ALMA MATER STUDIORUM
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Small fiber neuropathy in a patient with familial Ichthyosis: a case report

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Objective

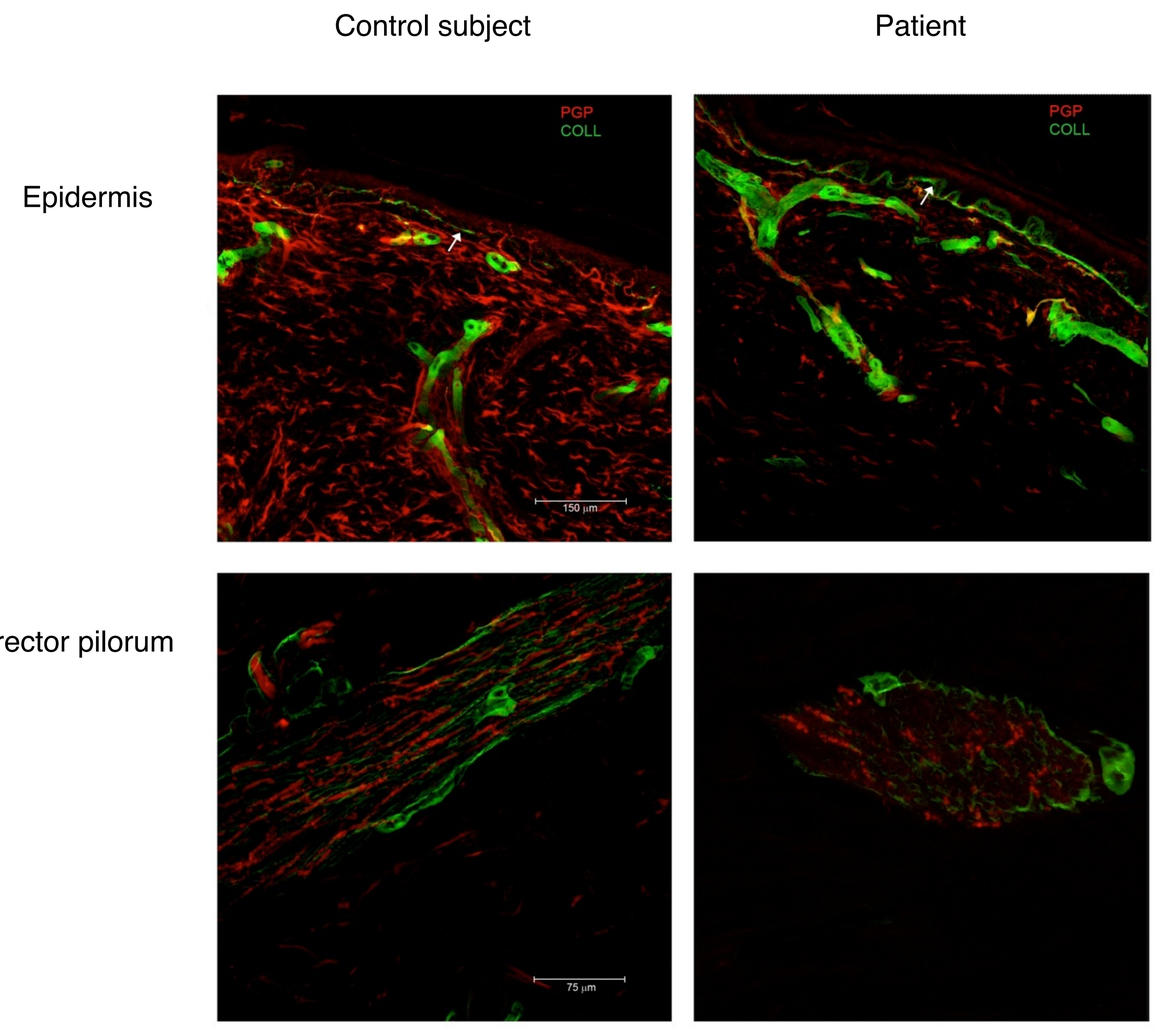
To describe a patient with isolated familial ichthyosis complaining of burning dysesthesias.

Material and methods

A 58 years-old patient with familial ichthyosis from birth started to complain of burning dysesthesias at the age of 51 years: these were described as a pinprick either a thermal sensation localized mainly distally in the legs. Six years later he started to referred autonomic symptoms including: profuse sweating in the upper part of the body, flushing and palpitations usually triggered by physical exercise and improved with rest. A long history of erectile dysfunction was also present. The patient underwent to neurological examination, a full serum screening to exclude predisposing causes for peripheral neuropathy, electromyography (EMG) to exclude peripheral large nerve fiber involvement, laser evoked potentials (LEPs) and skin biopsy (SB) to study somatic and autonomic small nerve fibers.

Results

LEPs and SB disclosed a small fiber neuropathy (SFN)mainly involving somatic fibers and the distal site with a length-dependent pattern. Normal EMG findings excluded the concurrent involvement of a large fiber neuropathy.



LEGEND FOR FIGURE
A confocal study of somatic and autonomic patterns of innervation in the patient and a control subject.
Leg somatic and autonomic innervations disclosed by confocal microscope (x20 for epidermis and x40 for muscle arrector pilorum) in the patient and an age-matched control subject. Nerve fibers are marked in red by a pan-neuronal marker PGP 9.5 whereas the collagen staining is shown in green.
Epidermis: free-ending PGP immunoreactive fibers are evident in the epidermis of the control whereas the patient showed a marked decrease of such fibers. The basement membrane separating epidermis from dermis is marked by collagen staining and indicated by an arrow.
The muscle arrector pilorum showed a rich density of fibers running in a longitudinal and wavy pattern in the control subject but these fibers were poor with a deranged pattern of innervation in the patient.

Discussion and Conclusion

Isolated ichthyosis has not been previously associated with SFN although a neuropathic involvement is part of the clinical spectrum of several ichthyosis syndromes, such as Mednik Syndrome[1], Cednik Syndrome[2] or Resfum's disease. We hypothesize for this patient a common genetic basis for the development of SFN and the familial ichthyosis by altered SNAP29, synaptosomal-associated protein 29 kDa. Interacting with SNARE proteins SNAP29 has a role in proper dermal differentiation but also in protein trafficking and autophagosomes metabolism[3] potentially affecting peripheral nerves when abnormal. Loss-of-function mutations in SNAP29 cause Cednik syndrome but a milder alteration of this protein could explain the association between isolated ichthyosis and SFN in our case. However to overcome this speculation a more detailed analysis of our patient and his family mainly involving genetic and functional evaluations is required.

References

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