LETTER TO THE EDITOR
Iran J Allergy Asthma Immunol
In press.

Varicella-associated Pseudofasciitis: A Postviral Hyperinflammatory Soft Tissue Reaction Mimicking Necrotizing Fasciitis in Children

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Received: 28 September 2025; Received in revised form: 22 February 2026; Accepted: 11 March 2026

Dear Editor,

Varicella (chickenpox) is usually self-limiting in healthy children but can lead to severe soft tissue complications, most notably necrotizing fasciitis (NF). NF following varicella is well known for rapid progression, severe pain, and high mortality. Importantly, several studies have associated the use of nonsteroidal anti-inflammatory drugs (NSAIDs), particularly ibuprofen, with an increased risk and severity of postvaricella NF, likely by masking early symptoms and facilitating deeper bacterial invasion.[1–3] Consequently, pediatricians have been trained to urgently rule out NF whenever significant soft tissue swelling occurs after chickenpox.

Over the last 4 years at our tertiary pediatric infectious disease center, we observed a reproducible postvaricella inflammatory clinical pattern that mimics NF but is sterile, immune-driven, and self-limited. During this period, we observed this clinical presentation in more than 10 previously healthy children (predominantly male, aged 2–10 years). These patients presented within one week of varicella rash onset with marked swelling and erythematous skin changes, frequently involving the genital region or trunk. The dramatic appearance initially raised concern for NF. Yet, these children were afebrile or had only low-grade fever, were hemodynamically stable, well-appearing, and lacked the severe disproportionate pain or rapid deterioration typical of NF. Importantly, none had chronic NSAID exposure; only a few patients received a single dose of ibuprofen after the onset or recognition of soft-tissue swelling for mild pain or low-grade fever.

Laboratory findings demonstrated normal or only mildly elevated C-reactive protein (CRP) levels and erythrocyte sedimentation rates (ESR), while all cultures remained sterile. Imaging by ultrasound or magnetic resonance imaging revealed fascial thickening and edema without abscess, gas, or necrosis. Empirical broad-spectrum antibiotics failed to induce improvement. In contrast, administration of a single dose of intravenous immunoglobulin (IVIG, 1–2 g/kg; Intratect 5%, Biotest Pharma GmbH, Dreieich, Germany; exclusive agent in Iran: Darman Ara Co) was followed by clinical improvement within 24–48 hours, representing a temporal association rather than established causality. This observation should not delay evaluation for necrotizing fasciitis when clinically suspected. Immediate surgical consultation is warranted in the presence of severe disproportionate pain, bullae, crepitus, hemodynamic instability, or rapidly rising inflammatory markers. However, true necrotizing fasciitis still requires urgent surgical evaluation and treatment.[4]

We provisionally use the descriptive term "varicella-associated pseudofasciitis" to describe this postviral inflammatory presentation. Distinguishing it from true NF is essential to avoid unnecessary and potentially harmful interventions. Compared with NF, this entity shows:

- Stable general condition and vital signs
- Absence of high-grade fever or septic shock

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Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

• Pain that is mild or proportionate to swelling
• Normal or slightly elevated inflammatory markers
• Sterile cultures
• Lack of necrosis or gas on imaging
• Rapid, reproducible response to IVIG administration

The findings suggest a possible immune-mediated mechanism. Several immunologic mechanisms may hypothetically explain this observation:

• Immune complex deposition in fascial microvasculature, triggering complement activation and localized vascular inflammation.
• A cytokine-mediated inflammatory response increases vascular permeability and edema.[5,6]
• T-cell dysregulation and loss of regulatory balance, resembling other postviral inflammatory conditions, such as multisystem inflammatory syndrome in children.[7]

A limitation of this report is the absence of detailed immunologic marker evaluation, including cytokine profiling, which precludes confirmation of the proposed immune-mediated mechanism. The absence of bacterial superantigens and toxins differentiates this process from streptococcal NF.

These immunological pathways explain the benign clinical course and rapid response to IVIG, which likely acts by neutralizing autoantibodies, modulating complement activation, and dampening cytokine storms rather than directly targeting pathogens.

Clinical Impact and Call to Action

Misdiagnosing this benign entity as NF can lead to prolonged broad-spectrum antibiotic use, unnecessary surgical exploration, and significant parental anxiety. In contrast, early recognition of varicella-associated pseudofasciitis—a descriptive term for a sterile, postvaricella immune-mediated fasciitis—allows for timely immunomodulation with IVIG, sparing children invasive procedures and accelerating recovery.

With varicella still prevalent in many regions and vaccine coverage incomplete, we believe this postviral hyperinflammatory soft tissue syndrome deserves wider recognition among pediatricians, infectious disease specialists, and immunologists. Increased awareness may help clinicians recognize this presentation and consider it in the differential diagnosis of postvaricella soft tissue swelling, potentially avoiding unnecessary invasive interventions in children with a self-limited inflammatory process. This report is intended to increase clinical awareness only.

This report reflects clinical observations rather than a controlled clinical study, and the findings should be interpreted with appropriate caution.

STATEMENT OF ETHICS

This letter describes general clinical observations encountered during routine medical practice and does not involve systematic collection or analysis of identifiable patient data. No individual patient information is reported. Therefore, according to institutional and international publication ethics guidelines, formal ethics committee approval was not required. All information presented has been fully anonymized.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

Not applicable.

DATA AVAILABILITY

Upon reasonable request (via the corresponding author's email address).

AI ASSISTANCE DISCLOSURE

Limited AI-assisted language editing was used.

REFERENCES

1. Mikaeloff Y, Kezouh A, Suissa S. Nonsteroidal anti-inflammatory drug use and the risk of severe skin and soft tissue complications in patients with varicella or zoster disease. Br J Clin Pharmacol. 2008;65(2):203-9.
2. Zerr DM, Alexander ER, Duchin JS, Koutsky LA, Rubens CE. A case-control study of necrotizing fasciitis during primary varicella. Pediatrics. 1999;103(4 Pt 1):783-90.
3. Choo PW, Donahue JG, Platt R. Ibuprofen and skin and soft tissue superinfections in children with varicella. Ann Epidemiol. 1997;7(7):440-5.

4. Schröder A, Gerin A, Firth GB, Hoffmann KS, Grieve A, Oetzmann von Sochaczewski C. A systematic review of necrotising fasciitis in children from its first description in 1930 to 2018. BMC Infect Dis. 2019;19(1):317.
5. Nie J, Zhou L, Tian W, Liu X, Yang L, Yang X, Zhang Y, Wei S, Wang DW, Wei J. Deep insight into cytokine storm: from pathogenesis to treatment. Signal Transduct Target Ther. 2025;10(1):112.
6. Fahey E, Doyle SL. IL-1 family cytokine regulation of vascular permeability and angiogenesis. Front Immunol. 2019;10:1426.
7. Graciano-Machuca O, Villegas-Rivera G, López-Pérez I, Macías-Barragán J, Sifuentes-Franco S. Multisystem inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection: role of oxidative stress. Front Immunol. 2021;12:723654.