side, the left eye winking with possible closure was noticed. The meningeal signs were negative, no signs of cerebellar damage. There were no other pathologies observed on physical examination. The blood tests were within normal limits.

Due to a progressive peripheral paralysis of the left facial nerve (VII) and all accompanying symptoms, the neuroinfection was suspected. The lumbar puncture was performed showing the signs of central infection (Erythrocytes: 36.00/ml; Neutrophiles: 15.00/ml; Lymphocytes: 747.00/ml; Glucose: 3.0 mmol/ml; Chlorides: 118.00 mmol/ml; Proteins: 1329.00 mg/ml) and arousing the suspicion of viral etiology. Taking into consideration all the results obtained and the patient's state, the herpetic infection was the most probable cause, hence anti-oedematous (Mannitol 20%, corticosteroids), analgesic (Gabapentin) and anti-inflammatory drugs were administered immediately and the patient was transferred to the Infectious Diseases Department.

The progression of the left facial nerve paralysis was observed, resulting in the left lagophthalmos. In order to prevent corneal abrasions, the local treatment was implemented (Hypromellose solution, Ophthalmo-Azulen/Guaiazulenum).

The targeted medication (acyclovire 500 mg 3x/day) was prescribed after receiving the results of PCR liquor tests – the herpetic etiology was confirmed (Varicella-Zoster Virus (**VZV**) — DNA). The diagnosis was meningoencephalitis accompanied by Ramsay-Hunt syndrome.

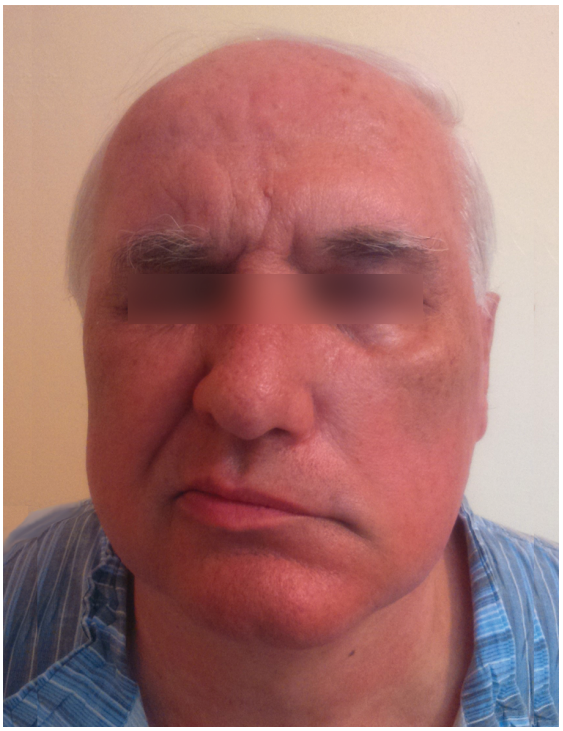

Fig. 2: Patient photography 2

The evaluation of the paralysis of the facial nerve, using the House-Brackmann Grading Scale (HBG Scale; 17), was performed at the beginning of the hospitalization — 3/4 points. Having noticed the severity of the patient's state, the dosage of antiviral was elevated to 750 mg, 3 times a day. The secretion from the left ear canal required the otolaryngologist's consultation, which resulted in the antibiotic therapy (cefuroxim 500 mg).

On the eleventh day of hospitalization, the worsening of hearing was noticed. The otolaryngologic examination revealed acute otitis media on the left side. Audiometry showed the loss of hearing – the right ear: 42,1%, the left one: 89%. The perforation of the left tympanum and the intensified secretion from the left ear canal were also spotted.

After 3 weeks of the therapy, facial nerve paralysis evaluation was repeated, showing the aggravation of the patients state – score: 5 (total paralysis). The everyday rehabilitation with specially selected exercises constituted a crucial part of his recovery.

During the whole hospitalization the patient complained about severe pain of the left side of the face and ear, which was successfully (VAS<3) treated with analgetics (gabapentin, paracetamol, codeine). Geratam, pentoxyfilline, C and B-complex vitamins were administered to improve the recovery.

The patient was discharged after 21 days with the following orders: a one-week intake of oral acyclovire (400 mg, four times a day), analgetic therapy, local eye preventive therapy.

Approximately two weeks later (on day 37), the control EEG and infectologist's examination were performed. The paralysis of the left facial nerve was still visible, though a slight improvement was noticed. There were no signs of central nervous system damage. The patient still complained about severe pain in the left facial area, so the control in the Pain Management Clinic was advised. The control otolaryngologist's examination revealed a mild improvement in audiometry (the loss of hearing — the right ear: 31%, the left one: 80,5%), which resulted in the severe impairment of hearing . The further intake of magnesium and vit. B-complex together with periodical control visits were advised.

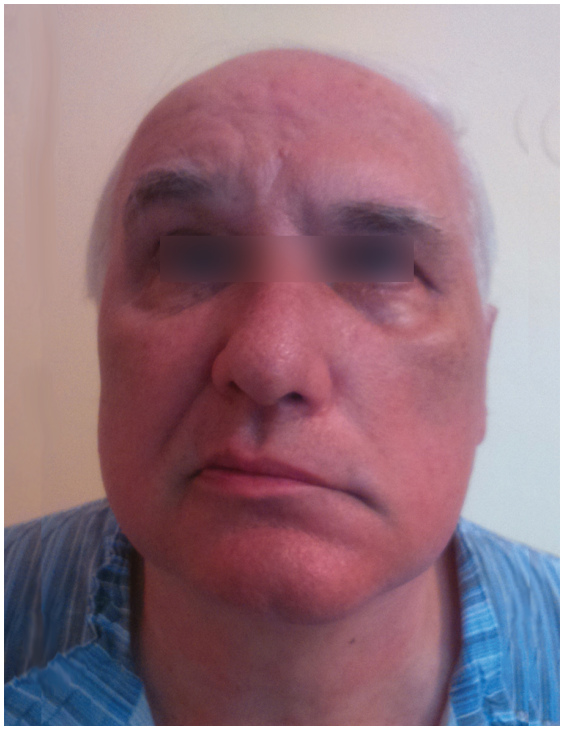

Fig. 3: Patient photography 3

As the patient was staying with his 70-year-old wife, her vaccination against **VZV** was recommended (even though she had already undergone chickenpox and shingles).

Discussion

Typical manifestations of herpes zoster infection, caused by its peripheral spread, are commonly known as a rash situated in a course of an occupied dermatome, often accompanied by a severe achiness. The pain may precede the appearance of vesicles by 42–72h with the dermatomes from T3 to L3 being most frequently involved [2].

Reactivation of **VZV** can occur when the host's immune system deteriorates, for example due to a cold, some severe infections, periods of intensified stress, post-vaccination condition or immunosuppressive treatment. The fact that a **VZV** infection can be one of the signs of another severe disease process developing in the organism such as neoplasm or systemic disease, cannot be ignored. The detailed analysis of the case in question excluded all the assumed causes of the disease so that the patient's age was considered the main potential risk factor. Reactivation of **VZV** happens regardless of age. Nevertheless,

it seems that people in their sixth decade of life and later are more vulnerable to such incidents.

However, some other rarely met complications of VZV's reactivation cannot be forgotten by the clinician. During the retrograde spread of the virus, when the CNS is involved, the characteristic rash does not have to be present (zoster sine herpete), which makes the diagnosis more difficult. Moreover, meningeal irritation signs are often negative, while the pleocytosis and elevated levels of CSF protein are found. CNS involvement can appear as myelopathy, encephalitis, meningitis, meningoradiculitis, cerebellitis, vasculopathy, acute disseminated encephalomyelitis (ADEM) and others [4,5]. Only a few cases of immunocompetent patients suffering from CNS complications have been described in the literature [1].

The patient in question had the viral meningoencephalitis confirmed. Symptomatic meningoencephalitis is described as headache (which does not answer to antianalgesics), cognitive changes, fever, photophobia, meningitis, vomiting, focal neurologic symptoms/signs [2–7]. **VZV** meningitis is definied as: symptoms and/or signs of meningeal inflammation without evidence of brain parenchymal involvement; CSF leukocyte count over $5x10^6$/l; a negative CSF bacterial culture; the absence of a non-infectious etiology [4].

It can be diagnosed through CSF and serum collection, followed by the Polymerase Chain Reaction (PCR) test in order to detect **VZV** DNA or the presence of intrathecal synthesis of anti-VZV antibodies. PCR may be false negative in the first 2 days of disease [8].

The diagnosis cannot be based only on the clinical sign because several recent studies have confirmed its low sensitivity. The absence of the clinical sign was noticed in more than a third of cases of CNS infection [4]. Computer Tomography (CT) scans are useful to exclude other potential causes of the involvement of CNS symptoms – such as hemorrhage or tumor, although Magnetic Resonance Imaging (MRI) is more sensitive and specific, but it is not available in every unit.

The second severe complication of **VZV** reactivation, diagnosed in the case in question, was Herpes Zoster Oticus (HZO) with facial nervy palsy. The most important risk factor of its appearance is age. RHS occurs in only 0,2% of all herpes zoster cases, which confirms the rarity of this manifestation [9]. It is described as an unilateral facial weakness accompanied by otalgia and herpetiformis lesions (ipsilateral ear, hard palate, anterior 2/3 of the tongue). Also, there can be noticed the involvement of Corti's (hearing loss) or Scarpa's (vertigo) ganglions [10] — both of which were found in the patient. Other frequent symptoms are: tinnitus, nausea, vomiting, and nystagmus. These eighth nerve involvement's features can be explained by the proximity of the geniculate ganglion to the vestibulocochlear nerve within the bony facial canal [11].

The pain which is associated with HZO in RHS is described as deep, dull, radiating to the ear. The analysis of a vast group of patients with RHS reveales a better prognosis for the cases without otalgia [12]. Sometimes, other symptoms like lacrimation, nasal congestion and salivation are also found.

RHS has a worse prognosis for complete recovery of facial nerve function than idiopathic facial palsy and it is statistically more prone to lead to persistent synkinesis [11, 13].

Moreover, patients aged >61 years achieve a significantly worse final status [1]. The coincidence of diabetes mellitus or essential hypertension even worsen the prognosis.

The standard treatment of **VZV** reinfection affecting CNS is complex and consists of drugs from several groups — antiviral, analgesics, antioedematous. It is recommended to supply 10–15 mg/kg of acyclovir, every 8 hours for 3 weeks, but the exact length of the therapy depends on a particular case [8, 14].

In the case discussed, the intravenous antiviral therapy lasted 21 days and then the oral drug was administered for the next 7 days (400 mg, 5 times a day). The dosage has to be modified in case of the renal insufficiency. It should be administered as soon as possible — the best results of acyclovir therapy are guaranteed when the therapy is initiated within 72 hours of lesion onset. Antiviral therapy may also reduce postherpetic neuralgia (PHN) by inhibiting viral replication and limiting neural damage [15, 16]. Yet, in antiviral trials approximately 20% of patients above 50 years of age continue to have pain, despite the prompt treatment [14]. Corticosteroids (high doses of dexamethasone or pulse methylprednisolone) were advised in the case presented here due to CNS involvement and **VZV**-induced facial paralysis. According to the literature, the therapy should be short (3–5 days) to minimize the risk of adverse effects [8]. Nevertheless, the benefits of such treatment have not been proved yet [15].

The long-term and frequent complication of **VZV** reactivation is postherpetic neuralgia (PHN). It is definied as unilateral, dermatomal-distribution pain, which lasts for more than 3 months after zoster. The incidence of PHN appearance increases with age — 80% of cases concerns patients over 50 years of age [6]. In addition, more than 40% of zoster patients >60 years of age experiences chronic pain [15].

As it is difficult to treat PHN and no universal therapy exists, it is the patient's and the clinician's role to decide what is bound to bring the relief. The first-line medications are: tricyclic antidepressants, gabapentin, pregabalin, and lidocain patches. The second- and third-line ones are: opioids, tramadol, 5% lidocaine patch, capsaicin cream, or 8% capsaicin patch [7]. Medical interventions are often combined.

PHN complications discussed above affected the patient in question. That is why, the man was sent to the pain management clinic to be provided with the most effective therapy.

Except for the post-infectious complications, which are under regular control by specialists, no evidence of herpes zoster having a predictive nature in this case was found.

Conclusions

Although Varicella Zoster Virus most frequently affects the group of pediatric patients as well as the immunosupressed adults, it should not be forgotten that the infection can also occur among completely different and unexpected hosts.

Having analysed the case in question, the patient's age seems to have been the main risk factor.

What also makes the case worth considering is the occurrence of herpes zoster oticus and the involvement of central nervous system, which are rather rare. These both manifestations of the illness can lead to severe and debilitating complications.

Therefore, every physician should always stay alert while diagnosing patients with such symptoms, particularly the elderly ones.

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Comment:

Description of that case is fully justifiable - it has educational valors. It is even more instructive because of not having predictional character (i.e. for neoplasmatic process) and demonstrating complications which doctors may rarely seen nowadays. That case concerns and reminds about complication which might be forgotten today in vaccination era. However that nonstandard complication should be considered by present, well educated, ambitious physicians in differential diagnosis - especially on a level of primary care.

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