Familial primary localized cutaneous amyloidosis: An uncommon disorder secondary to oncostatin M receptor-β mutation manifested by early-onset persistent familial pruritus

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Introduction

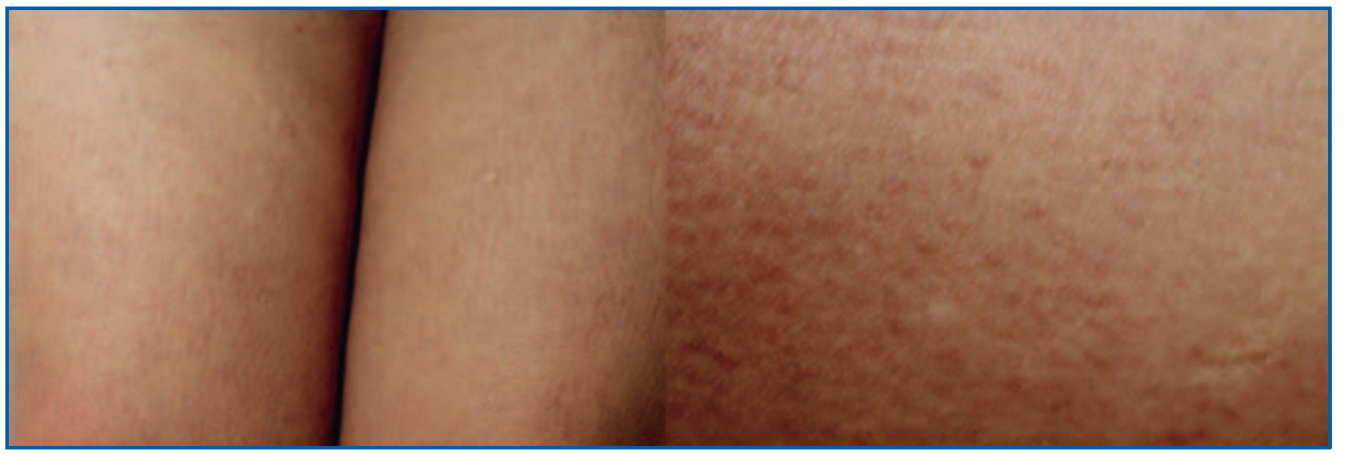
Primary localized cutaneous amyloidosis (PLCA) are a group of disorders characterized by the isolated deposition of cutaneous amyloid material that can either **keratinocyte** derived (macular amyloidosis [MA] and lichen amyloidosis [LA]) or **immunoglobulin light chain** derived (nodular amyloidosis). MA and LA represents a spectrum of sporadic disorders of unknown etiology, although **familial cases** have occasionally been reported (10% of cases), being much more common in South Americans, Middle Easterners, and Asians.

Case Report

A 15-year-old girl presented with **persistent pruritus** refractory to multiple topical and oral treatments mainly involving the **lower extremities** since infancy. Physical exam disclosed **pruritic brownish net-like macules and papules** predominantly in shins, calves and ankles (Fig. 1). Similar lesions, but less apparent were also noted in the upper arms. The patient's mother (Fig. 2), a maternal aunt, her grandfather and great grandfather presented a similar clinical picture, showing an autosomal dominant inheritance pattern (Fig.3). Skin biopsies disclosed a discrete acanthosis, and occasionally focal deposits of aggregates of a **hyaline Congo-red positive material** in the **papillary dermis** (Fig.4). With the suspicion of familial PLCA a genetic test with exome capture and analysis of the oncostatin M receptor (OSMR), interleukin (IL)-31 receptor a (IL31RA) and GPNMB genes was performed showing an heterozygous missense mutation of the **OSMR gene (c.1916A>7)**, that was also detected in the patient's mother. Treatment with topical corticosteroids, calcineurin inhibitors, laser and phototherapy have been prescribed with partial responses.

Figure 1. Brownish net-like macules and papules on shins of the patient.

Figure 2. Brownish papules on tights of patient's mother.



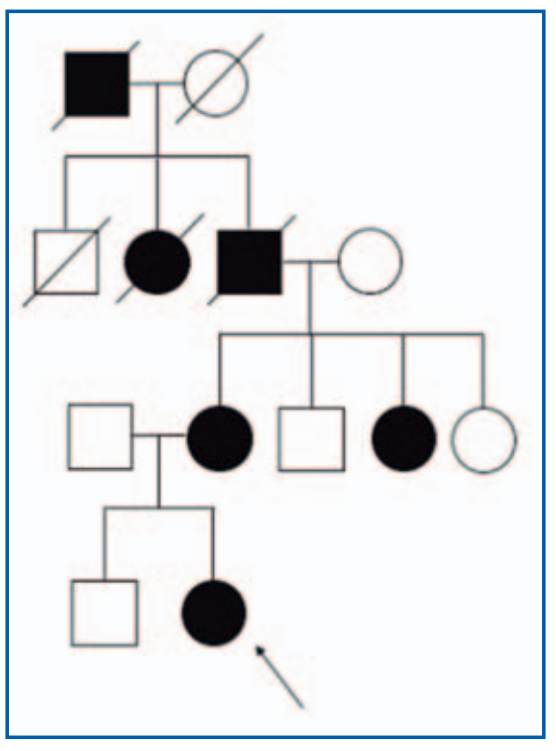
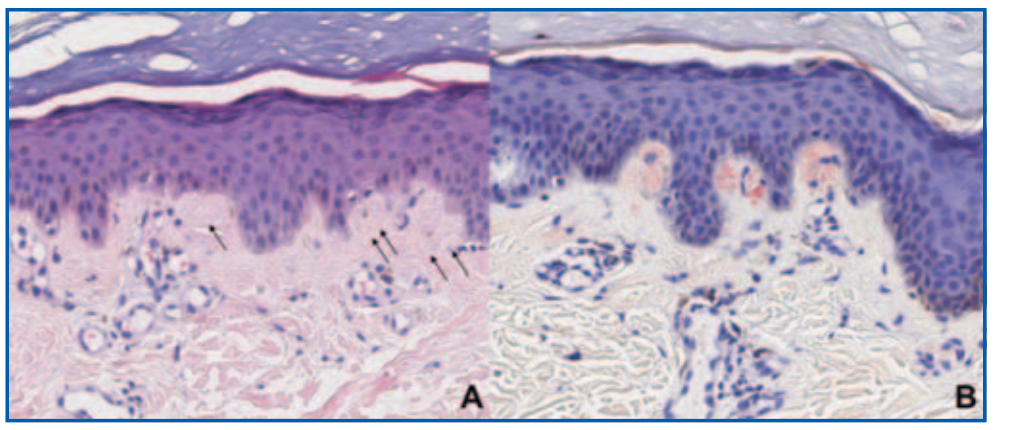


Figure 3. Family tree showing an autosomal dominant inheritance pattern.

Figure 4. Focal deposits of aggregates of a hyaline Congo-red positive material in the papillary dermis. A. Hematoxylin and eosin staining x100. B. Congo Red staining x100.



Discussion

Pathogenic mechanisms involved in familial PCLA are still unknown. Mutations in **OSMR**, **IL31RA** and **GPNMB** genes have been identified. OSMR gene encodes OSMRβ, that forms an heterodimer with IL31RA to generate IL-31 receptor, needed for IL-31 activation. Mutations in these genes show the **key role of IL-31 in the pruritus** associated to this disease and points out a potential benefit of targeted therapies against this interleukin (i.e, nemolizumab), in the treatment of these patients. Most probably, **amyloid deposits** represent a **secondary event** from a continuous and recurrent **scratching** in accessible areas in this rare and particular form of "Familial primary localized pruritus".

Conclusions

We report a new kindred with patient with familial PLCA secondary to a **missense OSMR mutation (c.1916A>7)** clinically manifested by an early onset and **persistent pruritus** mainly involving the lower extremities that later evolved to a **characteristic PLCA lesions**.

References

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