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Case Report

Fatal varicella in immigrants from tropical countries: Case reports and forensic perspectives

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ABSTRACT

The primary Varicella Zoster Virus (VZV) infection results in varicella, a generally benign, self-limiting disease in immunocompetent children. Despite the usual course a possible fatal evolution of the primary infection is observed predominantly in immunocompromised subjects and in adults, especially emigrating from tropical regions. Two cases of fatal varicella have been investigated and discussed. Death occurred in two patients over 40 years of age, coming from South Asia and receiving chronic immunosuppressive therapy. The forensic expert must be cautious and consider all clinical records in managing fatal varicella cases, bearing in mind risk factors and pre-existing conditions such as age, geographical provenance and pathological comorbidity, which may lead to a bad prognosis irrespective of therapies. Based on the severe and fatal course observed in the reported cases, an extension of the immunization program appears advisable for immigrants from tropical countries, especially before scheduled immunotherapy.

1. Introduction

Varicella Zoster Virus (VZV) is a worldwide highly contagious herpes virus and the primary VZV infection is responsible for varicella (or chickenpox) [1]. Apart from neonates, infants, and pregnant women, groups at higher risk for severe complications and death include immunocompromised subjects and adults. The primary VZV infection typically occurs during childhood however a higher incidence of infection during adulthood has been observed in many tropical regions [1]. Indeed, a higher seronegative prevalence among adults has been demonstrated in Saudi Arabia, India and Sri Lanka [2,3] with associated significant morbidity and mortality. The reasons for the higher susceptibility among young adults in tropical settings are poorly understood and may relate to properties of VZV, climate, population density and risk of exposure [4].

Here we report two cases of fatal visceral varicella occurring in over-40-year-old immunocompromised patients both having immigrated from South Asia. The related forensic perspectives are discussed and advisement of an extension of the immunization program for immigrants from tropical countries, especially before scheduled immunotherapy, is reaffirmed.

2. Cases

2.1. Case 1

A 42-year old Asian woman from Sri Lanka (Ceylon) was admitted to the hospital complaining of severe abdominal pain and nausea for about twelve hours. Clinical history was negative, except for an autoimmune uveitis in treatment with corticosteroids and Azathioprine. A tentative diagnosis of acute dyspepsia was made and she was treated with antiemetics, tramadol/paracetamol and a spasmolytic. One day later she was discharged after the resolution of nausea and abdominal pain. Ten hours after discharge hematuria associated to incessant bleeding of the tongue and scarce papulae and petechiae scattered in the trunk appeared and she was re-admitted to the hospital. The virologic analysis, performed thorough polymerase chain reaction in blood, revealed the massive presence of VZV DNA particles. Visceral varicella was diagnosed, and an antiviral therapy with acyclovir was initiated. The lingual artery was identified as the origin of bleeding, resistant to repeated surgical hemostatic interventions. Despite those therapies associated to hemodynamic support, the patient died three days after the first medical consultation displaying hepatitis and multi organ failure (MOF) evolving in disseminated intravasal coagulation (DIC). Diffuse papule and petechiae were observed at the external

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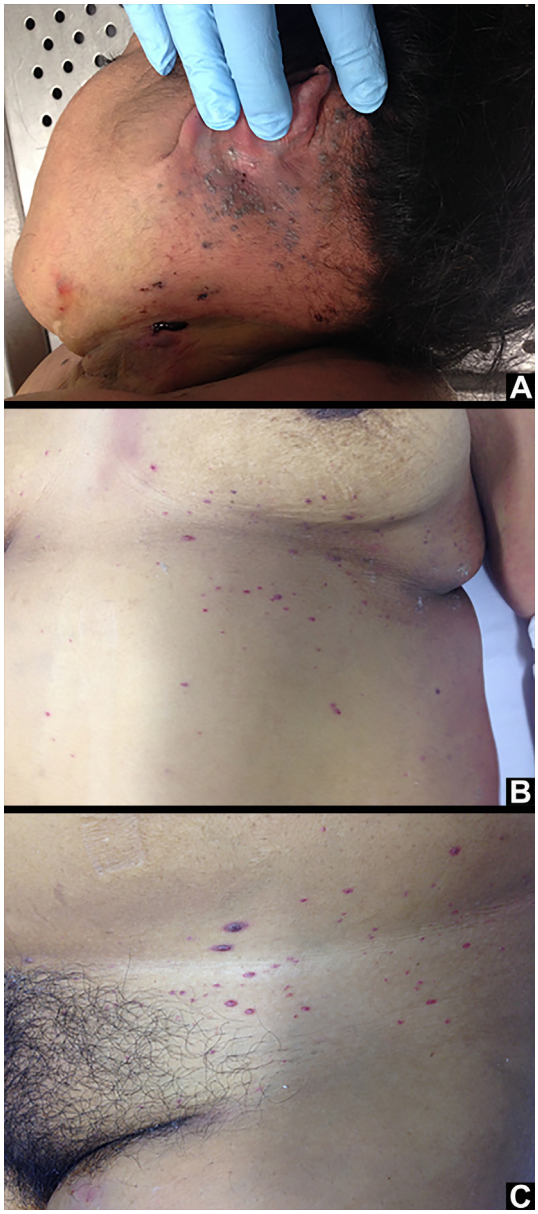

Fig. 1. Diffuse skin papule and petechiae becoming focally confluent in the mastoid region (A), under the breasts (B), and in the inguinal region (C).

examination of the corpse (Fig. 1). A comprehensive forensic autopsy including histopathological study, showed an early interstitial pneumonia (Fig. 2) associated to multiple focal hemorrhages in several organs (Figs. 3 and 4), corroborating the clinical diagnosis of DIC.

2.2. Case 2

A 44-year old Asian male from Bangladesh was admitted to the hospital complaining of severe abdominal pain associated with fever, headache and nausea. In the clinical history, rheumatoid arthritis treated with methotrexate and methylprednisolone therapy was reported. Abdominal pain was managed with ketoprofen and ranitidine and the patient was discharged. He was re-admitted to the hospital 4 h later because of the increasing abdominal pain and bloodspotted vomitus. A herpetic esophagitis was suspected because of vesicular lesions with ulcers observed during esophagogastroduodenoscopy. Virologic analysis, performed thorough polymerase chain reaction in blood, revealed the massive presence of VZV DNA particles. Visceral varicella was diagnosed, and prompt antiviral therapy with acyclovir was started. Despite the continued therapy with associated hemodynamic support, the patient died three months later displaying hepatitis, vesicular rash, and a progressive MOF evolving in DIC. Only external examination of the corpse was ordered by the Prosecutor.

3. Discussion

Two cases of fatal visceral varicella in apparently healthy patients over 40 years of age are reported. Both the subjects showed formerly unspecific symptoms including alteration of liver function blood tests, followed by vesicular rash, MOF syndrome and DIC. Despite an initial misleading clinical presentation, the diagnosis of VZV infection was made within two days by the virologic analysis of blood; IgG were negative demonstrating that a primary infection occurred during adulthood. They were in treatment with chronic immunosuppressive therapy. Both came from the South Asia area.

Primary infection results in varicella (chickenpox) which is a common and extremely contagious acute disease that occurs in epidemics among preschool and school-aged children. It is characterized by a generalized vesicular rash which is distinctive and readily recognized [5]. Visceral VZV dissemination is the clinical evidence of internal organ involvement [6,7]. In visceral varicella, skin lesions may appear after organ involvement or can even be absent throughout the course of the disease, delaying the diagnosis or making it less likely to be considered. Indeed, as described in the literature, the diagnosis of visceral varicella is sometimes cumbersome: both diagnosis and treatment are often delayed, and the diagnosis is often made postmortem [8,9]. The most common complications of visceral varicella are interstitial pneumonitis and meningoencephalitis [9]. However, coagulation disturbances and the involvement of other organs, such as the liver and the pancreas have also been reported, especially in immunocompromised patients [10–15]. At the beginning, both our cases showed fairly unspecific symptoms including alteration of liver function blood tests, followed by vesicular rash, MOF syndrome and DIC,

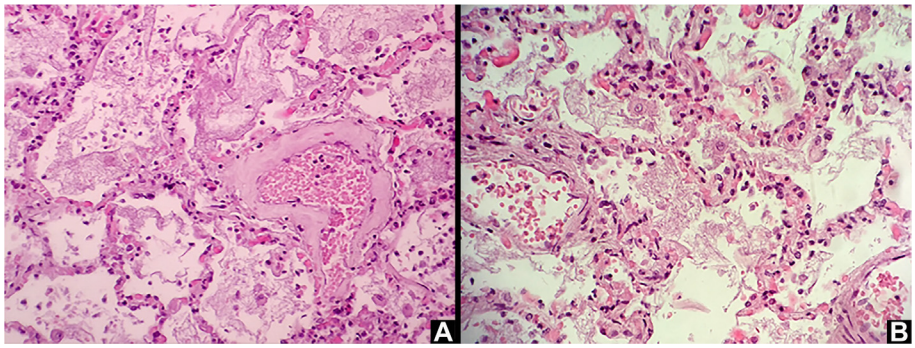

Fig. 2. Interstitial pneumonia (H&E). Alveola containing fibrin and mononucleated cells (A). Thickening of alveolar septa related to massive congestion of capillaries with lymphocytes, mononucleated cells and neutrophil granulocytes (B).