

Pigmented Purpuric Dermatoses in Mixed Cryoglobulinaemia Associated with Rheumatoid Arthritis and Hepatitis C Infection

Daisuke Sawamura, Yoshihiro Ohata, Akihiko Shibaki and Hiroshi Shimizu

Department of Dermatology, Hokkaido University Graduate School of Medicine, N15W7, Kita-ku, Sapporo 060-8638, Japan.

E-mail: smartdai@med.hokudai.ac.jp

Accepted January 25, 2005.

Sir

Cryoglobulinaemia is characterized by the presence of immunoglobulins that undergo reversible precipitation at low temperatures. The patients can show variable clinical manifestations depending on the amount of serum cryoglobulin and their living environment (1, 2). We here report a case of cryoglobulinaemia with initial pigmented purpuric dermatosis.

CASE REPORT

A 47-year-old Japanese woman presented with a 3-year history of rash on her lower legs. The eruption tended to worsen in winter. She had suffered from rheumatoid arthritis (RA) for 6 years and hepatitis C virus (HCV) infection for 4 years. Upon physical examination,

punctate purpura and pigmentation were scattered over her lower legs and their coalescence formed irregular red-brown patches (Fig. 1A). Routine laboratory tests were within their normal ranges. Antinuclear antibodies, antineutrophil cytoplasmic antibodies and cryoglobulins were not detected. Rheumatoid factor was 451 IU/ml and HCV RNA was 750 k copies/ml. Morning stiffness and erosive polyarthritis were noted. Histological examination of the skin lesion demonstrated a moderate perivascular lymphocytic infiltrate with extravasated erythrocytes (Fig. 1B). Some siderophages were seen in the dermis. There was no specific deposition in direct immunofluorescence. From those results, we made a probable diagnosis of chronic pigmented purpura and treated her with topical corticosteroids.

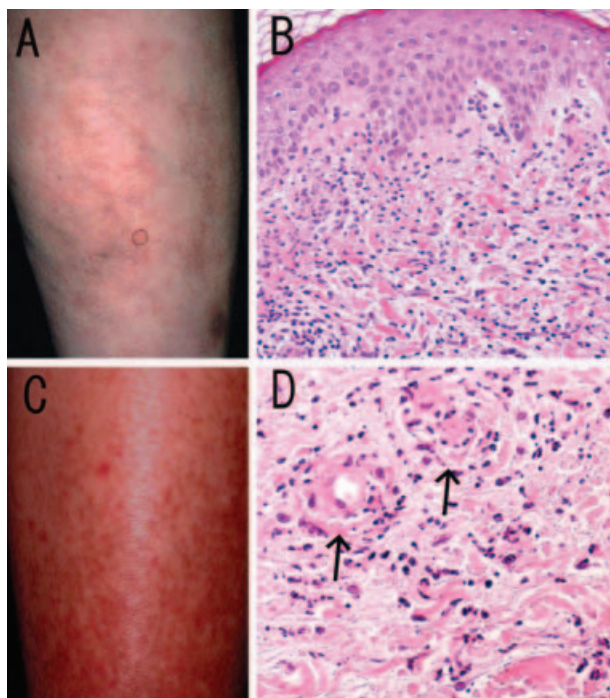


Fig. 1. (A) Punctate purpura with pigmentation was seen on the first visit. The circle indicates a biopsy site. (B) The biopsy revealed a moderate perivascular lymphocytic infiltration with extravasated erythrocytes. (C) On the second visit, widespread palpable purpura was found on the lower legs. (D) The biopsy specimen revealed a perivascular infiltration of neutrophils and lymphocytes with nuclear dust and fibrinoid necrosis of vessel walls (arrow).

Two months after the first visit, she returned because of a rapidly appearing eruption which was different from the previous eruption. The eruption consisted of multiple 3–8-mm, palpable purpura lesions on the shins and ankles of both legs (Fig. 1C). After a detailed interview, she disclosed that she stood outside, in the snow for 2 hours before appearance of the eruption. The biopsy specimen showed perivascular infiltration of neutrophils and lymphocytes with nuclear dust and fibrinoid necrosis of vessel walls (Fig. 1D). Direct immunofluorescence detected IgM and C3 deposits in blood vessels. Routine laboratory tests were within their normal ranges. At that time, serum cryoglobulin was positive and a diagnosis of cryoglobulinaemia was finally made. Immunoelectrophoresis of the serum protein failed to detect the M-component. Involvement of peripheral nerves and kidneys was not observed. Treatment with oral corticosteroids resulted in improvement and serum cryoglobulins returned to negative.

DISCUSSION

There are three categories of cryoglobulinaemia, grouped according to the class of the immunoglobulins that make up the cryoprecipitate (3). Type I, the essential form, comprises monoclonal immunoglobulin

associated with lymphoproliferative disorders. In type II, the cryoglobulins are polyclonal IgG and monoclonal IgM, with rheumatoid factor activity and in type III, IgG and IgM rheumatoid factors are polyclonal. The present case was classified as type III because of lacking M-component in the serum protein. Type II and type III are mixed cryoglobulinaemias, which are frequently associated with autoimmune and infectious diseases. Basically, intravascular deposits of cryoglobulin cause the essential form, while mixed cryoglobulin immune complexes activate complement leading to leukocytoclastic vasculitis (4). Mixed cryoglobulinaemia can present with different clinico-serological patterns (1, 2). The patients may show only one or two typical features among purpura, arthralgias, peripheral paraesthesiae, mild hepatitis, or rheumatoid factor seropositivity. Alternatively, some patients have typical mixed cryoglobulinaemia findings, but without serum cryoglobulins (2).

Our case was finally diagnosed as mixed cryoglobulinaemia related to RA and HCV based on the clinical and histological findings. Although the involvement of either RA or HCV, or both, was controversial, this case offered an interesting proposal that mixed cryoglobulinaemia might present the features resembling pigmented purpuric dermatosis. Histologically, mixed cryoglobulinaemia resulted in neutrophilic leukocytoclastic vasculitis, while lymphocytic perivascular infiltration was the initial pattern of pigmented purpuric dermatosis (4). However, in the older leukocytoclastic vasculitis lesions, the number of neutrophils may be decreased and the number of lymphocytes increased, so a predominance of lymphocyte infiltration might lead to the designation of a lymphocytic vascular reaction rather than a neutrophilic reaction (4). We think that the repeated appearance of low levels of cryoglobulin could result in pigmented purpuric dermatosis. Furthermore, serological testing for cryoglobulins might fail until strong exposure to cold, as in this case, suggesting that repeated cryoglobulin tests might be necessary for the correct diagnosis.

REFERENCES

1. Dammaco F, Sansonno D, Piccoli C, Tucci FA, Racanelli V. The cryoglobulins: an overview. *Eur J Clin Invest* 2001; 31: 628–638.
2. Ferri C, Zignego AL, Pileri SA. Cryoglobulins. *J Clin Pathol* 2002; 55: 4–13.
3. Brouet JC, Clouvet JP, Danon F, Klein M, Seligmann M. Biologic and clinical significance of cryoglobulins. *Am J Med* 1974; 57: 775–788.
4. Barnhill RL, Busam KJ. Vascular diseases. In: Elder D, Elenitsas R, Jaworsky C, Johnson B, et al., editors, *Lever's histopathology of the skin*, 8th edn. Philadelphia: Lippincott-Raven, 1997: 185–208.