

Keratosis Pilaris Atrophicans

One Heterogeneous Disease or a Symptom in Different Clinical Entities?

IN THIS ISSUE of the ARCHIVES, Baden and Byers¹ describe 21 cases of keratosis pilaris atrophicans (KPA). He considers KPA as one disease entity.¹ However, our opinion differs in view of the arguments presented here. Keratosis pilaris (KP) is a skin symptom associated with different diseases, mostly of ectodermal origin. By definition, keratinous plugs are observed in the follicular orifices surrounded by a variable degree of erythema. When the keratotic papules are followed by atrophy, one speaks of KPA. Atrophy is preceded with or without inflammation. There is much confusion on KP and KPA entities, especially because different overlapping syndromes have been described and many synonyms are used in both dermatologic and genetic literature.²⁻⁴ In this editorial, we present our opinion and arguments on diseases with KPA.

KERATOSIS PILARIS ATROPHICANS

We distinguish four distinct clinical entities that show KPA. These are keratosis pilaris atrophicans faciei (KPAF), atrophoderma vermiculata, keratosis follicularis spinulosa decalvans (KFSD), and, as proposed, folliculitis spinulosa decalvans.³ Rand and Arndt³ believe that these forms are different stages of a single process of KPA. Baden and Byers¹ also propose that KPAF, atrophoderma vermiculata, and KFSD should be headed under KPA. Baden and Byers consider KFSD to be similar to KPAF, with the difference that in the former condition, the scalp is also involved. In our opinion, the classification of diseases with KPA is as shown in the **Table**.

Keratosis pilaris atrophicans faciei, also called *ulerythema ophryogenes*,⁵ is a disorder characterized by redness and atrophic scarring of the eyebrows. The symptoms are present at birth or from infancy on. The inheritance pattern is most probably autosomal dominant.⁴ Associations of KPAF with Noonan's syndrome and woolly hair have been described.^{5,6}

Atrophoderma vermiculata, also called *atrophoderma reticulata*, *acne vermoulante*, *folliculitis ulerythematosa*, *folliculitis ulerythematososa*, and *honeycomb atrophy*, is characterized by reticulate atrophic

cicatricial elements on the cheeks. Symmetrical small atrophic skin pits with sharp edges are observed with a worm-eaten appearance. The disease is always limited to the face and starts after the age of 5 years. It is most probably of autosomal recessive inheritance.⁴

KERATOSIS FOLLICULARIS SPINULOSA DECALVANS

Keratosis follicularis spinulosa decalvans, also called *keratosis follicularis decalvans*, was described for the first time by Lameris⁸ in the Netherlands under the name *ichthyosis follicularis*. Siemens,⁹ who described some Dutch patients and others of the original Bavarian family, proposed the name KFSD.⁹ Several Dutch publications followed on the descendants of the original family living in the Netherlands.¹⁰ The disease is characterized by follicular hyperkeratosis of the skin, corneal dystrophy, and photophobia. Other prominent findings are scarring alopecia of the scalp and absence of eyebrows and eyelashes. Real serious inflammation is absent in X-linked KFSD. In our study, encompassing the largest pedigree,

See also page 469

we also described hyperkeratosis of the calcaneal region of the soles and a high cuticle on the nails.⁷ About 50% of the female carriers are symptomatic. Symptoms in carriers are dry skin, minimal follicular hyperkeratosis, and mild hyperkeratosis of the soles. Usually, the symptoms improve spontaneously in an extreme way in puberty. Pedigree analysis showed X-linked inheritance in three family studies.^{7,11,12} Almost complete expression in women can be explained by skewed lyonization. Harth et al¹³ described such a case in a woman with a fully expressed KFSD.

In the large Dutch family, which had originated from the original Lameris (Siemens) family and which had been extensively investigated by us,⁷ Oosterwijk et al¹⁴ located the gene to Xp21.2-p22.2.^{7,14} In 54 individuals (including 21 affected males), DNA linkage analysis was performed using DNA probes covering

Classification of Keratosis Pilaris Atrophicans*

Keratosis Pilaris Atrophicans Type/Inheritance	Clinical Characteristics	Associations/Remarks
Keratosis pilaris atrophicans faciei; inheritance? AD?	Keratosis pilaris atrophicans always in the eyebrows (atrophy), and keratosis pilaris also at other sites	Noonan's syndrome, ⁵ woolly hair ⁶
Atrophoderma vermiculata; inheritance? AR?	Follicular papules and reticulated atrophy (honeycomb)	Lichen spinulosa, Down's syndrome
Keratosis follicularis spinulosa decalvans; X-linked	Follicular papules, absent eyebrows and lashes, scarring alopecia (atrophy)	Photophobia, corneal dystrophy, nail abnormalities (high cuticula)‡
Folliculitis spinulosa decalvans; familial/AD?†	Persisting inflammation after keratosis pilaris atrophicans, atrophic scarring, especially on the scalp	Confusion with folliculitis decalvans and keratosis follicularis spinulosa decalvans, described in siblings

*AD indicates autosomal dominant; AR, autosomal recessive.

†Suggested as separate entity, formerly described as keratosis follicularis spinulosa decalvans with AD inheritance.

‡Described for the first time by van Osch et al.⁷

the X chromosome. Multipoint analysis placed the gene defect between DXS16 and DXS269. These studies are being extended to other KFSD families. The pedigree analysis has proved the X-linked inheritance in KFSD.⁷

Other reports indicated clinical and genetic heterogeneity in KFSD.^{15,16} One of the major clinical and genetic problems is the confusion with a variant characterized by persisting pustular elements, especially on the scalp. Pustular eruptions in this disease begin at puberty. Instead of improvement, this variant exacerbates in puberty. We suggest that a better name for this form would be *folliculitis spinulosa decalvans* (FSD). Guillet et al¹⁶ described two different clinical courses in both a father (case 2) and son (case 3) and a sporadic case in a boy (case 1). Cases 2 and 3 showed autosomal dominant inheritance, and clinically the description of the disease was also different from Siemens' KFSD. Guillet et al¹⁶ also reported aminoaciduria. Aminoaciduria has been described once before in a case report by Grosshans et al,¹⁷ with an unknown inheritance pattern.¹⁷ Aminoaciduria is only (though controversial) associated with monilethrix in which KP (without atrophy) is associated with koilonychia and moniliform hairs.¹⁸

There is also confusion with ichthyosis follicularis. The name *ichthyosis follicularis* is a misnomer and actually indicates keratosis pilaris (=follicularis). A syndrome closely resembling KFSD, was described by Eramo et al.¹⁹ This was defined by keratosis pilaris (that was called ichthyosis follicularis), alopecia and photophobia. There was no scarring that distinguished it from KFSD. These authors agreed that the choice of the term *ichthyosis follicularis* is arbitrary and that the term (*hyper*)*keratosis follicularis* would have been a better designation.¹⁹ We propose that this entity should be called *keratosis follicularis (nonatrophicans)*, *alopecia*, *photophobia*, or *KAP syndrome*.

The case report by Britton et al²⁰ illustrates another problem. It concerned a sporadic case with congenital gen-

eralized alopecia, widespread keratosis pilaris, neurosensory deafness, and reticulated hyperkeratosis. There was no atrophy. The conjunctivas were mildly injected, and the nails were hypoplastic. Actually this case, described as KFSD, was compatible with the later described *keratitis, ichthyosis, and deafness* (KID) syndrome.²¹

FOLLICULITIS SPINULOSA DECALVANS

Except for X-linked KFSD (Siemens) that goes into remission at puberty, the other described so-called KFSD variant continues with inflammation. X-linked KFSD is not a real inflammatory process. The inflammation in the misnomer KFSD variety begins at puberty, whereas in X-linked KFSD (Siemens), the inflammation is not present or mild and regresses at puberty. Therefore, we prefer to call this form FSD. The clinical course is completely different from KFSD (Siemens). The pattern of inheritance is also different and most probably autosomal dominant.^{3,15,16} The name of our choice probably causes problems with the poorly circumscribed and heterogeneous entity folliculitis decalvans.²²

OCULAR ABNORMALITIES AND KERATOSIS PILARIS (NON)ATROPHICANS

Ocular abnormalities may be observed in nonatrophic forms of KP, but more often in atrophic forms. In monilethrix, a syndrome characterized by moniliform hairs, koilonychia and KP (without atrophy), juvenile cataracts are found. Cataract has been described in woolly hair that can be associated with KPAF.

In KFSD, ocular abnormalities such as photophobia and corneal dystrophy are not pathognomonic. Similar ocular abnormalities are found in the KAP syndrome described by Eramo et al.¹⁹ One of their patients also showed a pendular nystagmus and corneal vessels coming from the limbus at 36°. The photophobia can be explained by scattered subepithelial opacities in the

Bowman's membrane.¹¹ Vascularization of the cornea is rarely observed. There are two opinions on the origin of corneal dystrophy. Some consider the opacities to arise from irritation of a more viscous product of meibomian glands forming hard prickles. In other articles, the corneal affection was considered primary. This was confirmed by a corneal biopsy specimen, in which abnormal epithelium and absence of Bowman's membrane were observed.^{7,10,11}

COMMENT

Based on clinical presentation,⁷ pedigree analysis,^{7,10,11} and DNA analysis,¹⁴ X-linked KFSD (Siemens) is delineated as a homogeneous entity. Expression of KFSD in women can be explained by nonrandom X-inactivation (Lyon hypothesis). The KFSD (Siemens) leads to scarring without any evident or mild inflammation. Folliculitis spinulosa decalvans is a better name for the persisting inflammatory KFSD. The clinical course and inheritance pattern of FSD is different. Other disease entities with KPA are KPAF and atrophoderma vermiculata, which are, respectively, most probably inherited in an autosomal dominant and autosomal recessive manner. The issue of genetic heterogeneity vs clinical entities will be resolved when the underlying biochemical defect(s) are unraveled by DNA linkage analysis or mutation detection. This will facilitate final conclusions on inheritance patterns and carrier detection. The most progress has been made in KFSD.^{7,14}

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