

Invited Comment

What is IFAP Syndrome?

In this issue, Mégarbané et al. [2003] describe two brothers with "IFAP syndrome" (ichthyosis follicularis, alopecia and photophobia). After having studied this interesting paper, I am asking myself whether IFAP syndrome can still be taken as one single clinicogenetic entity.

McLeod [1909] described three cases of "ichthyosis follicularis" associated with baldness. His report fell into oblivion until Zeligman and Fleisher [1959] reported additional cases. Traupe [1989] gave a comprehensive review of IFAP syndrome. A hallmark of this disease is the presence of thorne-like projections of follicular hyperkeratosis, giving the skin a feeling of a "nutmeg grater" [Zeligman and Fleisher, 1959; Eramo et al., 1985].

In recent years, however, several authors have described atypical patients in whom follicular hyperkeratosis was not a prominent finding. Rather, a generalized lamellar desquamation was present [Boente et al., 2000], or well demarcated psoriasiform lesions involved the gluteal fold, the buttocks or the limbs [Boente et al., 2000, Sato-Matsumura et al., 2000]. In these patients, additional extracutaneous lesions in the form of inguinal hernia or ectrodactyly were present.

From a clinical point of view it appears as if we are dealing with two different entities described under the same name. This perspective may be supported by the following argument. In "classical" IFAP syndrome as described by McLeod [1909], only boys show the full-blown syndrome [Keyvani et al., 1998], whereas female carriers may present a linear pattern of involvement reflecting functional X-chromosome mosaicism [König and Happle, 1999]. By contrast, the phenotype characterized by psoriasiform patches can be transmitted from a mother to her daughter who do not show any X-inactivation pattern but, conversely, a rather symmetrical arrangement [Sato-Matsumura et al., 2000]. The cases described by Mégarbané et al. [2003] appear to belong to this "psoriasiform" category.

Other reports [Martino et al., 1992; Bibas-Bonet et al., 2001] mention the presence of additional anomalies such as aganglionic megacolon or hypoplasia of corpus callosum, which raises the question whether such cases may represent examples of a contiguous gene syndrome.

The issue is becoming even more complicated because Cambiaghi et al. [2002] described "classical" IFAP syndrome in two unrelated girls who were diffusely affected without any sign of functional X-chromosome mosaicism. In these cases, an X-linked "recessive" mode of transmission with lyonization in females can be excluded. Does this mean that there are three different IFAP syndromes?

However it may be, the report of Mégarbané et al. [2003] that will give us further food for thought in order to ultimately solve the nosological conundrum of what we presently call "IFAP syndrome."

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Received 3 March 2003; Accepted 23 April 2003
DOI 10.1002/ajmg.a.20353

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