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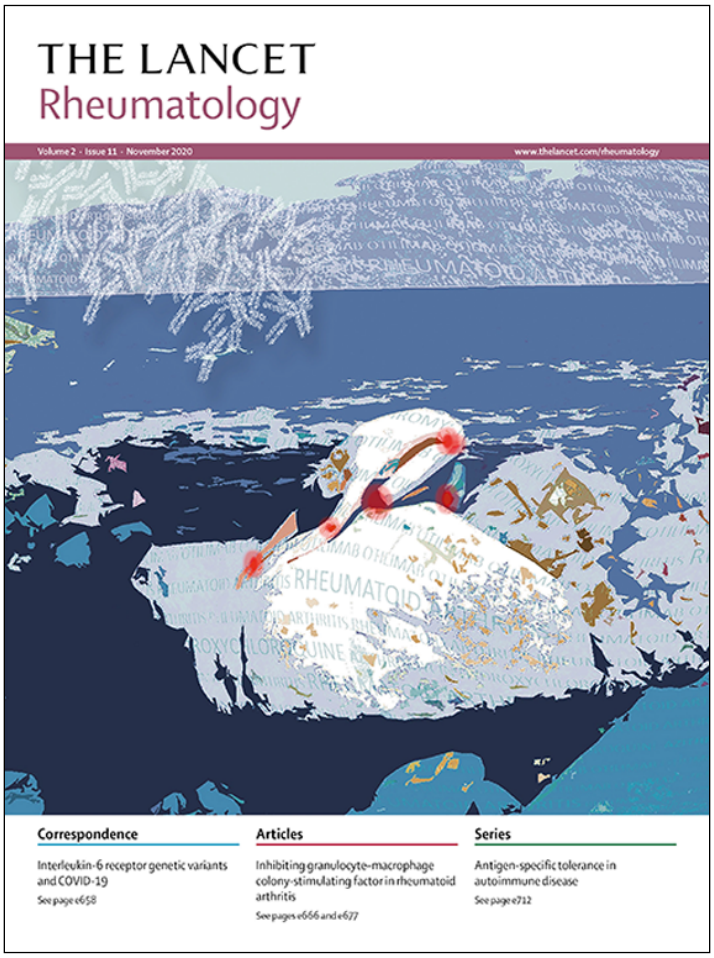

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Familial chilblain lupus with *TREX1* mutation and cerebrovascular disease

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A woman aged 24 years with a history of cerebral infarction presented with eruptions on the acral regions that had relapsed in winter since her childhood. On examination, we observed brownish erythema and dark red scaly papules on the fingers and toes (figure A, B). The patient's younger sister, mother, and maternal grandfather had similar eruptions (figure D, E, F). Magnetic resonance angiography showed multiple cerebral aneurysms in the patient (figure H, I, J). There was no evidence of intellectual disability or basal ganglia calcification. Laboratory tests showed normal blood cell counts and complement: positive for antinuclear antibodies at 1:80, positive for anticardiolipin antibodies at 27·1 IU/mL, and negative for antidouble-stranded DNA antibodies and cryoglobulins. Multiple enlarging cerebral aneurysms and a previous cerebral infarction were found in the patient's younger sister (figure L), although neither anticardiolipin antibodies nor other coagulation abnormalities were detected. The previously reported heterozygous *TREX1* (pAsp18Asn) mutation 53G→A was identified in the family and familial chilblain lupus was diagnosed.

Chilblain lupus erythematosus is a rare and unique form of chronic cutaneous lupus erythematosus that is characterised by chilblains, which are cold-induced eruptions on the acral regions. A familial form of chilblain lupus erythematosus, related to heterozygous mutations in *TREX1* and *SAMHD1*, has been previously reported. To date, there have been two case reports of familial chilblain lupus that have included cerebral vasculopathy presenting as multiple cerebral aneurysms, narrowing cerebral arteries, or cerebral infarction. Chilblains with family history and systemic symptoms might suggest the presence of hereditary autoinflammatory diseases.

Avoiding cold exposure, applying topical corticosteroid, or taking systemic immunosuppressive agents can be therapeutic options. In this case, administration of systemic prednisolone (1·0 mg/kg per day) improved the acral eruptions and the cerebral aneurysms. Because of the occurrence of hyperlipidaemia, the prednisolone dose was gradually tapered to 5 mg/day. Both the skin and the cerebral lesions have remained stable for 6 months. Familial chilblain lupus can present with various symptoms in a family with identical gene mutations. Recognising that cerebral infarctions and aneurysms can occur in familial chilblain lupus cases is important. Further investigation is needed to better understand the pathomechanisms and to prevent such severe complications.

Contributors

Written consent for publication was obtained from the patient. TN, TY, IY, NO, HU, HK, and YM contributed to the patient's care. NK analysed the genetics. All authors contributed to the writing of the Clinical Picture.

Declaration of interests

We declare no competing interests.

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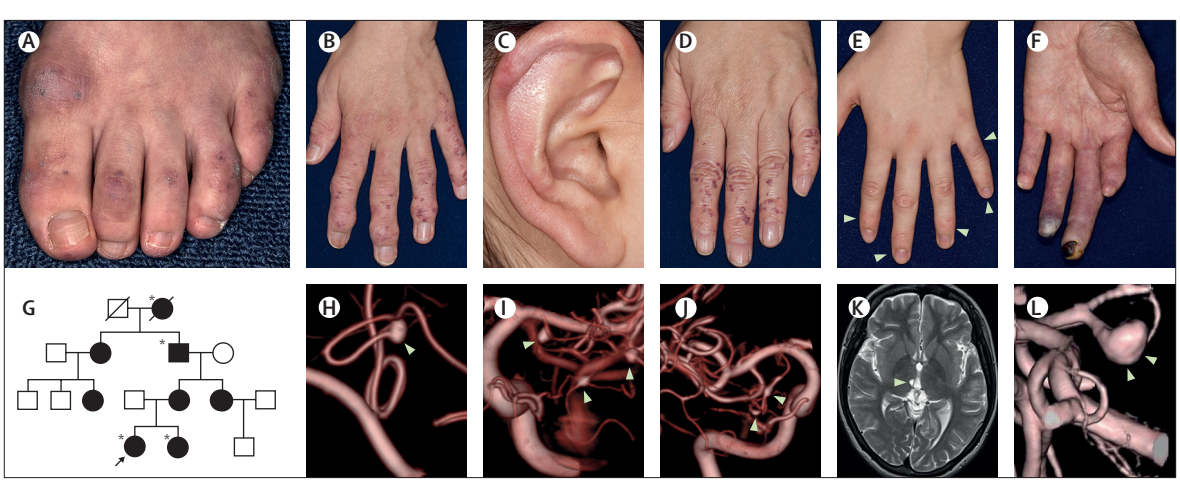

Figure: **Familial chilblain lupus with TREX1 mutation and cerebrovascular disease**
Brownish erythema are observed on the toes (A), fingers (B), and auricles (C) of the patient. Skin presentations of the hands of the patient's mother (D), younger sister (E; green arrowheads), and grandfather (F). Identical *TREX1* mutations were detected in all photographed family members. (G) The family tree showing female (circle) and male (square) members (including the patient [arrow]), with acral eruptions (black) and cerebrovascular disease (asterisk), or no skin lesions (white). Deceased family members are indicated by a diagonal line. The three-dimensional reconstruction of digital subtraction angiography taken of the patient shows multiple fusiform aneurysms on the posterior inferior cerebellar artery (H), the small vessels of the anterior temporal artery region (I), and the anterior temporal artery (J). Aneurysms are indicated by green arrowheads. MRI analysis of the patient's younger sister shows an old cerebral infarction in the right hypothalamus (K; green arrowhead). The three-dimensional reconstruction of digital subtraction angiography shows a 4 mm aneurysm in the middle cerebral artery (L; green arrowheads).