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Disseminated herpes simplex virus and varicella zoster virus co-infection in a patient with idiopathic thrombocytopenic purpura

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ABSTRACT

Concomitant disseminated herpes simplex virus (HSV) and varicella zoster virus (VZV) infection is a rare event. We describe a case of disseminated HSV and VZV infection in an 80-year-old patient many years after splenectomy for idiopathic thrombocytopenic purpura (ITP). This is the first case of disseminated HSV-1 and VZV infection with molecular evidence of the simultaneous presence of both viruses in two different body sites (the skin and cerebrospinal fluid). This adds to the three reports of patients developing cutaneous disseminated herpes zoster multiple years after splenectomy for ITP.

Case presentation

An 80-year-old immunocompetent woman was transferred to our institution from a community hospital where she was admitted two days earlier for altered level of consciousness. She was bradycardic and hypotensive, which lead to an imminent intubation. The family reported that two days earlier she started to become less responsive to verbal stimuli with visual and auditory hallucinations. The family also noticed small vesicles on her posterior neck of 1-day duration. The next day, upon presentation to our institution, the lesions became generalized. The patient had idiopathic thrombocytopenic purpura (ITP) treated by splenectomy 30 years ago; she had no history of atopic dermatitis.

In our emergency department, she was hypothermic (36.3 °C), hypotensive (82/38 mmHg), sedated on mechanical ventilation (respiratory rate 16 breaths-per-minute). The patient was responding to painful stimuli. The skin was covered diffusely with palpable erythematous 3–5 mm papules; most of which had a central translucent vesicle, others had a necrotic hemorrhagic center, and other papules were frankly necrotic (Fig. 1C–F). Over the left lateral neck and extending towards the nape, the papules were mostly necrotic and confluent into a necrotic ulcerating plaque (Fig. 1A and B).

Her white blood cell count was elevated (16,800 per mm^3) with 99% polymorphonuclear cells and an elevated lactic acid (3.06 mmol/L). Arterial blood gas analysis revealed low pO2 and low oxygen saturation of 89.4%. Her chemistry panel was otherwise normal.

Computed tomography of the brain was non-revealing. A lumbar puncture (LP) was done and the patient was started empirically on ceftriaxone and vancomycin. Acyclovir at 10 mg/kg was added after the lumbar puncture.

Results of the LP showed normal glucose level in the cerebrospinal fluid (CSF) (81 mg/dL), elevated protein (0.68 mg/dL; upper limit of normal 0.50), no white blood cells nor red blood cells, negative bacterial antigens and negative Gram stain. Polymerase chain reaction (PCR) for herpes simplex virus (HSV)-1 came back positive.

A skin biopsy was done and showed intraepidermal vesiculation (Fig. 2A), swollen pale keratinocytes with enlarged slate-grey nuclei and multinucleated giant cells consistent with a herpetic infection (Fig. 2B). Since HSV and varicella zoster virus (VZV) infections cannot be differentiated on histological basis, a PCR for HSV 1, 2 and VZV was ordered and came back positive for both HSV-1 and VZV.

PCR for VZV was then ordered on the CSF fluid and came back positive. As per the family, the patient had varicella primary infection as a child.

The patient was admitted to the intensive care unit, where she was in status epilepticus despite optimal anti-epileptic treatment; then unfortunately passed away.

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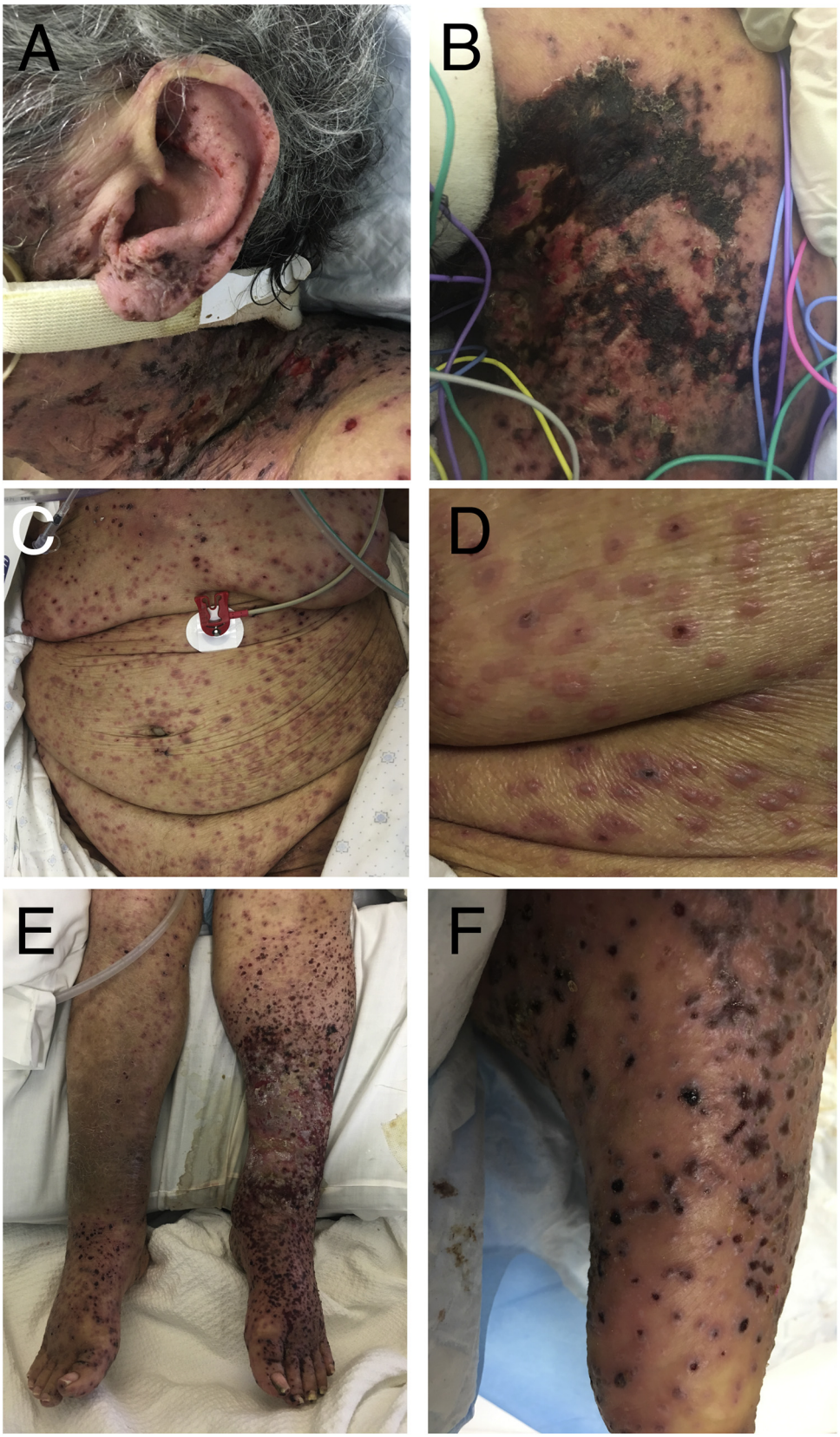

Fig. 1. Skin upon presentation to the emergency department.
(A)Left lateral neck showing necrotic papules and confluent into a necrotic ulcerating plaque. (B) Necrotic ulcerating plaque over posterior neck and upper back. (B and C) Diffuse palpable erythematous 3–5 mm papules over abdomen; some with a central translucent vesicle, others with necrotic hemorrhagic center. (D and E) Necrotic papules over lower extremities, more pronounced over the left leg.

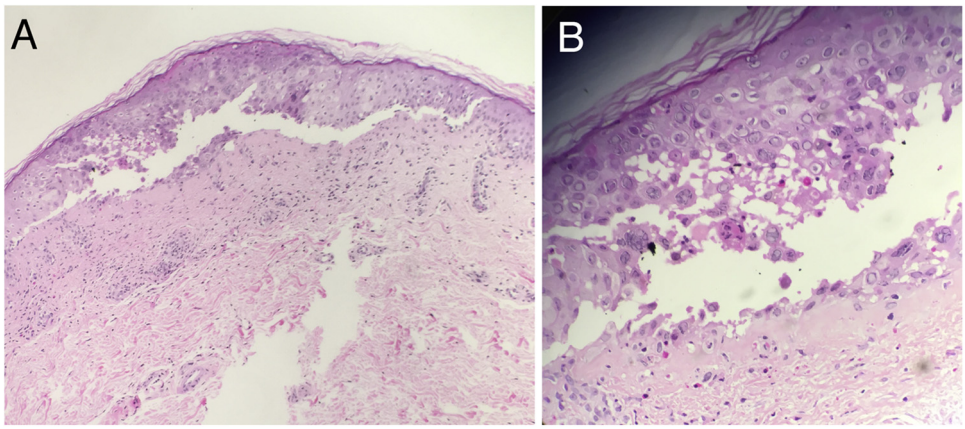

Fig. 2. Histopathology of skin biopsy.
(A) **At low power** — intraepidermal vesiculation. (B) **At higher power** — swollen pale keratinocytes with enlarged slate-grey nuclei and multinucleated giant.

Discussion

Viruses of the herpesviridae family are enveloped DNA viruses; they are frequent and important human pathogens [1]. Within this family, HSV1-2 and VZV are the human neurotropic viruses that can undergo latent infection in the dorsal root ganglia during the entire life of the host, from which they can reactivate and lead to human morbidity and mortality [1].

Reactivation can lead to disseminated disease; whereby there is diffuse skin involvement and/or different organ systems are concomitantly affected. Disseminated herpes zoster (DHZ) is rare and most frequently affects immunocompromised patients. It is defined arbitrarily as involvement of more than 2 contiguous dermatomes, presence of more than 20 vesicles outside the initial dermatome, or systemic involvement [2]. Disseminated herpes simplex virus (HSV) and varicella zoster virus (VZV) have been reported individually in both immunosuppressed and immunocompetent adults [3].

To the best of our knowledge, this is the first case of disseminated concomitant HSV and VZV with molecular evidence of the simultaneous presence of both HSV-1 and VZV viruses in two different body sites (the skin and CSF). A previous case of disseminated HSV and VZV co-infection in a patient taking thalidomide for multiple myeloma has been reported; however, viruses were isolated individually from two different sites; cultures from a skin vesicle only grew VZV, and cultures from the endotracheal tubes only grew HSV-1 [4].

Co-infection of HSV and VZV has been rarely reported. Isolated localized central nervous system co-infection with HSV and VZV has been reported in immunocompetent patients [5]; as well as cases of isolated localized skin co-infection by HSV and VZV in immunocompetent patients [6].

Waning cell-mediated immunity is believed to play a major role in increasing the incidence of herpes zoster in elderly individuals, particularly since antibody titers levels do not change or could even rise with age [7]. It has been well established that patients with altered cell-mediated immunity, such as elderly patients, HIV infected patients and patients with hematologic malignancies, have both higher incidence rates of herpes zoster and higher risks of herpes zoster related complications including its dissemination [8,9]. However, this case adds to the three reports of patients developing cutaneous disseminated herpes zoster many years after splenectomy for ITP [10,11]. The authors of the previous reports postulated that splenectomy might not increase the occurrence of HZ but may increase its risk of cutaneous dissemination [10]. Other authors have argued that since no other patients with a splenectomy without a history of ITP developed DHZ, it is probable that ITP is the risk factor for DHZ rather than the splenectomy itself [12]. Yu et al. suggested that functional defects in regulatory T cells might contribute to the pathogenesis of ITP [13]. Hence, although the mechanism of reactivation of VZV is not completely understood, it is likely that in patients with an underlying immunologic condition such as ITP, VZV-specific immunity is disturbed. Additional research is needed to further elucidate the relationship between ITP and VZV-specific immunity.

The potential cross-reactivity among viruses of the used *artus*-PCR Kits have been tested and refuted by the manufacturer. Hence both the skin and CSF samples were truly infected with both VZV and HSV-1.

Conclusion

This is the first case of disseminated HSV and VZV infection with molecular evidence of the simultaneous presence of both HSV-1 and VZV viruses in two different body sites (the skin and CSF). Cell-mediated immunity plays a major role in VZV-specific immunity, however, the mechanisms of reactivation of VZV are still not completely elucidated, and in immunologic conditions such as ITP it is likely that the VZV-specific immunity is altered. Additional research is needed to further elucidate the relationship between splenectomy in patients with ITP and VZV-specific immunity.

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Competing interests

None declared.

Ethical approval

Not required.

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