Meningitis Caused by Reactivation of Herpes Zoster Virus

Meningite por Reativação do Vírus Herpes-Zóster

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Abstract

Herpes zoster, caused by the reactivation of the varicella zoster virus, remains latent in the sensory nerve ganglia after primoinfection. It is usually manifested by a painful vesicular rash distributed in a dermatome and may be associated with neurological complications. Involvement of the central nervous system is uncommon, especially in the immunocompetent young patients.

A 17-year-old male adolescent with a personal history of varicella diagnosed in the first year of life, presented headache, phonophobia, photophobia and fever, associated whit neck stiffness and a cluster of vesicular cutaneous lesions in the right dorsal region. Deoxyribonucleic acid polymerase for the varicella zoster virus in the cerebrospinal fluid was positive. The patient underwent a total of 14 days of intravenous acyclovir therapy with total remission of symptoms.

In immunocompetent individuals with prompt therapeuthic institution, complete resolution of the condition is expected, with no sequelae in the medium-to-long term.

Keywords: Encephalitis, Varicella Zoster; Herpes Zoster; Herpesvirus 3, Human; Meningitis, Viral; Virus Activation

Resumo

O herpes-zóster, causado pela reativação do vírus varicela zóster, permanece latente nos gânglios sensoriais das raízes dorsais, após infeção primária. Habitualmente manifesta-se por erupção vesicular dolorosa distribuída ao longo de um dermátomo e pode estar associado a complicações neurológicas, apesar do envolvimento do sistema nervoso central ser raro, sobretudo em doentes imunocompetentes.

Adolescente de 17 anos, com história de varicela diagnosticada no primeiro ano de vida, observado no Serviço de Urgência por cefaleia, fonofobia, fotofobia e febre, com rigidez da nuca e um aglomerado de lesões cutâneas vesiculares na região dorsal à direita. A pesquisa de ácido desoxirribonucleico de varicela zóster no líquido cefalo-raquidiano foi positiva. O adolescente realizou 14 dias de terapêutica com aciclovir endovenoso, com remissão total dos sintomas.

Em indivíduos imunocompetentes com rápida instituição de terapêutica, é expectável uma resolução completa desta condição, sem sequelas a médio e longo prazo.

Palavras-chave: Ativação Viral; Herpes-Zóster; Herpesvírus Humano 3; Encefalite por Varicela Zóster; Meningite Viral

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Introduction

Varicella zoster virus (VZV) is an exclusively human herpesvirus that remains latent in cranial nerves, dorsal roots and autonomic ganglia, after a primary infection.[1,2] Herpes zoster, or zona, is caused by the reactivation of this virus and manifests as unilateral vesicular rash and acute neuritis distributed along one or two dermatomes, after anterograde replication along the sensory neuron.[1-3] Its incidence is higher in elderly and immunocompromised patients,[3] with a higher risk of complications. Herpes zoster is rare in childhood and adolescence, with the exception of immunocompromised children, with an estimated incidence at pediatric ages of 0.45-2.39 / 1000, and a higher incidence in adolescents older than 15 years old.[4,5] When it develops in childhood or adolescence, it usually occurs in cases of early primary infection, especially those in the first year of life.[4,5] The most frequent complication is postherpetic neuralgia, followed by other neurological complications, such as peripheral motor neuropathy, meningitis, encephalitis and myelitis.[1,3] Central nervous system infection by VZV, which occurs mainly in immunocompromised patients,[1,2,6] is rare in children, with few cases currently reported.[2-3,6-11] In some cases, the associated complications may manifest before the evidence of typical skin lesions, which can difficult the diagnosis.

The authors present a case of a previously healthy adolescent, diagnosed with varicella zoster meningitis and late cutaneous manifestation.

Case Report

The authors present a case of a 17-year-old male with a personal history of varicella infection diagnosed at the age of nine months, with no other relevant personal or family history. He was admitted in the emergency department (ER) complaining of a severe pulsatile headache, localized in the frontal and occipital region since the day before. On the day of the admission he also presented with nausea, phonophobia, photophobia and persistent fever of maximum value 38.3ºC.

The physical exam, including neurological examination, was normal. A computed tomography (CT) scan of the brain was performed showing no alterations. The adolescent was discharged upon the improvement of symptoms with analgesics. He then returned to the ER on the fifth day of illness, due to the maintenance of fever, awakening and worsening of the headache intensity, now described as holocranial with posterior cervical irradiation. Physical examination showed neck stiffness with no other signs of meningeal or focal neurological abnormalities. A painless cluster of small vesicular cutaneous lesions in the right dorsal region at T5 level was noticed on the same day (Fig. 1).

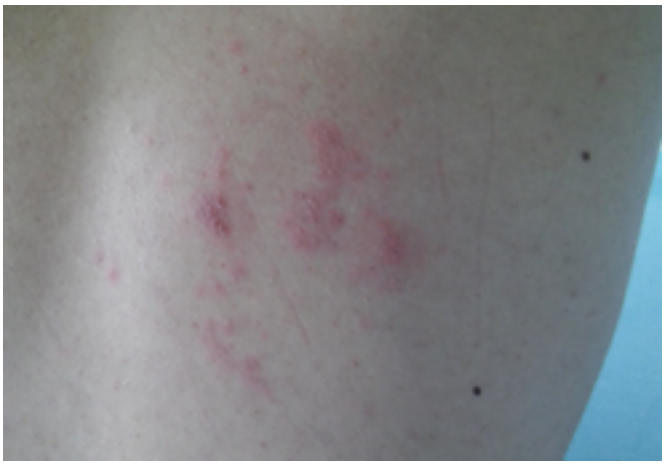

Figure 1. Vesicular cutaneous lesions in the right dorsal region (T5 level).

The laboratory evaluation provided the following results: white blood cells (WBC) count of 8400 leukocytes/µL with 68.3% neutrophils and a C-reactive protein of 1.4 mg/L. A new CT scan of the brain was performed, with no alterations. Cytochemical examination of the cerebrospinal fluid showed proteins of 124 mg/dL, glucose of 42 mg/dL (for a previous blood glucose of 95 mg/dL) and pleocytosis with 790 WBCs/µL (90% of mononuclear cells). He was hospitalized under empirical therapy with intravenous ceftriaxone (100 mg/kg/day) and acyclovir (30 mg/kg/day). Clinical setting manifested with good general condition and apyrexia from the first day, as well as resolution of headache and meningeal signs after 48 hours of therapy. Polymerase chain reaction (PCR) for deoxyribonucleic acid (DNA) screening of VVZ in the cerebrospinal fluid was positive. An electroencephalogram and magnetic ressonance imaging on the sixth and ninth days of hospitalization (respectively) did not show any abnormal features. Complete healing of the cutaneous lesions was observed on the seventh day of hospitalization and no pain or dysesthesia was ever reported. The patient underwent a total of 14 days of intravenous acyclovir therapy (with ceftriaxone discontinuation on the 5th day). He was discharged on the 15th day of hospitalization with evidence of clinical improvement.

Discussion

Reactivation of VZV is uncommon in children, particularly in the pediatric age[6,11] and is more commonly described in children infected in utero or during the first year of life,[4,5,11] as described in the present case.

Cell-mediated immunity is thought to be an important factor in increasing the incidence of herpes zoster with age because antibody titers remain unchanged or may even increase with time, which explains the low incidence in immunocompetent children.[3] However, the pathophysiological mechanism underlying the transition from latency to active viral replication is still unknown.[1]

In case of reactivation of this virus, there is anterograde active replication along the sensory neuron. Subsequently, clinical

manifestations in the form of unilateral vesicular rash and acute neuritis distributed along one or more dermatomes[1-3] become evident. Although a rash may occur in any dermatome, thoracic and lumbar dermatomes are most commonly involved, affecting up to 44% of cases in childhood.[5,12] The most common symptoms, that may precede the rash, include pain, burning, allodynia or itching in the affected region.

VVZ complications, like central nervous system involvement, have historically been associated with the subgroup of immunocompromised individuals. However, with the aid of PCR-based tests, such complications have been increasingly recognized in immunocompetent patients,[9] as showed in the present case. Central nervous system infection by VZV is rare in children and meningitis as a complication of herpes zoster occurs in only 0.5% -2.5% of cases.[3]

The pathophysiology of the process underlying VZV encephalitis is currently considered to be an immune-mediated vasculitis, whose pattern of brain vessel involvement and degree of brain injury reflect the host immune status.[9] Typical clinical manifestations include high fever, headache and neck stiffness, associated with the onset of vesicular rash on previous days. Rare cases with seizures, ataxia, hemiplegia or coma have been described in the literature.[13] Risk factors for the development of herpes zoster encephalitis are the involvement of cranial or cervical dermatomes, two or more previous episodes of herpes zoster, disseminated herpes zoster, and compromised cellular immunity,[14] none of which has been identified in our patient.

The diagnosis of VZV meningitiss can be particularly difficult when neurological manifestations of reactivation of this virus occur without the presence of characteristic skin lesions, as well as when the skin rash occurs months or days before or after the onset of neurological disease.[8,9] The possibility of reactivation of the virus without skin lesions has been increasingly recognized, manifesting only by atypical painful syndromes, distributed by dermatomes, a condition called zoster sine herpete.[1] Then, a high index of suspicion is necessary for the etiological diagnosis of neurological complications, in order to enable the early initiation of appropriate therapy. In the described case, the observation of typical skin lesions, after the onset of clinical manifestations of meningoencephalitis, allowed a more targeted diagnostic approach.

After clinical suspicion, the diagnosis may be suggested by cytochemical characteristics of the fluid, with the presence of pleocytosis and predominance of mononuclear cells, which point to a viral etiology. That diagnosis can be later confirmed by cerebrospinal fluid PCR for VZV, usually preferred as it is a fast, low cost and high sensitivity method.[1,8]

Regarding therapy, intravenous acyclovir[9] is recommended for a minimum of 7 days. Its early administration until 72 hours after the onset of the vesicular rash not only reduces pain, but also induces the remission of neurological symptoms and decreases viral replication.[3,15] Although medium and long term effects of herpes zoster meningoencefalitis are not well known, when diagnosed and treated early, VZV meningoencephalitis presents a good prognosis in immunocompetent individuals, with complete recovery,[3,15] as observed in the present case.

With this case, we intend to illustrate the diagnostic approach of herpes zoster meningoencephalitis, in order to optimize the diagnosis and institute early therapy.

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