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LETTERS TO THE EDITOR

Clinical, histopathological, and dermatoscopic characterization of eruptive pseudoangioma developing after COVID-19 vaccination—A case-series

To the Editor,

Eruptive pseudoangioma (EP) is an acute, benign, self-limiting exanthem characterized by the sudden appearance of small cherry angioma-like lesions over the body. EP develops due to transient dilatation of dermal blood vessels as a result of "dermal hypersensitivity reaction". Reported for the first time by Cherry et al.[1] EP is believed to be a paraviral dermatosis. The role of insect bite hypersensitivity reaction has also been suggested. Often pediatric patients may experience prodromal symptoms, but adult cases are invariable asymptomatic.

Clinically, the lesions are asymptomatic bright red macules and papules with blanched perilesional halos, resolving on their own within 2–15 days. Often a clustering of cases is seen in the summer and spring seasons. Histopathological features include capillary dilatation with plump endothelial cells and perivascular lymphocytic infiltration without vasculitis.

Herein, we present a series of 53 patients who developed EP following the recombinant ChAdOx1 nCoV-19 coronavirus vaccine, also known as Covishield™, COVID-19 vaccination, between February and November 2021 (Figure 1A–D). EP was clinically diagnosed, by two independent senior dermatologists. Dermatoscopic and histopathological features were correlated in all the patients.

The most commonly affected age group was 18–30 years (n = 49;92.5%). Five (9.4%)patients complained of mild pruritus. The latency between vaccination and eruptions was 5.3 ± 3.8 days. Prodromal symptoms including respiratory distress, transient fever, and diarrhea were recorded in 22 (41.5%) individuals. Twelve (22.6%) subjects had leukocytosis. Neutrophilia (n = 5;9.4%) and eosinophilia (n = 9;16.9%) were also noted. The lesions resolved in an average of 16.7 ± 11.1 days (10–40 days) without any post-inflammatory hyperpigmentation. Past history of COVID-19 infection was present in 4 patients (2–3 months back), while 3 patients had a history of dengue infection before vaccination.

Dermatoscopy revealed red dots (histopathologically corresponding to dermal vascular dilatation and plump endothelial lining), surrounding dull red structureless-zone (lymphohistiocytic infiltration around vessels), and perilesional halo(due to dermal edema) (Figure 1E,F). Interestingly, there was an absence of perilesional halo in all the patients having EP on their face. The absence of purpuric globules and dots ruled out RBCs extravasation and vasculitis. COVID-19 RTPCR (repeated twice 3 days apart) and TORCH profile (serology for Toxoplasma, Rubella, Cytomegalovirus, and Herpes simplex), HbsAg, and anti-HCV antibodies of all the patients were negative.

Interestingly, in 47 (88.7%) patients, the onset of EP was after the second dose of vaccination. This latency suggests the role of delayed hypersensitivity reaction as one of the mechanisms of EP following vaccination. While the first dose of vaccine induces hypersensitivity, the second dose leads to the elicitation of the reaction.

Cases of EP following COVID-19 have been sparsely reported.[2,3] Till date, only 6 cases of EP secondary to COVID-19 vaccine have been reported in literature.[4,5] The proposed hypothesis is upregulation of cellular and humoral immunity against the spike protein in the viral vaccine stimulating a paraviral response.[5] In our experience, the estimated incidence of EP following COVID-19 vaccination is as low as 0.03%.

According to our results, EP is predominantly a disease of younger age groups. Corticosteroid-induced immunosuppression has also been postulated to trigger EP.[1] However, none of our patients had history of acquired or iatrogenic immunosuppression. The interesting observation of concurrent dengue fever in 3 patients reinforces the multidimensional paraviral pathomechanics.

In conclusion, our work simply aims at elucidating a new facet of the possible immunization-related pathogenesis at play in causing EP. The benefits of these vaccines exceedingly outweigh these adverse events. However, since lesions of EP can mimic vasculitis,

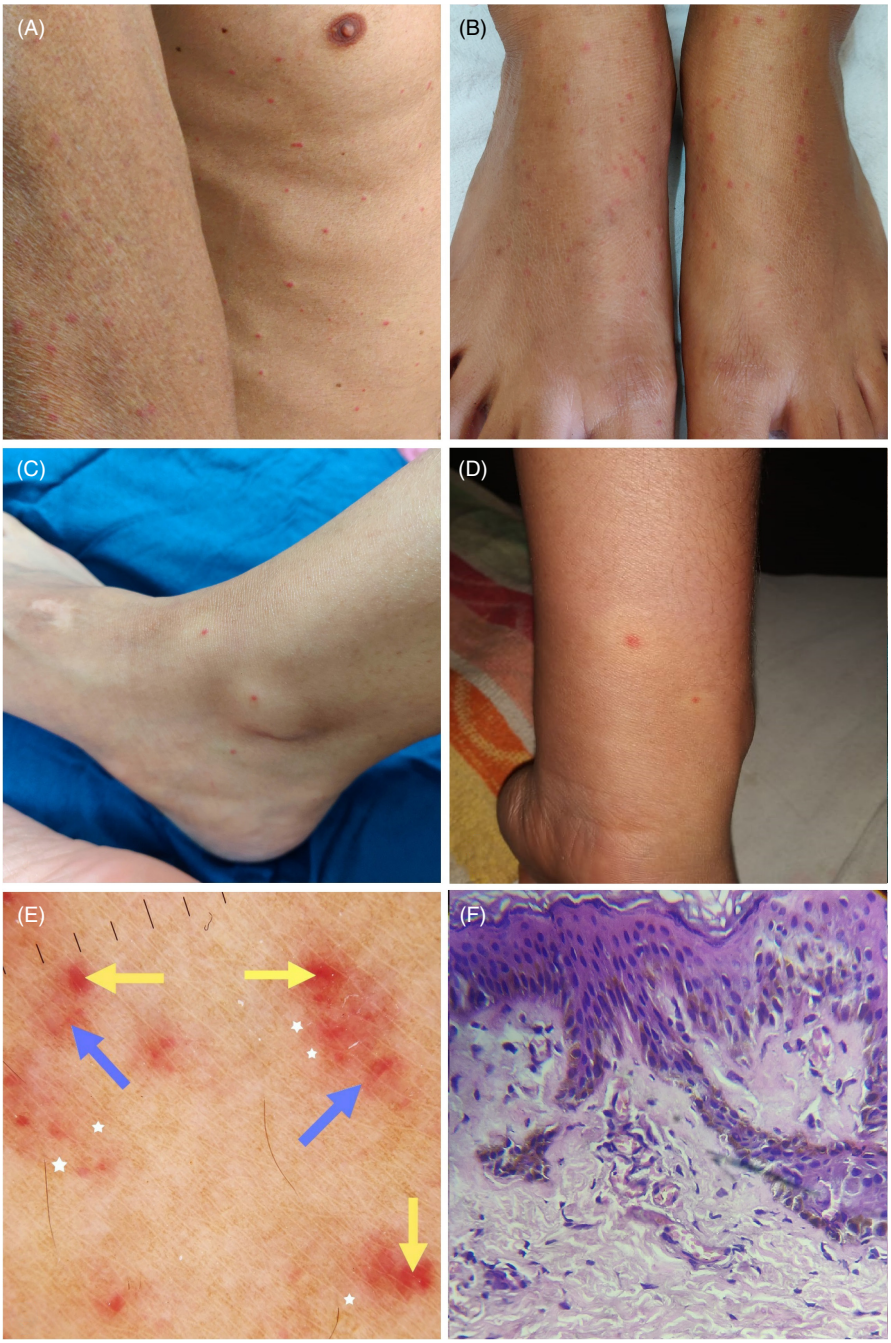

FIGURE 1 Multiple erythematous papules with perilesional halos (A) involving trunk and arms of a 52 year old male developing 6 days after vaccination, (B) over bilateral lower limbs of a 21 year old female developing 4 days after vaccination, (C) present over ankles and bilateral feet in a 27 year old female 3 days after vaccination, (D) over bilateral forearms in a 26 year old female 7 days after vaccination. (E) Dermatoscopic features included red dots (yellow arrow), surrounding dull red structureless-zones (blue arrow), and pale zones at periphery of lesions (white stars) as seen on Dermlite DL3 10× magnification. (F) Plump dilated superficial vessels with perivascular lymphohistiocytic infiltration in upper dermis and absence of red blood cell extravasation or features of vasculitis (Hematoxylin and eosin stain, 400×)

adrenergic urticaria, and vaccine-induced thrombotic thrombocytopenia, all cases must be subjected to histopathological confirmation.

Lack of controls and inability to assign causality were a few limitations of our work.

KEYWORDS

COVID-19, COVID-19 vaccine, eruptive pseudoangioma, eruptive pseudoangiomatosis, SARS-CoV-2

ETHICS APPROVAL

Due ethical approval was taken from institutional ethics committee. All patients gave written informed consent to be a part of this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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