DOI: 10.1002/cia2.12111

LETTER TO THE EDITOR

Journal of Cutaneous Immunology and Allergy
WILEY

Multicentric Castleman's disease presenting with cutaneous plasmacytosis

Castleman's disease (CD) is an uncommon lymphoproliferative disorder that can be divided into two clinical subtypes: unicentric and multicentric CD (MCD). A part of MCD is caused by HHV-8, whereas HHV-8–negative MCD cases remain idiopathic (iMCD).[1] Cutaneous involvement of MCD is rare and may overlap with cutaneous plasmacytosis (CP). Here, we report a case of MCD exhibiting CP.

An 80-year-old man was referred to us because of a 4-year history of asymptomatic, multiple, indurated, hyperpigmented papules/nodules and plaques on his trunk and face. He had old myocardial infarction and chronic epidural hematoma. The patient had low-grade fever and fatigue. Laboratory examination revealed anemia (Hb, 9.3 g/dL), hypoalbuminemia (2.2 g/dL), elevated CRP (18.18 mg/L), polyclonal hypergammaglobulinemia (IgG, 4710 mg/dL; IgA, 606 mg/dL; IgE, 26 492 U/mL), elevated sIL-2R (1765 U/mL), and elevated IL-6 (285 pg/mL). The serum IgG4 was not elevated (115 mg/dL). Computed tomography showed widespread lymphadenopathy with hepatosplenomegaly. He denied any further workups and treatments.

A skin biopsy taken from a nodule on the chest revealed variable-sized lymphoid follicles located in the upper to deep dermis (Figure 1B, uppermost panel). The infiltrate of the nodular follicles consisted of plasma cells, plasmablasts, and lymphocytes. Immunohistochemically (Figure 1B, lower panels), $CD138^+CD38^+CD21^+$ cells predominantly infiltrated in the margin of follicles, and some of them invaded into the inside of follicles, indicating the proliferation of plasma cells and marginal zone cells. The cells were positive for Bcl-2, but not for Bcl-6 or CD10, confirming that the proliferating cells originated from the marginal cells or plasma zone cells. Minor aggregation of $CD3^+$ T cells and $CD20^+$ B cells were observed. Monoclonality of plasma cells was not found as kappa and lambda light chain was equally stained. Stain for HHV-8 (LANA-1) was positive. Thus, the patient was diagnosed as having HHV-8-MCD.

The skin eruption in our case is clinically different from that of usual CP in that the multiple hyperpigmented lesions were more nodular and indurative than the usual CP. In addition, histopathologically, lymphoid follicles were prominent in our case, which differs from massive perivascular plasmacytic infiltration seen in ordinary CP. Thus, the skin lesion of our case seems to be a mimicry of the lymph node lesion of MCD. Although the diagnosis of CD is based on lymph node histology, the previous reported cases showed that lymph node and skin exhibited similar histological features,[2] in consistent with our case.

Based on the mechanisms of pathological action, cutaneous manifestations of CD can be categorized into three types: cytokine-related (hyperpigmentation, vasculitis-like lesion, and cherry hemangioma), immune complex-related eruptions (paraneoplastic pemphigus and xanthogranulomas), and nonspecific manifestations (pruritus).[3] Viral IL-6, which is produced by HHV-8, promotes an inflammatory state responsible for clinical manifestations and laboratory abnormalities (Figure 1C).[1,4] It is important to discriminate between the variants of MCD, because the individual types require different treatments. HHV-8-MCD is a distinct disease entity requiring a different management, that is, rituximab with or without etoposide or doxorubicin and antiviral agent.[4] In conclusion, we report a rare case of HHV-8-MCD presenting with CP.

Pawit Phadungsaksawasdi MD
Shinsuke Nakazawa MD
Reiko Kageyama MD
Yoshiki Tokura MD, PhD

Department of Dermatology, Hamamatsu University School of Medicine, Hamamatsu, Japan

Correspondence
Yoshiki Tokura, MD, PhD, Department of Dermatology, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan.
Email: tokura@hama-med.ac.jp

ORCID
Pawit Phadungsaksawasdi https://orcid.org/0000-0002-6537-2687
Yoshiki Tokura https://orcid.org/0000-0001-7452-6919

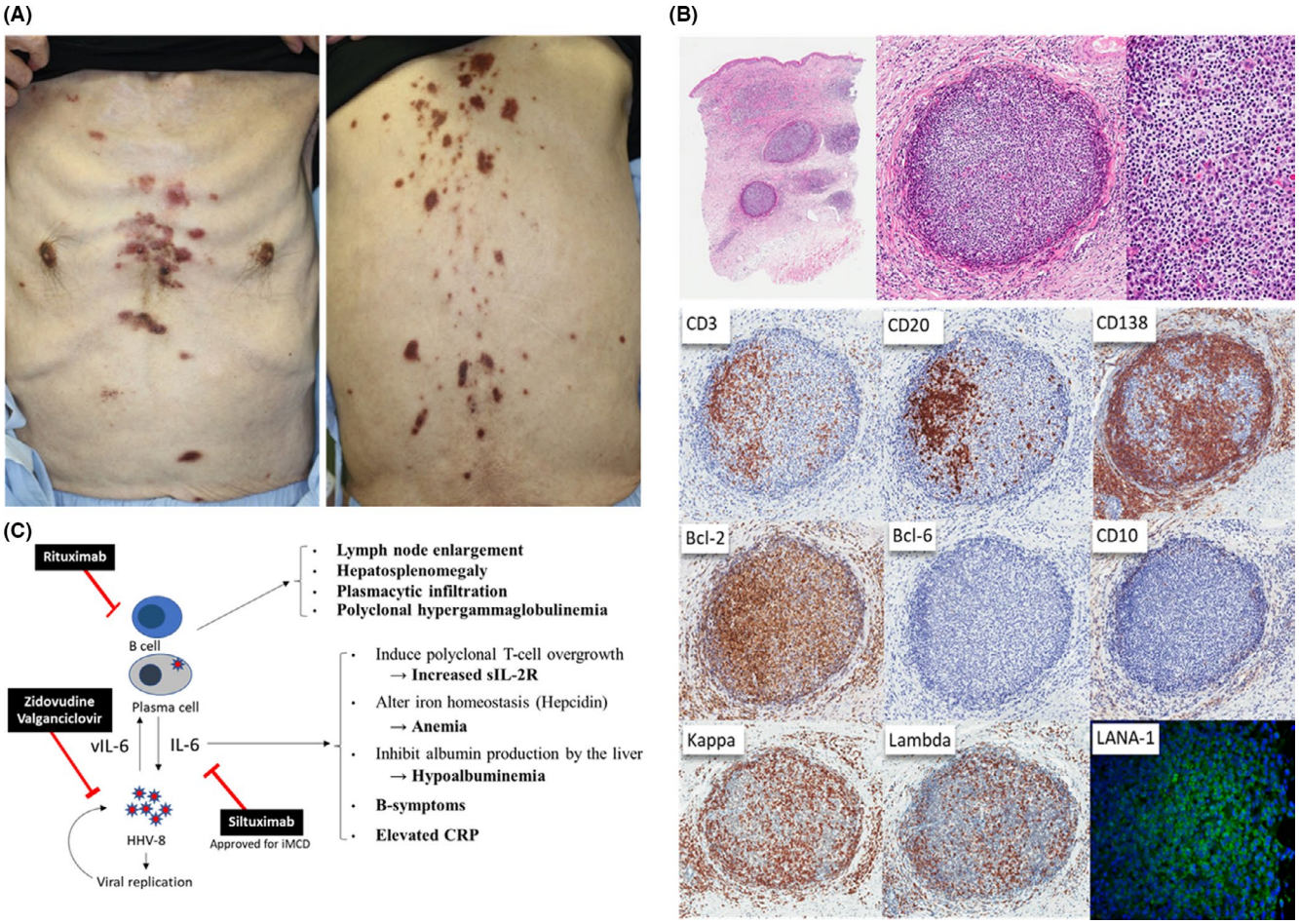

FIGURE 1 A, Skin manifestation; multiple indurated hyperpigmented papules, nodules, and plaques on the trunk. B, Skin biopsy; (uppermost panel; H&E) multiple nodular infiltrate of plasma cells, plasmablast, and lymphocytes; (lower three panels; Immunostaining. C, Pathogenesis of HHV-8–related MCD. HHV-8, Human herpesvirus 8; iMCD, idiopathic multicentric Castleman's disease; LANA-1, latency-associated nuclear antigen 1; sIL-2R, soluble IL-2 receptor

REFERENCES

1. van Rhee F, Voorhees P, Dispenzieri A, et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. Blood. 2018;132(20):2115–24.
2. Klein WM, Rencic A, Munshi NC, Nousari CH. Multicentric plasma cell arivant of Castleman's disease with cutaneous involvement. J Cutan Pathol. 2004;31:448–52.
3. Kim HJ, Han JH, Bang CH, et al. Cutaneous disorders associated with Castleman's disease. Acta Derm Venereol. 2019;99(11):984–9.
4. van Rhee F, Greenway A, Stone K. Treatment of idiopathic Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):89–106.