rule out hyaluronic acid, with a permanent filler seeming more likely. Polyacrylamide gel is more multivacuolated in appearance, whereas polyalkylimide is more granular; therefore, the substance involved in the present case could be polyalkylamide.[5,9]

In conclusion, we present a case of foreign-body granulomatous reaction with a good response to daily allopurinol 300 mg. This treatment could be a useful alternative in patients who do not respond to conventional therapy.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Hair Changes During Treatment With Trametinib☆

Cambios en el pelo asociados a trametinib

Dear Editor:

The mitogen-activated protein kinase (MAPK) pathway is the therapeutic target in a large number of neoplasias. MEK inhibitors such as trametinib have been used to treat solid tumors and blood cancers in adults, whereas its use in children is extremely rare.[1] Cutaneous manifestations associated with these therapies are frequent, but little data exists on hair abnormalities. We present the case of a girl who developed trichoschisis and trichorrhexis nodosa during treatment with trametinib.

A 2-year-old Caucasian girl with a history of neurofibromatosis type 1 (NF1), which had been diagnosed at the age of 9 months, and carrier of a de novo heterozygous mutation in c.7006G>T presented optic glioma and cervical plexiform neurofibroma with

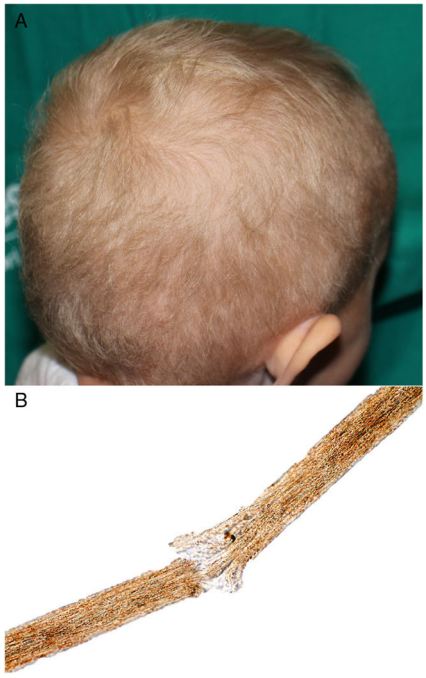

Figure 1 A, Sparse blond hair with a dry and dull appearance. B, Focus of transverse fracture with unraveled edges in the hair of a girl after 10 months of treatment with trametinib.

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Table 1 Cutaneous Manifestations of Pediatric Patients Treated with Trametinib.

Patient	Age, y	Sex	Neurofibromatosis	Tumor	Acneiform Eruption Days[a]	Angular Cheilitis Weeks[a]	Xerosis Weeks[a]	Seborrheic Dermatitis Days[a]	Folliculitis Weeks[a]	Paronychia Weeks[a]	Fine Hair
1	3	F		Astrocytoma		4	12				
2	9	F		Optic glioma	23					8	
3	10	M	X	Optic glioma			2		2	12	
4	13	F		Optic glioma		10	10		28	2	
5	13	F	X	Malignant tumor of peripheral nerve sheath	10		2		2		
6	13	F	X	Plexiform neurofibroma					1.5	12	X
7	15	F	X	Optic glioma	15		1.5	11			X
8	17	M	X	Astrocytoma	11	16	2	14	1		X
9 (this case)	2	F	X	Plexiform neurofibroma and optic glioma		38	40		40		X

Abbreviations: F indicates female; M, male.

[a] Time from start of treatment to appearance of clinical signs.

Source: modified from Boull C et al.[1]

involvement of the nerve roots and occupation of the spinal canal, vascular compression and a risk of involvement of the airways. Treatment was instated with trametinib, for compassionate reasons, at the age of 14 months. Ten months later, she was sent to our department due to the appearance of papules and pustules grouped in the dorsal area, some of which were umbilicated and clinically suggestive of molluscum contagiosum; the lesions had appeared several days earlier. The patient also presented erythematous papules on the tip of the nose and in the perioral region, angular cheilitis, and fine blond hair with a dull appearance; these manifestations appeared 2 months after beginning treatment (Fig. 1A). The patient had no hypertrichosis or trichomegaly and presented no other abnormalities on the skin or nails. She did not use chemical products or hairstyles that might cause traction. Study of the hair under an optical microscope revealed trichorrhexis nodosa and multiple trichoschisis fractures (Fig. 1B). Gram staining revealed gram-positive cocci on the surface of the skin lesions, PAS staining revealed no fungi, and immune staining for herpes virus was negative. The lesions improved after application of topical fusidic acid. As the change in the hair was only an esthetic alteration, it was decided, on consultation with the mother, not to indicate treatment. The patient was transferred to the city and long-term follow-up has therefore not been possible.

New targeted therapies have been developed in recent years to treat some solid tumors and hematologic cancers. Cutaneous manifestations are frequent in patients treated with MEK inhibitors.[2,3] Few cases of these reactions are recorded in adults and even fewer in children, for whom MEK inhibitors are not currently approved and are only indicated on compassionate grounds.[1] The most commonly described cutaneous alterations include acneiform eruptions, angular cheilitis, xerosis, folliculitis, and finer hair, as in our patient, as well as seborrheic dermatitis and paronychia[1–6] (Table 1).

Pilose dysplasias are malformations of the hair stem or bulb and may form part of a genetic syndrome or be nonspecific. Trichorrhexis nodosa is the most common pilose dysplasia and corresponds to a structural defect of the hair, characterized by transversal fractures in the hair stem, which takes on the appearance of a brush at each side of the break. Clinically, it manifests as white or yellowish particles joined to the hair stem. It usually affects head hair, but may appear on the eyebrows, eyelashes, or body hair. It occurs due to mechanical or chemical trauma in previously normal or abnormally fragile hair. Examples of physical trauma includes excessive brushing, hairstyles with traction, exposure to heat or ultraviolet light, trichotillomania, and scratching. Chemical trauma includes frequent washing, use of products for permanent waves, dyes, and exposure to salt water.[7] Congenital (proximal) trichorrhexis nodosa has also been linked to hypothyroidism, citrullinemia, argininosuccinic aciduria, Menkes syndrome, trichothiodystrophy, tricho-hepato-enteric syndrome, and one reported case in a patient treated with anti-TNF-α.[8,9] Trichoschisis is s transverse fracture of the hair that, although it has been linked to trichothiodystrophy, is not a specific finding and may be present in normal hair.

Treatment of these hair abnormalities is difficult and includes cutting off the damaged hair, using conditioners, and avoiding trauma. Treatment of the possible underlying causes must also be considered. Specific diets for specific deficits, use of minoxidil 5%, and sodium levothyroxine have been described, but only in isolated cases.[7,10]

In conclusion, we present the case of a pediatric patient with NF1 who presented trichoschisis and trichorrhexis nodosa during treatment with trametinib. Although abnormalities of the hair follicle associated with some targeted therapies are common, we have found no other cases in which the histologic characteristics of the hair, or the association of trichoschisis or trichorrhexis nodosa have been described in patients treated with trametinib, and we have found only 1 case describing a patient with uncombable hair and NF1.[11]

Determining the chronology of the appearance of the manifestations associated with these therapies is useful for predicting them and instating appropriate treatment, thereby avoiding having to reduce the dosage of or suspend the MEK inhibitors unnecessarily.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Actinic Keratosis and Primary Care Physicians: Factors Affecting the Decision to Treat or Not☆

Determinantes del tratamiento de las queratosis actínicas por médicos de atención primaria

Dear Editor:

Actinic keratosis (AK) is characterized by intraepidermal proliferations of dysplastic keratinocytes, and is more frequent in men and in individuals with low phototypes.[1] Despite its high prevalence and the risk of malignancy, awareness of AK is low among the general population and even among a percentage of primary care physicians (PCPs), and it is considered an underdiagnosed and undertreated problem.[2] European guidelines propose an active role of PCPs in treating patients with incipient lesions and referring them for ablative or cancerization field treatment.[3] In Spain, these patients are monitored by PCPs and referred to dermatology services in cases of diagnostic doubt or to plan the therapeutic approach.[4]

We evaluated the factors influencing the decision to treat AK in a sample of PCPs from the public health service of Andalusia, Spain. Based on factors reported in the literature to facilitate or hinder AK treatment, a questionnaire was developed and a focus group conducted with dermatologists and PCPs. The initial version of the questionnaire was evaluated by 10 PCPs to assess comprehension, feasibility, and completion time. The final version consisted of 13 questions, rated using a 5-point Likert scale. Information was collected about years of experience, the use of teledermatology and dermoscopy, hours of training in dermatology, and the level of self-reported dermatological knowledge relative to other PCPs. To assess the association between these variables and the decision to treat AK, a bivariate analysis was performed using either the Chi-squared test (for qualitative variables) or the student *t* test (for numerical variables). An exploratory factor analysis (EFA) was performed, followed by multivariate logistic regression in which the explanatory variables were those obtained in the EFA and the dependent variable was AK treatment.

After distributing the questionnaire to 381 PCPs, 98 (25.7%) responded, a response rate similar to that reported for other questionnaires with these characteristics.[5] The margin of error was 8.5%, with a 95% confidence interval (95% CI). Only 38.8% (95% CI 29.7–48.7) of PCPs reported that they had treated AK. Teledermatology and dermoscopy were used by 78.6% and 41.2% of respondents, respectively. Most respondents (66.3%) reported a level of dermatological knowledge similar to that of other PCPs. In the preceding 5 years they had received an average of 24.1 ± 44.9 hours of training in dermatology and 7.4 ± 12.1 hours dedicated specifically to skin cancer. The only variables that were statistically significant were the use of dermoscopy and self-reported dermatological knowledge. The results of the EFA (Table 1) explained 68.5% of the variance. The Cronbach alpha values (0.67–0.92) obtained confirmed the reliability of the selected determinants of AK treatment: perceived importance, necessary training, primary care organization, medical-legal considerations, and treatment costs. Table 2 shows the results of the logistic regression analysis. Medical-legal considerations was the variable with the greatest explanatory power, followed by perceived importance. Both were found to be direct determinants of the decision to treat AK by PCPs. No association was observed for necessary training, primary care organization, or treatment costs.

Our analysis allowed us to identify the factors that best explain the decision to treat AK by PCPs. To our knowledge, no such study has been previously carried out in Spain. We found that 38.8% of the respondents opted to treat AK, in line with the proportion (40%) reported by Halpern et al.[6] The most relevant determinant of the decision to treat AK was medical-legal considerations (i.e. fear of misdiagnosis or an adverse reaction to treatment). In our opinion, this insecurity could be due to insufficient training and overly heterogeneous guidelines, ultimately leading to a decision not to treat. In fact, the Spanish Society for Healthcare Quality (SECA)[7] recently pioneered a circuit of care for AK patients in Spain, and identified the functions of the different agents involved. The authors concluded that a lack of coordinated action is one of the barriers to quality of care

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