Novel treatment (new drug/intervention; established drug/procedure in new situation)

Clearance of seborrhoeic keratoses with topical dobesilate

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A patient with two seborrhoeic keratoses in the face received a single daily application of dobesilate cream during 6 months. Dobesilate achieved complete clearance of the seborrhoeic keratosis lesions with good cosmeses, suggesting that this compound is a safe and efficient candidate in the treatment of seborrhoeic keratoses.

BACKGROUND

Although seborrhoeic keratoses (SebKs) are very common benign tumours and represent one of the most disfiguring signs of skin ageing, their pathogenesis is poorly understood. Recently activating fibroblast growth factor receptor 3 (FGFR3) mutations in the epidermis were shown to be involved in the development of SebKs. It has been shown that dobesilate interferes with the FGF signals. Consequently, it seemed reasonable to test this compound for SebKs treatment.

CASE PRESENTATION

A 70-year-old woman with two SebK lesions in the face (figure 1A) received a daily application of 5% potassium dobesilate cream during 6 months. Complete clearance of the lesions was observed at the end of the treatment. Disappearance of the lesion was not accompanied with appreciable application-site reactions, skin atrophy, disturbances in pigmentation or skin thinning (figure 1B). The patient maintained results at 1 year follow-up visit.

DISCUSSION

SebKs are keratinocyte-derived benign skin tumours that never progress to acquire invasive features. SebKs are sharply demarcated brownish plaques with a verrucous

surface predominantly localised in the head, neck and trunk, varying in size from a few millimetres to one centimetre or more. The prevalence of SebK increases with age. About 80%–100% of people over 50 years display those benign skin tumours in some regions.¹ Because this tumour is benign, treatment is not mandatory. However, the lesions are often removed specially for cosmetic reasons. The treatment for SebK covers a range of operative procedures such as curettage, shave excision, electrodesiccation, cryotherapy and ablative laser. Unfortunately, recurrence, scarring and pigmentation changes are common problems with these techniques.² The use of topical and systemic drug therapies in the treatment of SebK has been proposed. These previously proposed therapies have shown some efficacy against SebK, though none is universally effective and SebK lesions tend to recur.² Little progress has been made in developing new medical therapies for SebK in recent years. The molecular mechanisms underlying the initiation and progress of SebK are not yet clear. However, several recent reports have implicated activating mutations of FGFR3.^{3–5} It is well established that this family of receptors shows strong affinity for sulphated glycosaminoglycans which constitute the extracellular matrix. In addition, glycosaminoglycans are required for the assembly of the molecular complex responsible of triggering the intracellular signalling

Figure 1 Clinical appearance of seborrhoeic keratosis lesions before (A) and after (B) dobesilate treatment.

cascade that mediates the biological activity of this growth factor system.⁶

Recently we have identified a new family of compounds that target both FGFs and their FGFRs. These compounds hinder the reciprocal association between these two proteins and, consequently, their biological activity.⁷ Dobesilate, (2,5-dihydroxybenzene-sulfonate), the best of this family of inhibitors, is a pharmacologically very safe compound, that has been used, as inhibitor of FGF signalling, in the treatment of several skin diseases caused by the anomalous functioning of this signalling system.^{8–10} It has been shown that dobesilate interferes with the binding of FGFRs to sulphated glycosaminoglycans.⁷ Consequently, it seemed reasonable to test this compound for treating SebK. The outcome of dobesilate treatment on these lesions is illustrated with the case presented in this report. According to these data, dobesilate should be investigated further as a possible treatment for SebKs.

Learning points

- ▶ SebKs are a major disfiguring problem of aged skin.
- ▶ Somatic activating FGFR3 mutations in human skin are associated with SebKs.
- ▶ Dobesilate interferes with coupling of FGF with its receptors.
- ▶ Dobesilate represents a possible pharmaceutical compound for the topical treatment of SebKs.

Competing interests None.

Patient consent Obtained.

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