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Stevens-Johnson syndrome induced by Vaxvetria (AZD1222) COVID-19 vaccine

To the editor,

A 65-year-old male patient with unremarkable medical history, except for recent administration of the second dose of Vaxvetria (AZD1222) COVID-19 vaccine, was hospitalized for a mucocutaneous eruption occurred 10 days after the injection. No adverse events were reported after the first dose. A prodromal phase characterized by headache, high fever, cough, impaired vision and joint and muscle pain started 3 days after the vaccine. At dermatological consultation, multiple, round-to-oval erythematous patches were observed, with ill-defined borders and purpuric centres giving the lesions an atypical targetoid appearance. The patches were widely distributed on face, trunk and limbs, sparing the scalp, palms and soles with an approximate body surface area (BSA) involved of 9% (Fig. 1a). Mucosal involvement was also presented with erosions and vesicles affecting both superior and inferior labial mucosae and glans penis (Fig. 1b). A skin biopsy was collected, and the histological report evidenced hyper-orto-parakeratosis with focal vacuolar degeneration of the basal layer and scattered apoptotic keratinocytes. Clinical and pathological findings were compatible with Stevens-Johnson syndrome (SJS), thus prednisone 1 mg/Kg/die was started and slowly tapered in 8 weeks, resulting in progressive improvement and complete clearance of lesions (Fig. 1c).

Blood examinations of the prodromal phase showed neutrophilia and low platelets along with elevated CRP (9.21 mg/dL), LDH (319 U/L) and fibrinogen (>700). Subsequently, an increase in CRP (14.73), creatine-kinase (299 U/L), LDH (345 U/L) and D-dimer (from 1984 to 2256 μg/mL) were noted with fibrinogen consumption. However, coagulation indexes

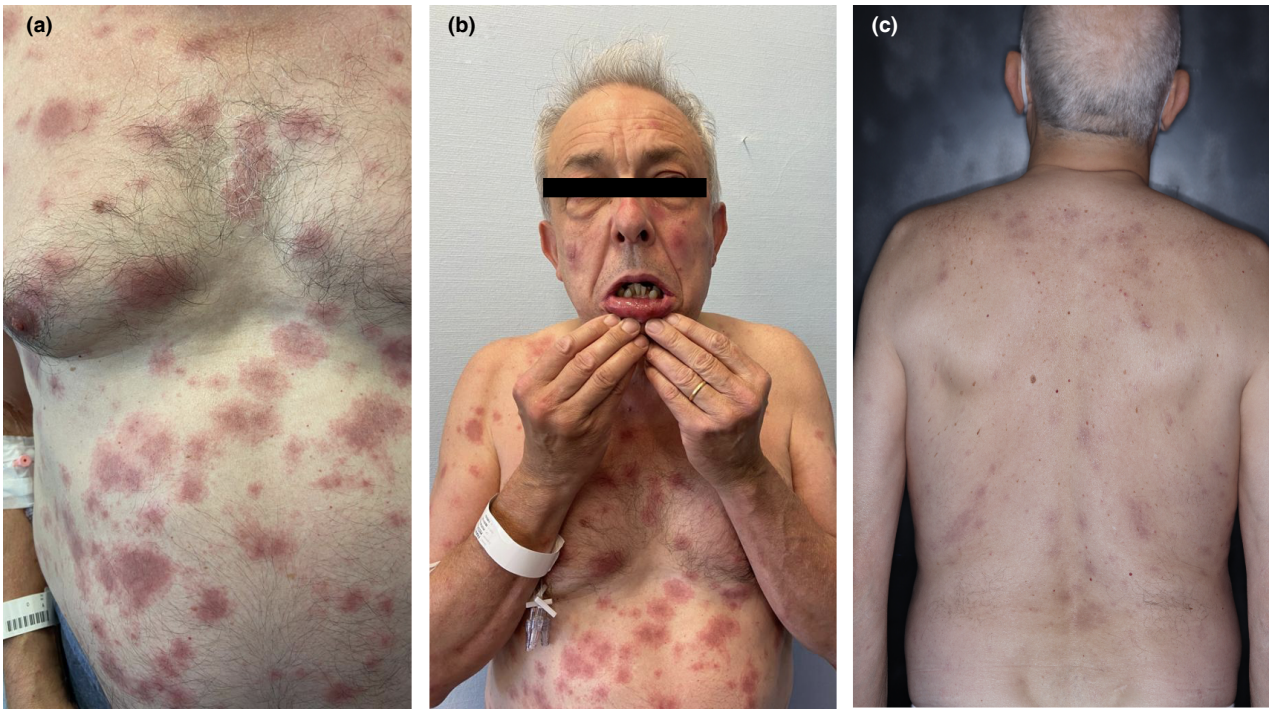

Figure 1 Clinical pictures showing cutaneous and mucosal involvement before (a, b) and after administration of corticosteroids (c).

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(PT and aPTT) appeared to be normal, excluding intravascular coagulation disease. A cranial CT angiography was performed due to persistence of headache, revealing superior sagittal sinus thrombosis (Fig. 2) for which the patient was started with Warfarin. A venous echo colour Doppler excluded deep vein thrombosis of lower limbs.

Stevens-Johnson syndrome is a rare life-threatening inflammatory mucocutaneous reaction, counting 1-2 cases per million each year. It usually begins with upper respiratory tract symptoms followed by the rapid onset of mucocutaneous lesions, characterized by diffuse erythematous macules with purpuric necrotic centres and overlying blistering. If involvement progresses, affected portions of the skin may slough, resulting in extensive superficial detachments.[1] Among the defined triggers of SJS, drugs are considered the most important. In our case, no new medications were introduced before the eruption onset. As it appeared 7 days after the administration of the second dose of Vaxvetria COVID-19 vaccine, we deposed for a probable causative association. The Naranjo score obtained was 5 even if an accurate score was not applicable. Vaccination-related cases have been described in the literature, the majority regarding childhood and varicella vaccination.[2] However, only a few cases of SJS after COVID-19 vaccination have been reported in the literature so far,[3–6] none of them regarding Vaxvetria vaccine. It has been hypothesized that due to individual genetic susceptibility, vaccine antigens may be preferentially expressed on the surface of keratinocytes, generating a CD8+ T lymphocyte immune response against epidermal cells (type IV hypersensitivity) then leading to apoptosis of keratinocytes and detachment at the dermal-epidermal junction with a latency of 5 days in most cases[7]

Intriguingly, our patient presented to the ER with thrombocytopenia and developed sagittal sinus thrombosis during hospitalization. Those manifestations are now known to be possibly linked to an autoimmune dysregulation induced by COVID-19 vaccination, presumably involving the production of antibodies against platelet factor 4, causing platelet consumption and thrombus formation.[8] Therefore, although not demonstrated, we may have observed antibody and cell-mediated hypersensitivity, induced by COVID-19 vaccination in the same patient in a short period of time.

During the current COVID-19 pandemic, vaccination is the safest available option to stop the pandemic and prevent severe disease. Given the large number of persons likely to be exposed to these drugs, vaccine safety is a critical issue: identifying and managing adverse reactions, while continuing to educate on the critical importance of vaccination is an objective of primary importance.

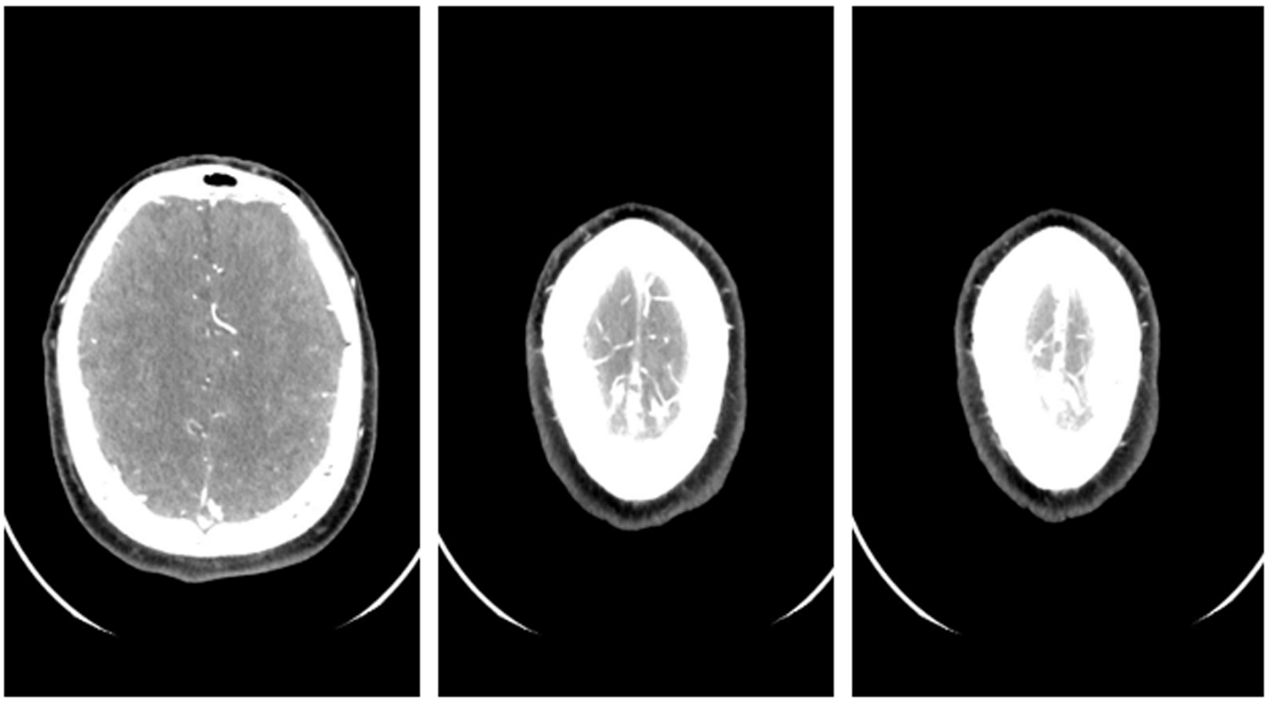

Figure 2 Radiological images from cranial CT Angiography conducted during hospitalization showing irregular uptake at superior sagittal sinus, compatible with thrombosis.

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Informed consent

The patients have given written informed consent to the publication of the case details.

Conflicts of interest

None of the authors have any conflict of interest to disclose.

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Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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‘COVID nose’ – A unique post–COVID pigmentary sequelae reminiscing Chik sign: A descriptive case series

Sir,

The novel coronavirus 2019 (COVID-19)-induced pandemic, attributed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been rampaging across the globe since last 2 years. A myriad of mucocutaneous manifestations have been observed with COVID-19 infection.[1] In this descriptive case series, we describe six Indian patients who developed localized freckle-like nasal hyperpigmentation following COVID-19 infection. We propose the term ‘COVID nose’ to delineate this unique delayed pigmentary outcome attributed to COVID-19.

Six patients presented to our dedicated post-COVID clinic over the course of this pandemic with facial pigmentation (Table 1). Institutional Ethics Committee approval and written informed consent from all these patients were obtained. They comprised of four females and two males (age range: 25–65 years, mean: 44 years). Accompanying comorbidity (diabetes mellitus-1, hypothyroidism and COPD-1) was noted in two patients (33%). History regarding medications, pre-existing dermatoses and arthritis was not elicited in any patient. Apart from the aesthetic disturbance owing to pigmentation, the condition was asymptomatic in majority of patients (5, 83%). All patients had experienced only mild COVID-19 symptoms, from which they had recovered with standard supportive care without any systemic complications. The interval between onset of COVID-19 symptoms and appearance of nasal pigmentation ranged from 15–27 days (mean 23.2 days). On cutaneous assessment, multiple discrete and few coalescing dark brown-to-black freckle-like macules was observed to be localized mainly over the tip and ala nose in most cases (100%) with occasional involvement of malar area (2, 33%) (Fig. 1a–c). Dermoscopy [DermLite DL4, contact/polarized, 10×] revealed areas of light-to-dark brown reticular pigment network over light brown background with perifollicular pigment clumping (Fig. 1d) Histopathological examination could not be carried out as the patients refused consent for biopsy. Routine blood parameters was within normal levels and serological tests for dengue and chikungunya viruses was negative. Treatment with topical skin-lightening agents (azelaic acid and hydroquinone) coupled with sunscreen led to significant resolution of pigmentation in 10–16 weeks.

Pigmentary alteration has rarely been directly attributed to SARS-CoV-2.[1] In China, there were televised reports of two COVID-19 affected physicians who developed darkening of

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