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Single Case

Treatment of Moderate-to-Severe Psoriasis in the Presence of Kaposi's Varicelliform Eruption

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Keywords
Psoriasis · Secukinumab · Herpes simplex virus

Abstract
Kaposi's varicelliform eruption (KVE) is a disseminated cutaneous infection usually induced by herpesvirus type 1 or 2, vaccinia virus or Coxsackie A16 virus in a patient with an underlying dermatosis. Risk factors for KVE reported in the literature include erythroderma, systemic sepsis, therapy with immunosuppressants such as methotrexate and systemic steroids, and therapy with systemic retinoids. The occurrence of KVE in psoriasis is rare and it predominantly appears in patients affected by erythrodermic psoriasis during immunosuppressive treatment. We report our experience of a remarkable case of a patient affected by severe erythrodermic psoriasis and KVE that healed after antiviral treatment and after having received secukinumab. After 1 year, psoriasis was cleared and no recurrence of KVE had occurred.

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Psoriasis and Kaposi's Varicelliform Eruption

Psoriasis is a chronic and inflammatory immune-mediated disease whose Th1–Th17 inflammatory background can promote the development of several comorbidities, such as metabolic syndrome, liver and infectious disease [1–7].

Kaposi's varicelliform eruption (KVE) is a disseminated cutaneous infection usually induced by herpesvirus type 1 or 2, vaccinia virus or Coxsackie A16 virus in a patient with an underlying dermatosis, including atopic dermatitis, acantholytic dermatoses (Darier's disease, Hailey-Hailey disease), mycosis fungoides, ichthyosis vulgaris, seborrheic dermatitis, pityriasis rubra pilaris, and burns injuries [8, 9].

Risk factors for KVE reported in the literature include erythroderma, systemic sepsis, therapy with immunosuppressants such as methotrexate and systemic steroids, and therapy with systemic retinoids [10].

The occurrence of KVE in psoriasis is rare and it predominantly appears in patients affected by erythrodermic psoriasis during immunosuppressive treatment [10–13].

Clinically, KVE usually appears as disseminated papulovesicular and vesiculopustular eruption or superficial/deep erosions in the area affected by the underlying dermatosis, and commonly it spreads over the entire body in 7–10 days. Skin eruption may be associated with fever, malaise, and regional lymphadenopathy [10, 12].

The clinical diagnosis of KVE is confirmed by PCR for viral DNA or by viral culture; both electron microscopy and immunofluorescence testing can be useful for diagnostic purposes [14].

The pathogenesis of KVE remains unclear; nonetheless, decreased barrier function, as occurs in erythroderma, and deficient host immune response, as in the course of immunosuppressive therapy, may increase the vulnerability of patients to herpes simplex virus (HSV) superinfection [13].

Additionally, it has been demonstrated that patients affected by psoriasis have a significantly increased risk of serious infections, particularly systemic viral infection, owing to intrinsic immunologic disturbances associated with the disease and the higher prevalence of comorbidities, unhealthy lifestyle factors, and/or a higher low-grade inflammatory state that can affect their infectious disease susceptibility [15].

In the presence of erythroderma, HSV infection should be suspected when vesicular lesions or erosions develop on the underlying dermatosis [12].

Complications of KVE can be severe, including herpetic keratitis and blepharoconjunctivitis resulting in blindness, and systemic viremia [16, 17]. Early recognition of HSV infection, discontinuation of immunosuppressive agents, and the introduction of appropriate antiviral treatment are important medical interventions to decrease the incidence of complications and viral infection relapse.

TNF-α inhibits both replication and antigen expression of herpes virus and it has been shown that partial or complete block of TNF-α inhibits this intrinsic antiviral activity with a severe impact on host defense [18]. Caution is recommended on the use of anti-TNF-α drugs in patients with psoriasis and HSV infection, although several authors report that these drugs can generally be safely restarted in the majority of patients with HSV after temporary cessation and introduction of conventional anti-viral therapy and infection resolution [19–21].

Secukinumab is a fully human monoclonal antibody that selectively neutralizes interleukin-17A that has been shown to be effective in the treatment of moderate-to-severe psoriasis, psoriatic arthritis, and ankylosing spondylitis, with a rapid onset of action and sustained responses, and a favorable safety profile [22–24]. Clinical data on the use of secukinumab in

HSV-infected patients is lacking. Secukinumab use in hepatitis has been reported in 5 patients with hepatitis B virus (HBV), in 3 patients with hepatitis C virus (HCV), and in 1 patient with HBV-HCV co-infection. None of these patients experienced a significant increase in liver enzymes or virus reactivation [25–27]. Although biologic therapies showed a minimal risk for viral reactivation in patients seronegative for HCV or HBV core antibody, a risk was found in patients with chronic HBV infection highlighting the need not to underestimate a concomitant antiviral prophylaxis [25, 28].

The authors here report their clinical experience with a patient affected by severe erythrodermic psoriasis, with widespread HSV infection.

Case Report

A 53-year-old male with a 36-year history of plaque psoriasis presented with erythrodermic psoriasis (fever, asthenia, lymphadenopathy, and extensive erythema and scaling with PASI 48, PGA 4, BSA 90%, DLQI 28). He had received methylprednisolone 16 mg/day for 14 days. The steroid dose was gradually tapered, and oral cyclosporine 4 mg/kg/day was initiated. After 9 days, the patient developed painful erosive lesions predominantly located on the upper chest and face with ocular and labial involvement (Fig. 1a–c) associated with persistent fever and malaise. Histologic examination showed intraepidermal vesiculation with ballooning degeneration of keratinocytes, intranuclear inclusions, and multinucleated giant cells along with mild dermal and follicular lymphocytic infiltrate (Fig. 2a, b). Viral culture and PCR assay from swab of nonmucosal skin was positive for HSV-1. Moreover, bacterial cultures from the lesions were positive for methicillin-sensitive *Staphylococcus aureus* and oral Candida infection was found. Severe hypogammaglobulinemia was detected. Erythrodermic psoriasis with KVE from HSV infection was diagnosed. Therapy was started with intravenous gamma globulin (0.4 g/kg/day) for 5 days, intravenous acyclovir (10 mg/kg/day) for 10 days, intravenous teicoplanin (400 mg/day) for 10 days, oral fluconazole (200 mg/day) for 14 days, and topical ocular antiviral agents. The lesions regressed completely within 10 days. After KVE healing, in January 2017, the patient received secukinumab at conventional induction dosage of 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance at 300 mg. In March 2018, the patient was still in treatment with secukinumab, psoriasis was cleared (PASI 0, DLQI 0, PGA 0, BSA 0) (Fig. 3a, b), and no recurrence of HSV infection was observed during 1 year of follow-up.

Conclusion

A patient affected by severe erythrodermic psoriasis had KVE that healed after antiviral treatment and after having received secukinumab. After 1 year, psoriasis was cleared and no recurrence of KVE had occurred.

Key Message

The authors report their clinical experience with a patient affected by severe erythrodermic psoriasis, with KVE, a disseminated cutaneous infection usually induced by herpesvirus.

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Statement of Ethics

The authors declare that the research was conducted in accordance with the World Medical Association Declaration of Helsinki. The patients have given their written informed consent to publish their case, including publication of images.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

A.C. and E.M. equally contributed to data collection as well as to manuscript preparation. All authors discussed the results and contributed to the final manuscript.

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Anna Campanati and Elisa Molinelli equally contributed to the manuscript

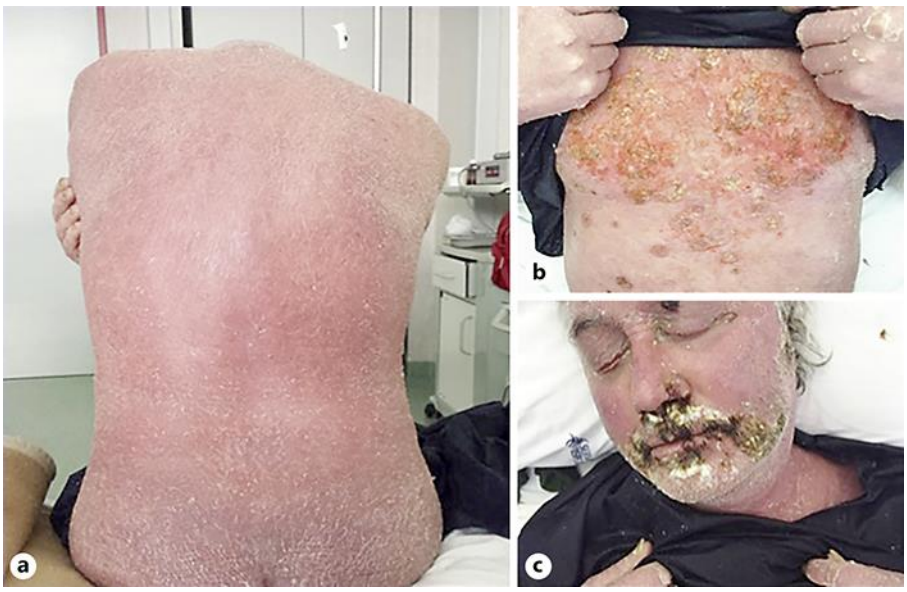

Fig. 1. KVE in erythrodermic psoriasis complicated by methicillin-sensitive *Staphylococcus aureus* superinfection (**a**) and characterized by vesicular and erosive lesions located on the upper chest (**b**) and face (**c**) with bilateral ectropion.

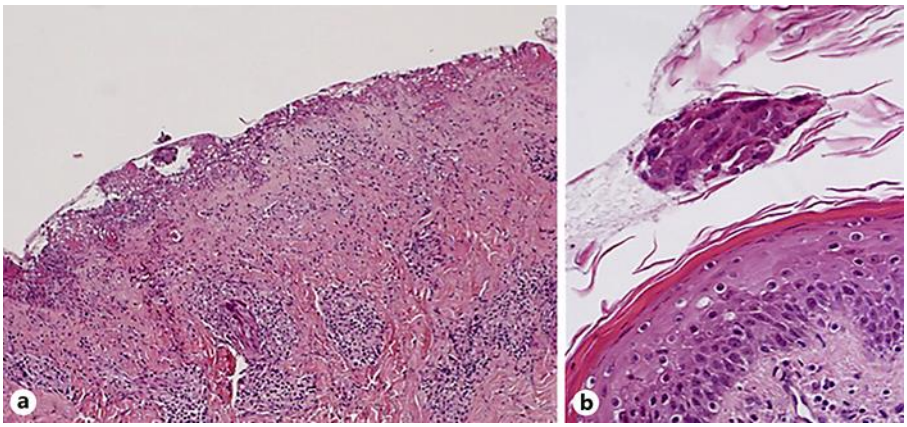

Fig. 2. Histology of the skin lesion showed mild dermal and follicular lymphocytic infiltrate (**a**) (hematoxylin and eosin staining, ×100 magnification) associated with intraepidermal vesiculation with ballooning degeneration of keratinocytes, intranuclear inclusions, and multinucleated giant cells (**b**) (hematoxylin and eosin staining, ×200 magnification).

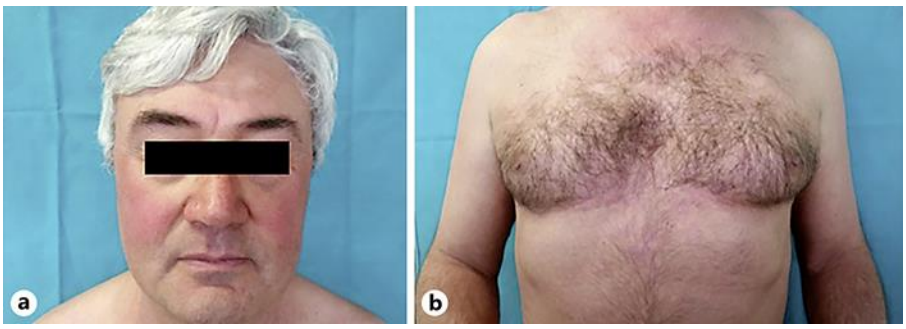

Fig. 3. Complete psoriasis clearance and no recurrence of KVE on the face (**a**) and chest (**b**) after 1 year of treatment with secukinumab.