

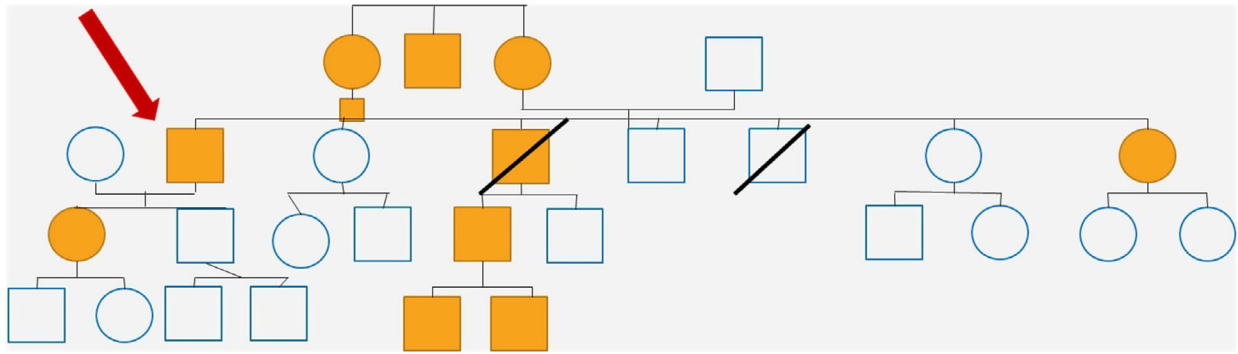


**Figure 2** Pedigree of the patient's family. Red arrow indicates the studied patient; filled symbols indicate members with cerebral lesions; open symbols indicate those not known to be affected; solidus indicates deceased.

vessels with gaps between the endothelial cells.<sup>2</sup> The main symptoms are neurological (seizures, headache, cerebral haemorrhage) and ophthalmological (decreased visual acuity, reduction of the visual field).<sup>3</sup> Cutaneous vascular malformations are seen in only 9% of patients with mutations, mainly those with a *KRIT1* mutation.<sup>4</sup> In descending order of frequency, capillary malformations, venous malformations and hyperkeratotic cutaneous capillary–venous malformation can be found.<sup>4</sup> Hepatic cavernomas have only been reported in two Italian families with a heterozygous pathogenic variant in the *CCM2* gene.<sup>5</sup> The unusual feature of our case was the concomitant presence of cerebral, cutaneous and hepatic cavernomas in a patient with a *KRIT1* mutation.

In conclusion, we report an unusual case of multiple cutaneous venous malformations revealing an FCC. The diagnosis of FCC should be considered in patients with multiple vascular malformations, neurological and/or ophthalmological symptoms, and a positive family history of cerebral cavernomas. Early diagnosis of familial cases with this condition is of great importance as it may be suitable for surgical correction, thus preventing severe brain damage.

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## Cholinergic pruritus responding to omalizumab

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Cholinergic pruritus is a rare condition characterized by generalized itch provoked by sweating without an associated rash. It is exacerbated by heat, exercise, emotion or activities of daily living.<sup>1</sup> The pruritus can be severe and have a considerable impact on the patient's life.

A 60-year-old man presented to our clinic in 2012 with a 9-month history of severe pruritus and a burning sensation that was induced by exercise and heat and relieved by cooling. The symptoms were not associated with a skin rash. He had a Dermatology Life Quality Index (DLQI) of 23/30 indicating an extremely large effect on his quality of life. The pruritus impacted many of his regular daily activities such as housework and shopping, including sexual activity. The patient had a history of asthma and depression for which he was taking fluticasone salmeterol and sertraline.

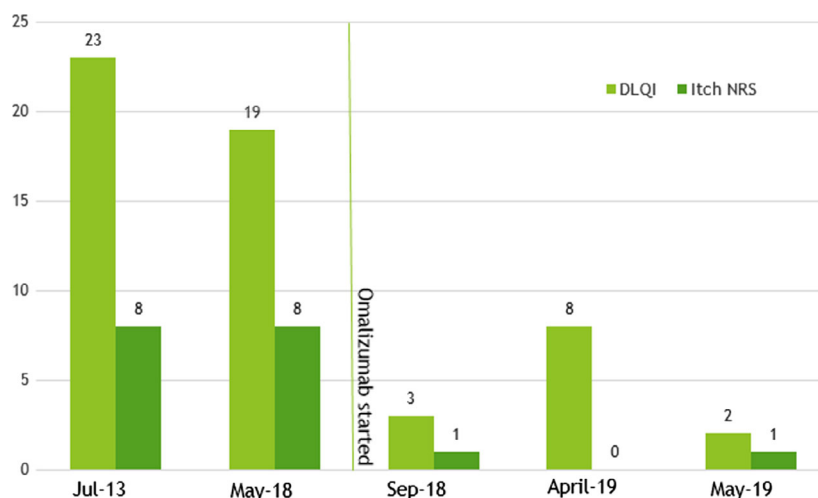


**Figure 1** Figure outlining Dermatology Life Quality Index (DLQI) and Itch Numerical Rating Scale (NRS) scores over time. Omalizumab was commenced in June 2018.

On physical examination, a few patches of vitiligo covering around 2% of the patient's body surface area were seen, but no other skin lesions and no dermatographism.

Laboratory investigations, including blood test screen (complete blood count, lactate dehydrogenase, liver, renal and thyroid function test, HbA1c, IgA anti-tissue transglutaminase antibody and pemphigoid antibody) for systemic causes of pruritus without rash yielded negative results.

Initial treatment for the cholinergic pruritus included a trial of several antihistamines, including fexofenadine 180 mg twice daily, in addition to ranitidine 150 mg twice daily and montelukast 10 mg once daily. Increasing the doses of antihistamine was not possible owing to sedation on higher doses. Danazol 200 mg three times daily, subsequently tapered down to 100 mg once daily, was added to the treatment regimen based on case report evidence in cholinergic pruritus.<sup>2</sup> The symptoms improved but after 2 years of therapy the patient developed tenderness in his left breast and mild gynaecomastia, thus danazol was discontinued. As a result, a trial of monthly subcutaneous injections of omalizumab 300 mg was initiated.

Prior to initiating omalizumab, the patient reported a DLQI of 19/30 and Itch Numerical Rating Scale (NRS) score of 8/10. Three months after starting omalizumab the patient experienced a dramatic improvement in his symptoms with a DLQI score of 3/30 and Itch NRS score of 0–1/10 (Fig. 1). His scores for itching, interference with regular chores, choice of clothes, and impact on sports and work were reduced with the disease having very little or no impact at all on these areas. The patient initially reported that there was complete resolution of his symptoms in the 2 weeks after receiving the omalizumab injection, and only mild pruritus in the following

2 weeks. This gradually improved and the patient reported that he no longer has any symptoms in between the injections. The slight increase in the patient's DLQI to 8/30 in April 2019 was probably due to incorrect administration of omalizumab injection intramuscularly that month because the patient reported that the injection was more painful than usual.

Cholinergic pruritus is a rare disease that may go undiagnosed owing to the lack of physical signs or misdiagnosed as cholinergic urticaria.<sup>3</sup> In our patient, danazol somewhat alleviated his pruritus but led to the development of breast tenderness and gynaecomastia. He was started on omalizumab based on reports of its benefit in treating cholinergic urticaria.<sup>4,5</sup> Omalizumab was effective in controlling the patient's symptoms and he was able to resume his regular physical activities including physiotherapy sessions for a shoulder injury. To our knowledge, this is the first report of cholinergic pruritus being treated with omalizumab, which is a treatment option worth considering for severe refractory cholinergic pruritus.

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### Acrodermatitis enteropathica-like skin eruption with neonatal seizures in a child with biotinidase deficiency

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An 8-year-old boy presented with recurrent seizures starting from day 6 after birth and skin lesions around his eyes and lips that had been present from 1 year of age.

Mucocutaneous examination revealed adherent scaling and crusting in the periocular and perioral region along with angular cheilitis, generalized xerosis, diffuse alopecia and follicular prominences over the scalp (Fig. 1a,b). The hairs were sparse, and hair microscopy showed trichorrhexis nodosa (Fig. S1). These acrodermatitis enteropathica-like skin lesions, history of neonatal seizures with delayed neurological development were suggestive of acrodermatitis dysmetabolica.

Further investigations for metabolic derangement showed absence of metabolic acidosis, and normal serum lactate and alkaline phosphate levels. Biotinidase enzyme assay showed an undetectable level, suggestive of biotinidase deficiency and confirming acrodermatitis dysmetabolica. The patient was started on oral biotin supplement 10 mg/day, following which all the facial lesions and generalized scaling cleared within 2 weeks (Fig. 1c). The patient was advised to take lifelong biotin supplementation and his antiepileptic medications were continued.

Acrodermatitis enteropathica-like skin eruptions are seen in patients with metabolic disorders.<sup>1</sup> Biotin is a water-soluble vitamin, which serves as an essential coenzyme for carboxylases that play crucial roles in the metabolism of fatty acids, amino acids and glucose.



**Figure 1** (a) Scaling and crusting over perioral and periocular region; (b) follicular prominences and diffuse alopecia; (c) improvement in the facial lesions after 2 weeks of oral biotin supplementation.