



Case report

Cryoglobulin induced skin ulceration

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Abstract

Lupus Erythematosus (LE) is a multi-organ auto-immune disease which results from complex interaction of genetic and environmental factors. The clinical spectrum ranges from minor cutaneous lesions to life threatening multi-organ dysfunction. The skin manifestations are variable and common and range from LE specific to LE non-specific cutaneous disease. Vasculitis is one of the most common non-specific skin lesion of Systemic lupus erythematosus (SLE) and appears as purpuric lesions, infarcts along lateral nail folds, peripheral gangrene, sub-cutaneous nodules and ulcers. Mixed cryoglobulinaemia (type II) is associated with connective tissue disorders including SLE. Skin manifestations are seen in 60-100% patients and are more common in females. The most common manifestation is palpable purpura of lower extremities seen in 30-100% which often is triggered in winter or on cold exposure. Skin infarction, hemorrhagic crusts and ulcers are seen in 25% of patients. Wide spread necrotic ulcers are seen in 10-25% of patients which are often exacerbated by cold.

Key words: SLE, skin ulcers, cryoglobulins

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Systemic lupus erythematosus (SLE) is a connective tissue disorder characterized by production of non-organ specific auto-antibodies with peak incidence between 15-40 years and female: male ratio of 6-10:1. Cryoglobulins are found in 11% of patients with SLE and may precede the manifestation of the disease by many years. About 6% of patients predominantly females develop chilblain like lesions on fingers, toes, nose, ears etc. and few may have cryoglobulins and cryofibrinogens in blood. Gangrene of tips of fingers and toes may develop insidiously due to occlusion of large or medium sized arteries as a result of vasculitis or thrombosis. Thrombotic episodes are more common in patients with anti-phospholipid antibodies. Leg ulcers occur in about 10% of patients.

Case report

An 18 year old girl presented to the out-patient department of Dermatology with ulceration on dorsa of both hands of 1 month duration. She is a known case of systemic lupus erythematosus which she had developed 3 years back and was on treatment for the same. The disease was in remission for 3 years. About one month back she developed diarrhea and was admitted in hospital and was started on oral antibiotics and IV fluids. She developed a swelling on dorsa of both hands in the area of IV line and had rubbed ice cubes on the swelling for about 20-30 minutes. This was followed by blistering and ulceration on the area in about a course of 2 weeks the ulcers became necrotic and increased in size. On examination 2 well defined ulcers were

present on dorsa of both the hands of the ulcers with surrounding erythema and the floor was covered with dry necrotic slough and the base was indurated. Peripheral pulses were normal. Erythematous macular rash was seen on the face and no other skin lesions were present. Routine blood examination revealed raised ESR and was high ANA titres. Serum was positive for cryoglobulins. Urine analysis showed proteinuria.



Fig 1. Necrotic ulcers on the dorsa of hand and forearm.

Based on the history, clinical findings and laboratory investigations a diagnosis of vasculitic ulcers was made probably induced by precipitation of cryoglobulins due to ice application. Patient was continued with the treatment of SLE and was referred to surgeon for the management of skin ulcers. In about 8 weeks the ulcers healed with scar formation.

Discussion

Cryoglobulins are circulating immunoglobulins that reversibly precipitate in the cold.

Symptoms are caused by vascular occlusion resulting from precipitation. They may be associated with wide spectrum of infections, connective tissue diseases and malignancies. The organs which are usually involved are skin, liver, kidney, nervous system etc.

Brouet et al. have classified cryoglobulinemia is classified into 3 types I, II and III¹.

Type I consist of single monoclonal immunoglobulins typically IgG or IgM. Type II and III are often termed mixed as they comprise both IgG and IgM components. Vasculitis associated

with mixed cryoglobulinaemia involved both small and medium sized blood vessels.



Fig 2. Necrotic ulcer on the dorsa of hand

For the demonstration of cryoglobulins venous blood was drawn into a warm syringe not treated with anti-coagulants, it was cooled to 4-5 °C and any precipitate noted, the precipitate re-dissolves on warming and allowed to clot at 37 °C while the patient was fasting as lipids may interfere with assay².

Symptoms are caused due to intravascular precipitation on exposed part after cooling and present as purpura, patchy livido reticularis, cold urticaria, Raynad's phenomenon and ulceration. Systemic symptoms include glomerulonephritis, arthralgias and fatigue.



Fig 3 shows ulcer with post-inflammatory scarring

Symptoms appear when cryoglobulin levels are more than 25 mg/dL more common than the right counterpart (Waldayer's hernia).

Conclusion

Cryoglobulins are circulating immunoglobulins and are found in 11% of SLE patients and may precede the manifestation of the disease by many years. Skin infarction, hemorrhagic crusts and ulcers are seen in 25% of patients. Wide spread necrotic ulcers are seen in 10-25% of patients which are often exacerbated by cold.

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Conflict of interest: None

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