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Letter to the Editor

Erythema Papulatum Centrifugum: A Clinically Distinct Dermatosis

To the Editor,

We would like to comment on "Erythema Papulatum Centrifugum: A Clinically Distinct Dermatosis. CLINI-AEDV Case Series."[1] This article presents a descriptive case series of 7 patients. The small sample size and lack of a control group make it difficult to draw conclusions regarding a causal relationship between EPC and the COVID-19 vaccine or cancer. Furthermore, most analyses are descriptive and lack inferential statistical tests, such as chi-square tests or regression analysis, making it impossible to assess relative risk or statistical associations. The sampling strategy is also unclear, and selection bias is likely because all patients were recruited from specialist clinics with demographic characteristics that may not be representative of the broader population.

The diagnosis of EPC is based on clinical observations and rash characteristics. There are no specific laboratory or biopsy tests to detect inflammation or indicators of paraneoplastic disease, which limits the reliability of establishing an association with cancer or the COVID-19 vaccine. The timing and chronology of vaccine-associated exacerbations are unknown, which may contribute to recall bias or observer bias among patients and physicians.

From an interpretive standpoint, additional insights may be obtained by reanalyzing previous data, such as by stratifying patients according to risk variables (e.g., cancer history, immunization, age, and genetic background) and evaluating relapse patterns. Establishing an international EPC database to increase the number of patients may enable meta-analysis and the use of inferential statistical methods, such as logistic regression or Cox proportional hazards models, to evaluate hypotheses regarding paraneoplastic and temporal associations with vaccination.

Questions for further discussion include the following: Is EPC actually associated with the COVID-19 vaccine, or is this a coincidental finding? How does its presence in patients with cancer support a possible paraneoplastic phenomenon? Should patients without cancer be monitored to assess long-term risk? To confirm biological associations, future research should be designed as multicenter prospective cohort studies including a control group and additional biomarkers. Imaging and molecular profiling methods may contribute to a better understanding of the pathophysiology of EPC and its relationship with cancer or immunity.

References

1. Allegue F, Zulaica A, Pastor-Nieto MA, et al. Erythema papulatum centrifugum: a clinically distinct dermatosis. CLINI-AEDV case series. *Actas Dermo-Sifiliogr*. 2025, http://dx.doi.org/10.1016/j.ad.2025.10.006. S0001-7310(25)00653-2 [in press].

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