Thus, pharynx is already known as a reservoir for BHS involved in invasive GAS infection.

In some cases of NSTI, the portal of entry is not identified.[5,8] Pharyngeal and perineal carriage of bacteria could be involved in NSTI in two ways: extrinsic contamination of a pre-existing skin disruption or intrinsic contamination by haematogenous dissemination and transient bacteraemia.[8]

Some authors report that a deep and non-penetrating tissue injury (20–30% of cases) may occur and stimulate a repair response and myogenic progenitor cell activation with increased vimentin expression.[8–10] Vimentin is a ligand for GAS with transient bacteraemia from carriage.[8,10] The same authors demonstrated that NSAIDs play a role, increasing the binding of GAS to injured muscular tissue.[9] The GAS adhesin that binds vimentin has not been identified. GBS could have a comparable receptor that binds vimentin.

This case of GBS NSTI with no identified portal of entry associated with pharyngeal and perineal carriage of the same strain supports an endogenous origin of this infection; moreover, NSAIDs may have played a role, increasing the binding of GBS to injured muscular tissue, as was demonstrated for GAS.[9] Additional experiments should confirm the role of vimentin expression in GBS NSTIs and the role of pharyngeal or perineal carriage in the development of streptococcal-related NSTI.

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Conflicts of interest

Chloé Charpentier, Camille Hua, Mélanie Darty, Romain Bosc, Nicolas De Prost, Emilie Sbidian, Camille Gomart, Paul-Louis Woerther, Asmaa Tazi and Olivier Chosidow have nothing to disclose. Floriane Kouby and Jean-Winoc Decousser report grants from Merck Sharp and Dohme, outside the submitted work.

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Interferon-beta as an enhancer of paraviral exanthema during influenza virus infection

Dear Editor,

We herein describe the case of a 33-year-old male patient who presented at our emergency department with concomitant flu symptoms and a maculopapular rash. The evening prior to consultation he had first noticed erythematous macules on the trunk

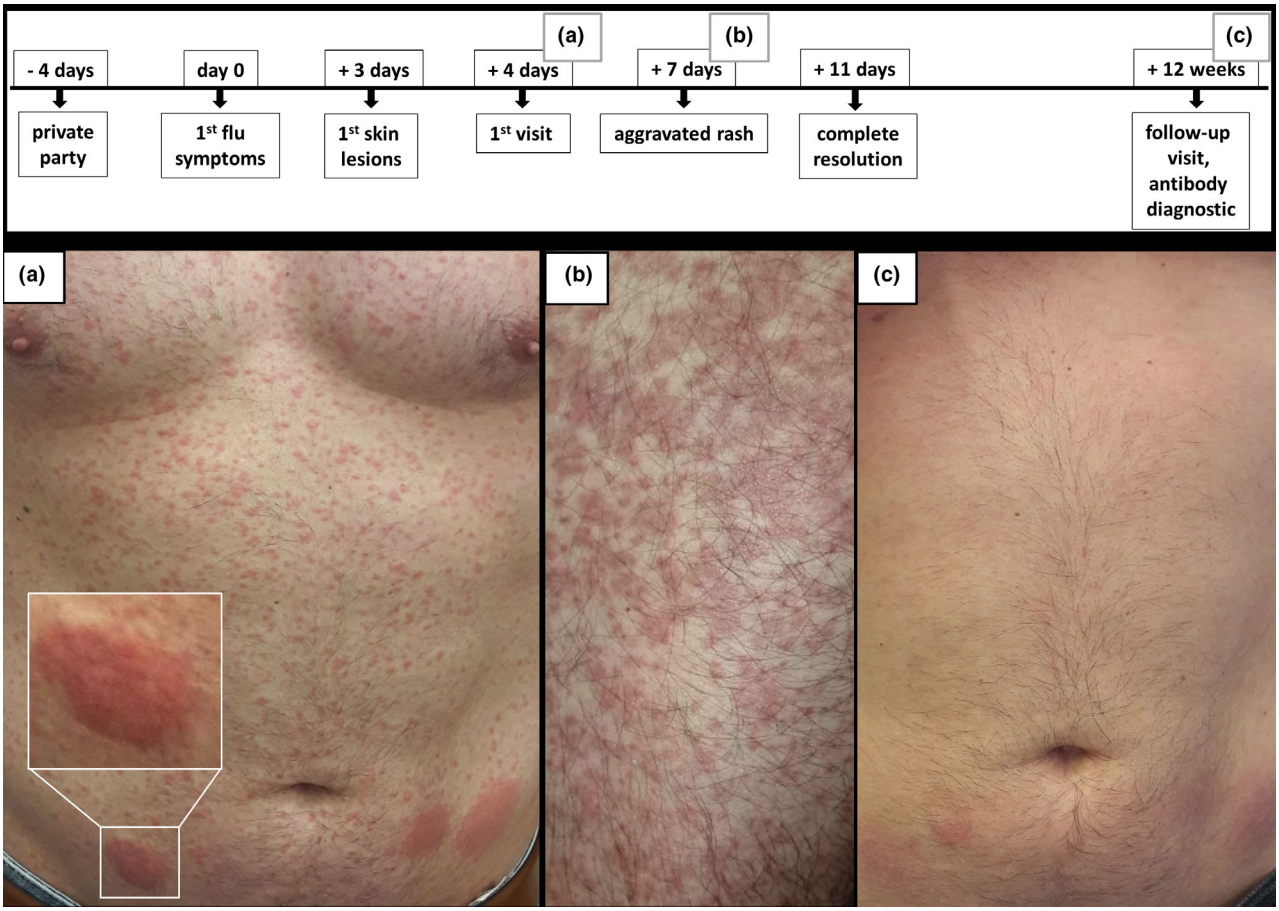

Figure 1 Timeline of clinical course and respective clinical findings. (a) clinical aspect (abdomen) during first visit/+4 days, (b) clinical aspect (left thigh)/+7 days (captured by the patient), (c) clinical aspect (abdomen) during follow-up visit/ +12 weeks

and arms, which had then rapidly progressed overnight. The rash was markedly pronounced at injection sites of interferon-beta (IFN-β) administered for relapsing remitting multiple sclerosis (RRMS; see Fig. 1a). Pruritus was moderate (3/10 numeric rating scale). Fever up to 38°C, fatigue, hoarseness and muscle and joint pain had begun four days prior to consultation. Another four days earlier, the patient and his family had visited a private party. Some of the guests as well as the patient's wife and children experienced equivalent flu symptoms albeit no skin eruptions.

Physical examination revealed neither abnormal auscultation findings concerning lungs and heart nor lymphadenopathy. The patient had been on IFN-β medication (Rebif® 44 mg subcutaneously three times per week) for almost a year. He reported about regularly occurring erythematous macules around the sites of injection. Apart from RRMS, there was no relevant comorbidity.

Paraviral exanthema during a respiratory tract infection was suspected; hence, the patient received a prescription for Methylprednisolonaceponat 0.1% to be applied once daily and an antipruritic lotion for repetitive use on demand.

At a follow-up visit 12 weeks after initial consultation, the patient stated he had applied topical treatment as prescribed. The lesions had initially progressed, though (see Fig. 1b). Within 1 week, however, the rash completely resolved without any modification of the treatment regimen simultaneously to resolution of the undulant fatigue and muscle and joint pain. Erythematous macules around injection sites were the only irregular skin finding at that point (see Fig. 1c). Serological analysis was highly suspicious for recent influenza A virus infection, whereas testing for other respiratory viruses including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) yielded unremarkable results.

Rashes associated with virus infections are frequent. They either result from direct viral induced cytopathic effects on epithelial cells or present themselves as so-called paraviral exanthema that are considered an immunological epiphenomenon in response to the infectious pathogen.[1,2] Sporadic reports of

exanthema during influenza exist.[3] Interestingly, the distribution pattern of our patient's rash suggests IFN-β injections as a trigger of immune response. The mechanisms involved in paraviral exanthema are not fully unravelled, yet. Type I IFN production, however, is considered a hallmark of the response pattern upon virus sensing.[4] It seems plausible that circulating endogenous interferons might contribute to the widespread efflorescences in paraviral exanthema as locally administered IFN-β has been shown to be capable of directly inducing inflammatory patches via CXCL10 as well as CCL2 induction and infiltration of corresponding CXCR3-positive T cells and macrophages.[5] Presumably, the local, inflammatory reactions upon IFN-β application persist awhile as our patient exhibited at least five of the alternately used injection sites at the same time. It seems likely that residing immune cells (e.g. tissue resident memory cells[6]) might locally enhance the generalized immunological paraviral exanthema.

As it is well known that interferons mediate antiviral responses, their therapeutic capacity against SARS-CoV-2 is currently being investigated in clinical trials with first promising results concerning early IFN-β treatment.[7] Heterogeneous paraviral rashes have also been reported in corona virus disease 2019 (COVID-19) patients,[8] and in a recent study including 103 COVID-19 patients, one individual had developed a maculopapular rash upon IFN-β treatment.[9] Therefore, this case report encourages systematic dermatological evaluation of skin eruptions in COVID-19 patients treated with interferons. Resulting knowledge might help to further dissect pathophysiological pathways in virus-induced exanthema in general.

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Dyskeratosis follicularis cured by superficial radiotherapy: long-term follow-up of 10 patients

Editor,

Dyskeratosis follicularis (DF), or Darier's disease, is a genodermatosis caused by a mutation in the ATP2A2 gene coding for Ca^{++} – ATPase.[1,2] DF is a chronically relapsing disease with keratotic papules especially in seborrhaeic areas with tendency to superinfections and malodours.[3] Treatment, such as antiseptics, antibiotics, corticosteroids and retinoids, does not result in cure.[3]

Superficial radiotherapy (SR) uses low-energy X-rays (20–100 kV) to kill cells by ionization of atoms. SR is mostly used to treat skin cancer but has been used to treat DF in a few cases during the last century.[4–9]

In this case series, we rapport the efficacy of the innovate therapeutic approach of treating dyskeratosis follicularis with superficial radiotherapy.

We treated 10 patients with histologically confirmed DF with SR in our centre from 2015 to 2019. The mean age was 50 years (range 19–81). The average number of years suffering from DF before SR was 27 (range 8–57 years). Eight patients suffered from between one and more than 10 yearly infections, and three of the patients had been hospitalized due to DF.

The X-ray generating system was a Gulmay D3100 (Xstrahl LTD, Surrey, UK). Patients received eight fractions of two grey with 20 kV (half-value-layer of 2 mm skin) every 2–3 days to a total dose of 16 Gray.

Eight out of 10 patients [30 out of 34 treated areas (90%)] responded with complete cure (Figs 1 and 2). The average observation time after cure was 33 months (range 14–68 months). One patient suffered from continuous skin infections and had complete response in four out of seven treated areas. She

