

Herpes Zoster in Palate: Atypical Presentation in Immunosuppressed Patient Secondary to Rituximab, a Case Report and Review of Clinical Manifestations and Management

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ABSTRACT

Herpes zoster (HZ) is caused by the reactivation of the latent varicella zoster virus (vZv). The cause of reactivation may be associated with predisposing factors such as age, stress or the impaired immune system and an association with autoimmune diseases has been seen. Its clinical presentation is characterized by the appearance of multiple vesicles that rupture quickly, leaving small, very painful ulcers that are distributed respecting specific dermatomes.

The diagnosis in most cases is clinical, and complementary tests may be necessary and differential diagnoses may be excluded in cases of atypical presentation.

The main sequelae after the disappearance of skin signs is postherpetic neuralgia, which is more common in the elderly. Early diagnosis and rapid initiation of treatment determine the prognosis, especially in immunocompromised individuals.

In this work we report a case of atypical clinical presentation in a woman with autoimmune disease, immunocompromised and belonging to the elderly population, being a clear example of the patient in whom special attention should be paid when establishing the diagnosis with the aim of emphasizing early detection and rapid establishment of appropriate treatment, avoiding deleterious outcomes.

KEYWORDS: Herpes Zoster, Palate, immunosuppressed, Rituximab, Acyclovir.

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INTRODUCTION

HZ occurs worldwide without seasonal variations of incidence. The incidence of HZ is age-dependent and ranges from 1.2 to 3.4 per 1000 persons per year among younger adults to 3.9–11.8 per 1000 persons per year in elderly patients (>65 years) [1]. According to a systematic review of studies from 2002–2018, the cumulative incidence has been estimated between 2.9–19.5 cases per 1000 population with female predominance [2].

Herpes zoster virus is caused by reactivation of the varicella-zoster virus, which establishes latency in the sensory ganglia after an initial infection such as chickenpox [3]. The reason for the reactivation of the virus is unknown and has been mainly related to predisposing factors such as age (>50 years), immunodeficiency [5], stress, sleep disorders, depression and autoimmune diseases [6,7,8].

Recently, studies have been carried out with biological therapy in the treatment of HZ. In a retrospective cohort study

with >2000 patients suffering from ankylosing spondylitis, treatment with TNF-alpha inhibitor infliximab did not increase the risk for HZ [16]. In patients with psoriasis, treatment with infliximab and etanercept increased the risk for HZ with an OR of 2.43 and 1.65, respectively [17]. JAK inhibitors bear an increased risk for HZ reactivation. Upadacitinib is an oral Janus kinase (JAK) inhibitor approved for rheumatoid arthritis. The incidence rate of HZ was 3.0 (2.6 to 3.5) for 15 mg upadacitinib and 5.3 (4.5 to 6.2) for the doubled dosage [18].

The initial symptoms of HZ are nonspecific and include fever, malaise, headache, followed by a prodrome that begins with paresthesia and subsequently a vesicular rash with an erythematous base over the skin region 2 to 3 days later and is accompanied by severe and lancinating radicular pain, as well as decreased sensitivity in the affected area [2,9]. The topography of the HZ is unilateral and does not cross the midline, the vesicles rupture forming small ulcers that begin to dry and crust, then symptoms begin to decrease and

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complete resolution usually occurs within 3 to 4 weeks [4]. The lesions are distributed unilaterally along the infected nerve, the most commonly affected dermatomes in descending order are the thoracic, trigeminal, cervical, lumbar and sacral regions [10].

In most cases, HZ presents a mild evolution with a favorable prognosis; in other cases, it may present various complications: otic, ocular involvement, bacterial superinfection, encephalitis, cutaneous and visceral dissemination. When the maxillary or mandibular branch is involved, the most frequent complications are necrosis of the alveolar bone or exfoliation of the teeth. Special clinical presentations include ophthalmic HZ, Ramsay Hunt syndrome, disseminated HZ, deep HZ, purpuric HZ, central nervous system HZ and postherpetic neuralgia (pHN) which is the most common chronic complication, especially in people over 60 years of age. Recurrent HZ is possible in elderly and immunocompromised patients [2].

HZ is generally diagnosed by the classic clinical presentation, however, in an atypical presentation the diagnosis can be difficult, making it necessary to resort to available diagnostic tests such as the Tzanck test, histopathology, immunofluorescence, electron microscopy, detection of antigens and antibodies, viral culture and polymerase chain reaction (pCR); Differential diagnoses must also be taken into account because early diagnosis of HZ is key to establishing appropriate treatment, thus avoiding deterioration in the quality of life of patients and possible complications inherent to the evolution of the disease [11].

There is no cure for HZ, its management consists of shortening the course of the disease, providing analgesia, preventing complications. Several studies have shown that the administration of systemic antiviral drugs in the HZ reduces inflammation, improves the healing process and reduces possible complications, in especially in immunocompromised patients [11,12]. Acyclovir was the first antiviral agent developed to treat HZ, today is the standard therapy of HZ, the recommended oral dose is 800 mg 5 times a day for 7-10 days, other options are 500 mg 3 times a day in uncomplicated cases or 10 mg/kg/day 3 to 5 times a day in severe cases or immunosuppression [2]. It has

been reported that valacyclovir and famciclovir have better bioavailability and pharmacokinetics, compared to acyclovir, which is why patients present a significant improvement, in addition to requiring less frequent dosing than acyclovir, 1000 mg every 8 hours for 7 days and 500 mg every 8 hours for 7 days, respectively [2].

CASE REPORT

The case of a 62-year-old woman is presented whose significant history includes systemic arterial hypertension, Sjögren's syndrome of 18 years of evolution and rheumatoid arthritis being treated with celecoxib, deflazacort, leflunomide, chloroquine and annual rituximab receiving the last dose 1 month later. prior to his current illness. It begins with bilateral otalgia, predominantly on the left, as well as fronto-temporal headache, later facial edema is added to the left side of the face with involvement of the eye, cheek, lips and neck, presence of hyperemia, heat and facial pain, areas of necrosis in At the level of the pyramid, nasal wing, cheek and oral cavity with the presence of vesicles in the frontal region and nose [figure 1A], with 24 hours of evolution, the presence of yellowish plaque on the soft and hard palate is added, delimited by a demarcation line that It divides the palate in two, differentiating the injured area from the healthy area [figure 1B]. In their complementary studies, Hb: 12.8 g/dl, Hct: 42.30%, platelets: 322,000, leukocytes: 9.71 mil/ul, lymphocytes: 5.50%, neutrophils: 82.80%, procalcitonin: 86 mg/dl, glucose: 86 mg/dl are reported. dl, urea: 41 mg/dl, BUN: 19.15mg/dl, cr:0.8 mg/dl.

Simple and contrast-enhanced computed tomography was performed, which showed no bone disease.

It was concluded that the patient had symptoms suggestive of herpes zoster infection, for which management with Acyclovir was initiated and due to the type of lesions present, mucormycosis was ruled out, for which debridement of the lesions was performed as well as a biopsy which was performed. It was reported without data compatible with this diagnosis.

After a week of treatment, clinical improvement and disappearance of the lesions were evident [figure 1C], so the diagnosis of herpes zoster with facial, ophthalmic and palate involvement was concluded.

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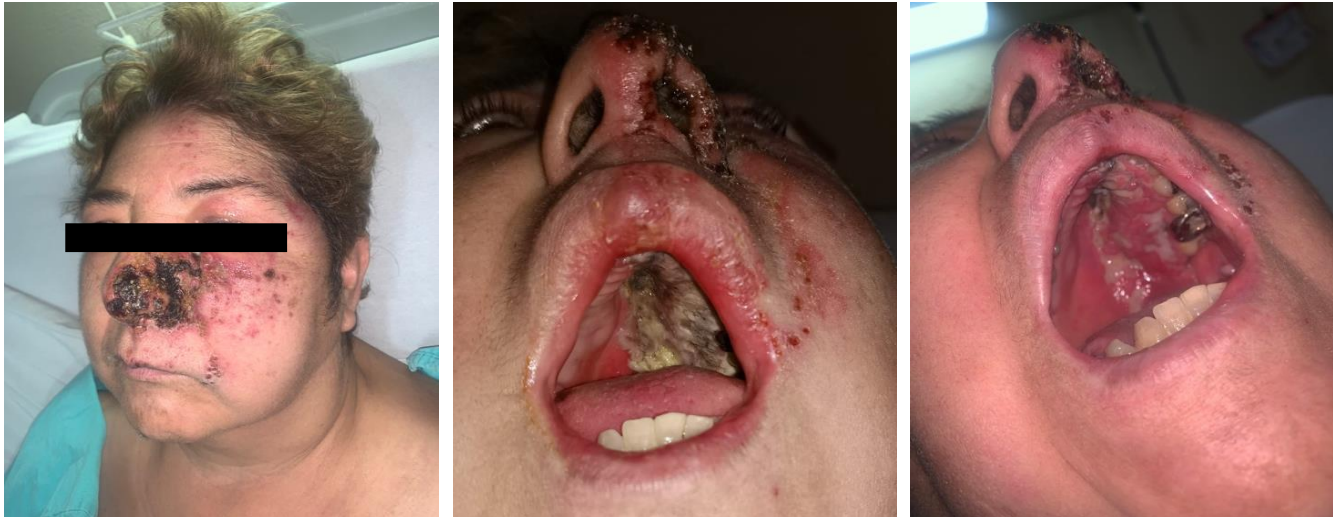


Figure 1: (A) Facial condition with vesicles in various phases in the frontal region, nasal region, nasolabial fold and cheek on the left side with purulent content and areas of necrosis, as well as eyelid edema and conjunctival hyperemia. (B) Oral involvement of the lips and soft and hard palate, showing the presence of yellowish plaque with well-defined areas of necrosis. (C) Disappearance of palate lesions after treatment with Acyclovir.

DISCUSSION

The exact cause of vZv reactivation in immunocompetent individuals is unknown, but a specific relative deficiency of cellular immunity has been suggested [13]. There is an association with autoimmune diseases and advanced age and female sex have been detected among the predisposing factors [5, 7]. The patient's history, in addition to being a woman over 60 years of age, includes an autoimmune disease due to rheumatoid arthritis and the recent administration of immunosuppressive drugs such as corticosteroids and rituximab, which is a B-cell antagonist monoclonal antibody. Recently published studies have related biological therapy with a higher risk of presenting HZ [16,17,18], so this patient meets several predisposing factors and in this particular case the state of immunosuppression secondary to the administration of Rituximab stands out and which we associate with the reactivation of the HZ.

Oral manifestations occur when the maxillary and/or mandibular branches of the trigeminal nerve are affected, however when the maxillary nerve is affected, vesicular lesions occur in the vestibular mucosa and palate; In cases in which the mandibular nerve is affected, the entire extension of the jaw, tongue and lip will be compromised unilaterally, even the lower teeth may present pain [14]. In the case presented, in addition to the involvement of the maxillary and mandibular branches of the trigeminal nerve due to the presence of multiple ulcers surrounded by an erythematous halo and areas of necrosis, the maxillary nerve was compromised, presenting lesions in the left palate where a yellowish pseudomembrane that does not cross the midline. The diagnosis of HZ in most cases is clinical, made from the appearance of the lesions that are generally typical for its diagnosis, vesicles that rupture quickly leaving small ulcers and that are distributed unilaterally along the infected nerve

[15]. In some cases, the clinical presentation represents a diagnostic challenge for the doctor, especially when it manifests with an atypical presentation in which differential diagnoses must be taken into account, as in the case presented in which the diagnosis of mucormycosis was ruled out because it was a Immunocompromised patient with lesions on the palate accompanied by necrotic areas.

In most cases, HZ presents a mild evolution with a favorable prognosis; in other cases, it may present various complications especially in people over 60 years of age and immunocompromised patients [2,4]. The development of these complications can be prevented with the rapid establishment of antiviral treatment. The patient in the reported case being a clear example of a candidate for early management with acyclovir.

CONCLUSION

Herpes Zoster virus infection is a common entity in the world and predominates in the elderly and female population; Reactivation of the virus may be associated with predisposing factors such as age, stress or an impaired immune system. There is a strong association between autoimmune diseases and the use of biological therapy with an increased risk of HZ reactivation due to the suppression of immune cell activation. In most cases it presents a mild evolution with a favorable prognosis, in other cases it may present various complications, especially in the elderly population and immunocompromised patients.

The diagnosis in most cases is clinical, and complementary tests and the ruling out of differential diagnoses may be necessary in cases of atypical presentation.

Early detection and rapid initiation of antiviral treatment prevents complications and reduces mortality in patients with herpes zoster.

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