

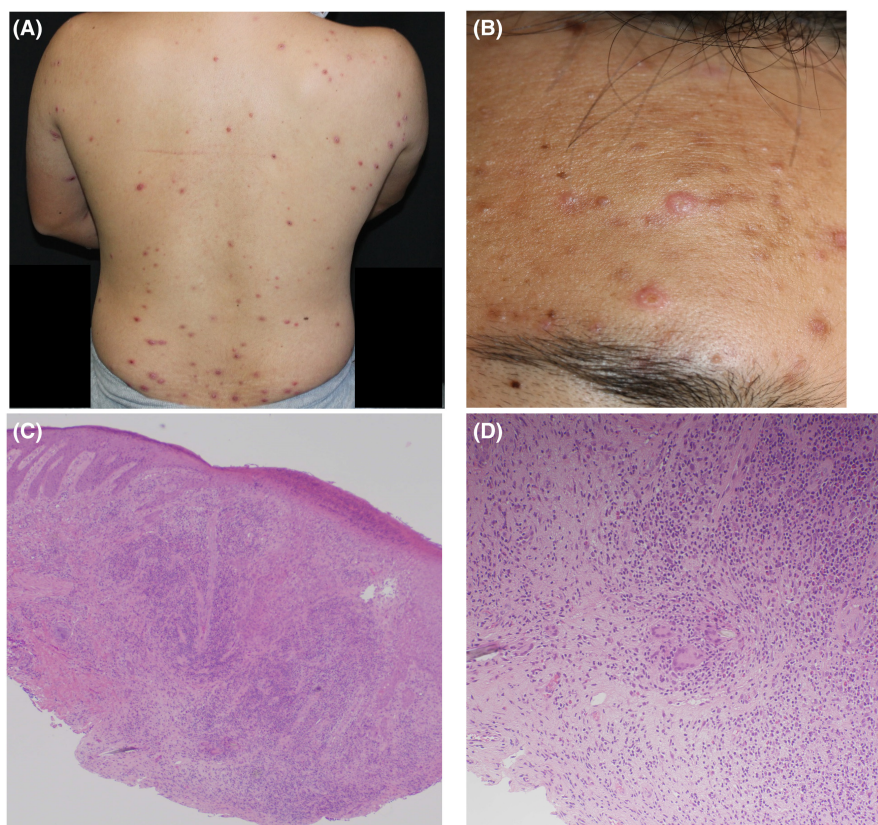
## CORRESPONDENCE

## Granulomatous reaction as a postherpetic isotopic response after primary varicella infection in a healthy adult

Postherpetic isotopic reaction (PHIR) refers to the development of new skin lesions at sites where prior herpetic skin lesions have been resolved. Herpes zoster (HZ) is the most common cause of PHIR; however, only a few cases of PHIR due to primary varicella infections have been reported.

A 22-year-old Japanese man with no relevant medical history presented with multiple vesicles throughout the body. The patient was diagnosed with primary varicella infection based on a positive Tzanck test. Three weeks after onset, new skin eruptions appeared in the regions affected by the primary rash. He had multiple nodules of 5–8 mm size and hues ranging from red to normal skin on his face, trunk, and limbs (Figure 1A,B). He had been vaccinated against varicella during childhood. No abnormal findings

were observed except for slightly low immunoglobulin (Ig) A and IgG (IgM: 37 mg/dL, IgA: 63 mg/dL, IgG: 734 mg/dL) in blood tests. Viral antibody examination revealed varicella-zoster virus (VZV)-IgM enzyme-linked immunosorbent assay (EIA) and VZV-IgG EIA titers of 0.03 and 6.8, respectively (both tests are positive at  $\geq 4.0$ ), indicating a previous infection. Histological findings showed epithelioid cells and granulomatous foreign body giant cells within the upper dermis, surrounded by marked neutrophilic and lymphocytic infiltration. No caseous necrosis, inclusion bodies, or residual viral particles were observed (Figure 1C,D). The patient was diagnosed with granulomatous reaction as PHIR after primary varicella infection. The nodules gradually improved with topical steroid, and no recurrence was noted.



**FIGURE 1** Clinical presentation of the patient. Multiple nodules on (A) the trunk and (B) forehead. A skin biopsy was obtained from the nodule on the forehead. Histological findings: epithelioid cell granuloma with inflammatory cell infiltrate (Hematoxylin and eosin stain, (C)  $\times 40$ ; (D)  $\times 1000$  magnification).

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Postherpetic isotopic reaction is a type of Wolf's isotope reaction (WIR), and some argue that WIRs are Koebner reactions.<sup>1</sup> However, Koebner reactions generally indicate the appearance of the same preexisting dermatosis on the injured skin. In the present case, a completely different eruption appeared after the primary rash. Thus, it was appropriate to describe it as a PHIR. Various skin manifestations have been reported in PHIR, with granulomatous dermatitis being the most common. According to Wang et al., the pathogenesis of granulomatous reaction as PHIR possibly encompasses post-infection nerve damage and residual virus particles, which may induce secretion of interleukin-4 and other chemokines, promote infiltration of inflammatory cells, and locally modulate immune and angiogenic responses.<sup>2</sup> Less nerve damage associated with primary varicella compared to that associated with HZ may be a reason for the infrequent PHIR phenomenon following primary varicella infection.

Several pediatric cases of granulomatous reactions as PHIR after primary varicella have been reported previously.<sup>3-6</sup> Two PHIR cases in adults were previously reported, but the patients were immunosuppressed hosts with myelogenous leukemia. Immunocompromised patients are susceptible to greater nerve damage by VZV.<sup>7</sup>

This is the first case of PHIR after varicella infection in a healthy adult. Histological findings supported the possibility of a hyperimmune response to residual viral particles, resulting in granulomatous dermatitis. Blood samples showed a slightly low level of immunoglobulins, but no other abnormalities were observed. Although the cause is unclear, the patient should be followed carefully for the future development of immune system diseases. Further studies are required to understand the mechanisms underlying PHIR after varicella infection.

## KEYWORDS

granulomatous reaction, postherpetic isotopic response, primary varicella infection, varicella-zoster virus

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## ETHICS STATEMENT

Informed consent: Informed consent was provided by the patient, and approval was received.


Approval of the research protocol: N/A.

Registration No. of the study/trial: N/A.

Animal studies: N/A.

## DATA AVAILABILITY STATEMENT

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

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