Received: 18 January 2023 | Revised: 26 January 2023 | Accepted: 16 February 2023

DOI: 10.1002/cia2.12300

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

Kikuchi-Fujimoto disease presenting with papular lesions on the elbows and knees

Kikuchi-Fujimoto disease (KFD) is a self-limited febrile lymphadenitis of unknown etiology, predominantly affecting the cervical lymph nodes of young adults.[1] Nodal lesions show paracortical necrosis with non-neutrophilic karyorrhexis, infiltration of $CD8^+$ T cells and myeloperoxidase $(MPO)^+$ histiocytes, and $CD123^+$ plasmacytoid dendritic-cell clusters, although necrosis may be absent depending on the disease phases.[1,2] Cutaneous lesions have been reported in up to 40% of cases.[3] The skin manifestations are variable, but often present on the upper body.[4–6] We report a case of KFD with papular lesions limited to the elbows and knees.

A 20-year-old man presented with a 2-week history of fever. Physical examination revealed non-tender lymphadenopathy of bilateral posterior cervical, axillary, and inguinal lymph nodes and non-pruritic erythematous papules on the elbows and knees (Figure 1A,B). Laboratory tests showed elevated levels of C-reactive protein (3.62 mg/dL) and serum lactate dehydrogenase (318 U/L; reference range, 124–222 U/L) and decreased white blood cell count (1700/μL). Anti-nuclear antibodies were negative. Computed tomography did not detect central lymph node swelling.

The skin biopsy specimen showed interface dermatitis, papillary dermal edema, and dermal infiltrate (Figure 1C). In the epidermis, spongiosis and pseudo-Pautrier abscesses were present (Figure 1D). The dermal lymphohistiocytic infiltrate was associated with karyorrhexis in the absence of neutrophils (Figure 1E). Most lymphocytes were positive for CD3 and contained both $CD4^+$ and $CD8^+$ cells, although most of the intraepidermal T cells were $CD8^+$ cells expressing TIA1, perforin, and granzyme B. The dermal infiltrate contained numerous $CD68^+$ (clones KP-1 and PG-M1) histiocytes (Figure 1F) that were comprised of $CD163^+$, MPO^+, and $CD123^+$ cells.

The lymph node biopsy specimen showed paracortical lymphohistiocytic infiltrate with karyorrhexis in the absence of neutrophils (Figure 1G). $CD8^+$ T cells predominated over $CD4^+$ cells (Figure 1H,I). $CD68^+$, $CD163^+$ histiocytes were abundant, and most of them expressed MPO (Figure 1J,K). Clusters of $CD123^+$ plasmacytoid dendritic cells were present (Figure 1L).

Although necrosis was not observed in the lymph node biopsy specimen, the diagnosis of KFD in the proliferative phase was made based on the histopathological and immunohistochemical findings.[1,2,4–6] Only supportive therapies with an oral non-steroidal anti-inflammatory drug and topical corticosteroid were given. Fever, lymphadenopathy, and cutaneous lesions resolved spontaneously in 5 weeks after the disease onset.

Cutaneous lesions of KFD are characterized by superficial and deep dermal lymphohistiocytic infiltrate, non-neutrophilic karyorrhexis, interface dermatitis, and papillary dermal edema.[4–6] Although spongiosis was observed in some cases,[5,6] presence of pseudo-Pautrier abscesses has not been reported. The reason why the cutaneous lesions in our case were limited to the elbows and knees is unknown, but their localization and the spongiotic epidermal changes suggest involvement of exogenous stimuli.

Differential diagnosis of KFD mainly includes SLE and lymphomas.[1] In our case, serum anti-nuclear antibodies were negative, and clinical signs suggestive of SLE other than fever and lymphadenopathy were absent. Histopathological and immunohistochemical

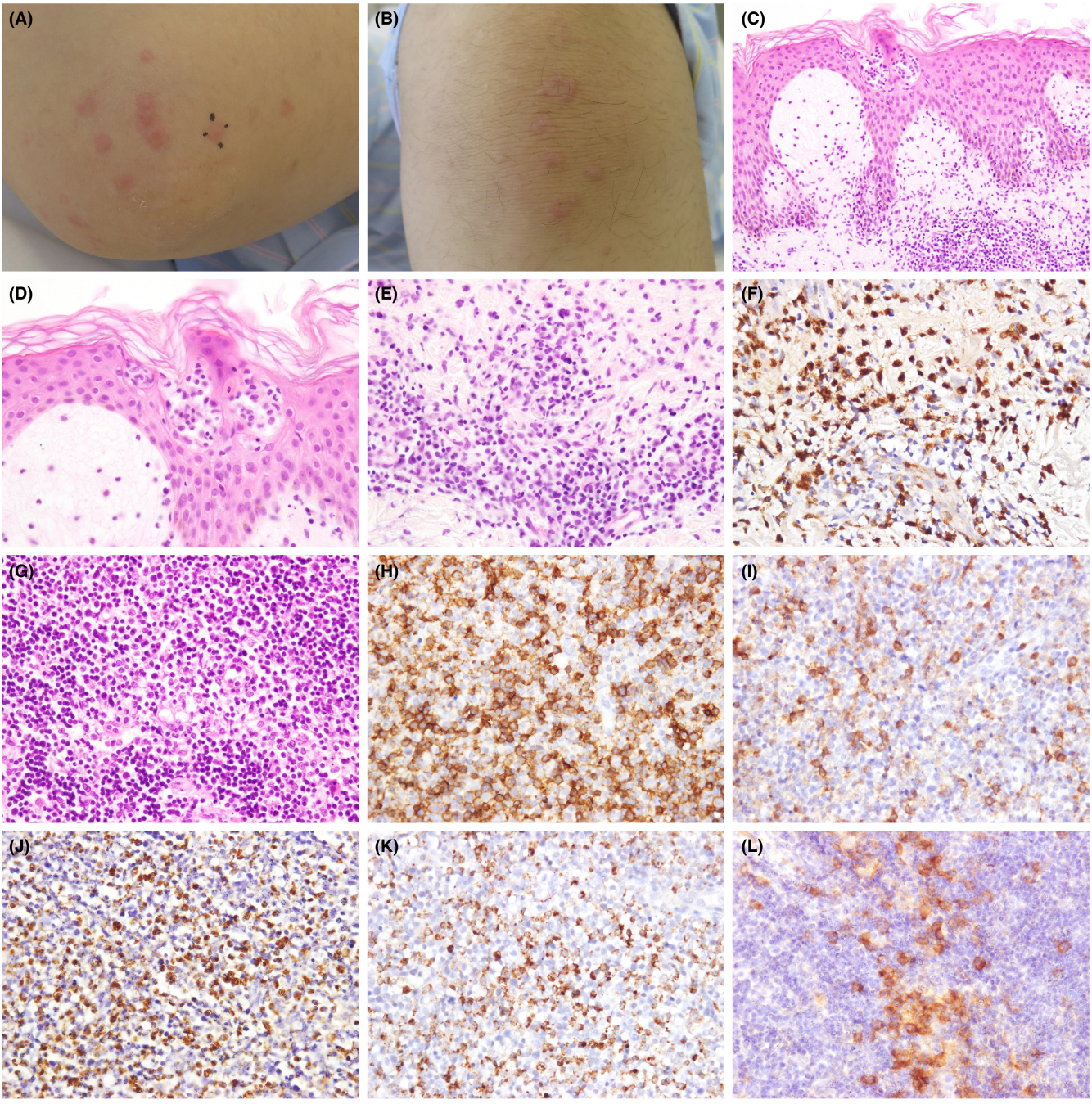

FIGURE 1 (A, B) Clinical features at presentation. Erythematous papules on the elbows and knees. (C) Interface dermatitis, papillary dermal edema, and dermal infiltrate (hematoxylin–eosin [HE], original magnification ×200). (D) Spongiosis and pseudo-Pautrier abscesses were also present (HE, ×400). (E) Dermal lymphohistiocytic infiltrate with karyorrhexis in the absence of neutrophils (HE, ×400). The dermal infiltrate contained numerous (F) $CD68^+$ (clone KP-1) histiocytes (×400). (G) The lymph node biopsy specimen showed paracortical lymphohistiocytic infiltrate with karyorrhexis in the absence of neutrophils (HE, ×400). In the paracortex, (H) $CD8^+$ T cells predominated over (I) $CD4^+$ cells (×400). (J) $CD68^+$ (clone KP-1) histiocytes were abundant, and most of them expressed (K) MPO (×400). (L) Clusters of $CD123^+$ plasmacytoid dendritic cells (×400).

findings of skin and lymph node biopsy specimens excluded both SLE and lymphomas.

In patients with cutaneous eruptions, fever, and lymphadenopathy, KFD should be considered. Immunohistochemical studies are useful for accurate diagnosis, especially in atypical cases.

ACKNOWLEDGMENTS

We thank K. Gunshin for her technical assistance.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

Journal of Cutaneous Immunology and Allergy

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

Approval of the research protocol: N/A.

Informed consent: Written informed consent was obtained from the patient.

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

Animal studies: N/A.

Izumi Takei MD[1,2]
Kazuhiro Kawai MD, PhD[1]
Mihoko Yamazaki MD, PhD[3]

[1]*Department of Dermatology, Kido Hospital, Niigata, Japan*
[2]*Division of Dermatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan*
[3]*Department of Nephrology and Rheumatology, Kido Hospital, Niigata, Japan*

Correspondence
Kazuhiro Kawai, Department of Dermatology, Kido Hospital, 4-13-3 Takeo, Higashi-ku, Niigata 950-0862, Japan.
Email: kazkawai@m2.kufm.kagoshima-u.ac.jp

ORCID

Kazuhiro Kawai https://orcid.org/0000-0001-9375-0713

REFERENCES

1. Pepe F, Disma S, Teodoro C, Pepe P, Magro G. Kikuchi-Fujimoto disease: a clinicopathologic update. Pathologica. 2015;107:120–9.
2. Sukswai N, Jung HR, Amr SS, Ng SB, Sheikh SS, Lyapichev K, et al. Immunopathology of Kikuchi-Fujimoto disease: a reappraisal using novel immunohistochemistry markers. Histopathology. 2020;77:262–74.
3. Kuo T. Cutaneous manifestation of Kikuchi's histiocytic necrotizing lymphadenitis. Am J Surg Pathol. 1990;14:872–6.
4. Spies J, Foucar K, Thompson CT, LeBoit PE. The histopathology of cutaneous lesions of Kikuchi's disease (necrotizing lymphadenitis): a report of five cases. Am J Surg Pathol. 1999;23:1040–7.
5. Kim JH, Kim YB, In SI, Kim YC, Han JH. The cutaneous lesions of Kikuchi's disease: a comprehensive analysis of 16 cases based on the clinicopathologic, immunohistochemical, and immunofluorescence studies with an emphasis on the differential diagnosis. Hum Pathol. 2010;41:1245–54.
6. Atwater AR, Longley BJ, Aughenbaugh WD. Kikuchi's disease: case report and systematic review of cutaneous and histopathologic presentations. J Am Acad Dermatol. 2008;59:130–6.