The simultaneous clinical presentation of cutaneous nodules with facial nerve palsy warrants a comprehensive search for underlying pathology. The differential diagnosis of a patient presenting with nerve palsy and cutaneous nodules may additionally include lymphoma, sarcoidosis, and Langerhans cell histiocytosis. Often in these cases a biopsy will allow for rapid diagnosis and lifesaving treatment.

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Topical N-Acetylcysteine for the Treatment of Lamellar Ichthyosis: An Improved Formula

Abstract: Topical N-acetylcysteine is gaining recognition as a useful and safe therapy for lamellar ichthyosis. We report a case of inherited lamellar ichthyosis that showed a good response to treatment with a new formula of N-acetylcysteine cream. With this new formula, which is described in the article in a practical manner, the odor of sulfur was minimized and we obtained excellent adherence to treatment.

Lamellar ichthyosis is a chronic, disabling disorder with significant effect on quality of life. Its management continues to be challenging, so new therapeutic strategies are always welcome.

CASE REPORT

A 5-year-old boy with lamellar ichthyosis has been followed by our Dermatology Department since birth. He was delivered as a collodion baby, and shortly after, he developed a characteristic phenotype compatible with lamellar ichthyosis. Based on histopathologic study and genetic testing of the transglutaminase-1 gene (*TGM-1*) from his DNA, the confirmatory diagnosis of lamellar ichthyosis was made. Parental genetic testing was also performed and showed that the patient had two heterozygous mutations in the *TGM-1* gene: one from the mother (mutation in exon 8 c.1222del5, pDAsp408VfsX21) and one from the father (mutation in exon 15 c.2278C>T, p.R760X). Since birth he had always been managed with topical emollients and keratolytic agents, such as urea (maximum 10%) and ammonium lactate creams, but with poor results. Oral retinoids were offered, but the parents preferred to postpone their use. We decided to prescribe 10% N-acetylcysteine in urea cream, but with a modified formula to improve the applicatio. To eliminate the intense sulfur smell we added a solution of 1.5% rosemary oil (Fig. 1). After a few weeks of topical twice-daily use we observed marked improvement, with a decrease in the ectropion, some hair regrowth, and a significant reduction in plaque thickness and desquamation. Tolerance was excellent (Fig. 2).

DISCUSSION

The usefulness of topical N-acetylcysteine in the treatment of lamellar ichthyosis has been shown in isolated case reports since it was first described (1–4). The inhibition of keratinocyte proliferation is thought to cause the therapeutic effect of this drug on hyperproliferative skin disorders without a cytotoxic effect (1). Its main drawback is the strong "rotten egg" odor that results once it is applied to the skin, which is caused by progressive oxidation of the N-acetylcysteine, which liberates sulfur-containing components. This is an inconvenience that leads to therapy rejection or withdrawal by many patients and physicians. Bassoti et al (3) mentioned the possibility of adding a fragrant essence to diminish this nuisance in a recent article, but did not mention anything about type or quantity. In addition to eliminating the "rotten egg" odor with rosemary oil, we improved the formula by using the nonionic

10% N-Acetylcysteine + Urea 5% in o/w emulsion formula

Ingredients*: Active ingredients and excipients for 100 g of final product

- N-acetylcysteine……10 g
- Urea……..……5 g
- Sodium hydroxide……..…2.5 g
- Neo- polycaprolactone (PCL) Base O/W cream (non-ionic emulsion)……..…..25 g
- Glycerin…….…….,,…5 g
- Rosemary oil……1.5 mL
- Sterile water…….…….51 mL

Equipment Required:

- Class A prescription balance
- Magnetic stirrer
- Test tube and beaker
- Laboratory thermostatic bath
- Mixer
- Glass stick

Method of Preparation:

Do not use metallic material during preparation.

1. Measure 55 mL of sterile water with a test tube and place in a beaker. Heat the water in the thermostatic bath up to 50ºC to 60ºC.
2. Weigh the N-acetylcysteine and the urea and dissolve them slowly with the magnetic stirrer.
3. Incorporate the glycerin and add the sodium hydroxide slowly. Dissolve them using the magnetic stirrer.
4. Measure the pH; must be between 4.5 and 5.0.
5. Weigh the Neo-PCL and melt it in the thermostatic bath up to 50ºC to 60ºC. Add the rosemary oil.
6. Remove the Neo-PCL from the bath. Incorporate the water phase into the oil (Neo-PSL) while shaking with the glass stick until it cools down.
7. Finally, reduce the particles and homogenize the mixture with the help of a mixer until it gets an ambient temperature.

Quality Control Procedures:

- Weight of final product
- Visual observation of ointment spread: white, slightly stiff ointment with no visible particles
- pH 4.5 to 5

Packaging

Package in tight, light-resistant containers.

Beyond-Use Date Assignment:

- The beyond-use date is 30 days†

Figure 1. Formula ingredients and procedures. *Acofarma Laboratory S.A. manufactures and sells all ingredients listed. All the ingredients were approved by the Spanish Drug Agency, which follows the legislation from the European Agency for the Evaluation of Medical Products. †Based on the recommendations of the U.S Pharmacopeial Convention for pharmaceutical compounding of nonsterile preparations.

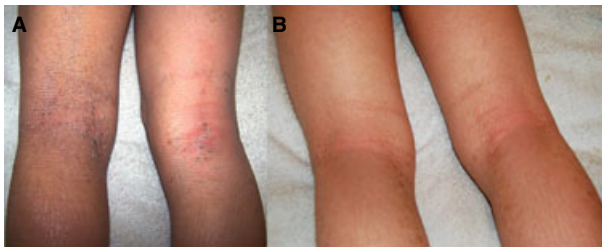

Figure 2. Improvement of the hyperkeratotic scales and desquamation on the legs 2 weeks after twice-daily use of 10% N-acetylcysteine cream. (**A**) Before treatment. (**B**) After treatment.

modern excipient neopentyl glycol (NEO)-polycaprolactone (PCL)–base oil/water (O/W) cream, which consists of liquid PCL, solid PCL, beeswax, several paraffinic esters, and fatty alcohol ethoxylate and in which the oil is the dispersed phase and water is the dispersion medium, instead of a water/oil (W/O) emulsion, cold cream, or NEO-PCL W/O base, in which water is the dispersed phase and oil is the external phase, as previously described (5). With this base, greater blendability is obtained without residuals or a greasy feeling. Another remarkable

difference in our formula is the way in which the active agents are added to the water phase of the emulsion to obtain better homogeneity in the final product. An effective and easy-to-use cream is obtained with this formula, making topical N-acetylcysteine an excellent therapy in the management of ichthyosis.

CONCLUSION

We report a case of inherited lamellar ichthyosis that showed a good response to treatment with a new formula of topical N-acetylcysteine cream. With this new formula the odor of sulfur was eliminated and we obtained excellent adherence in the use of N-acetylcysteine cream.

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Sinus Pericranii with a Hair Collar Sign

Abstract: Sinus pericranii is a rare vascular malformation in which the extracranial veins are connected to the intracranial venous circulation. It typically appears as a soft mass with a blue hue on the scalp. We describe a patient with sinus pericranii and associated hair collar sign.

Sinus pericranii is a rare anomalous communication in which the extracranial veins are connected to the intracranial venous system (typically a transosseous emissary vein connecting a scalp varix with the dural venous sinus). It has a variable clinical appearance. We describe an unusual finding of midline sinus pericranii with an associated hair collar sign.

A 53-day-old boy was seen for a congenital scalp nodule with surrounding hair growth. The nodule had been increasing in size since birth. It became red and swollen when he cried and was tender to touch. The infant was born via normal vaginal delivery without instrumentation.

Examination of the midline vertex of the scalp showed a soft, nonpulsatile nodule with surrounding dark terminal hairs forming an irregular hair collar (Fig. 1). The nodule was in the center of a light red capillary stain that became more obvious when the patient cried. There were no other midline defects.

Magnetic resonance imaging (MRI) with and without contrast showed findings consistent with sinus pericranii (Fig. 2). An appointment at a multidisciplinary vascular anomalies clinic for further examination and treatment is pending.

Sinus pericranii typically appears as a soft, fluctuant, pulsatile or nonpulsatile, blue or red mass fixed to the scalp. The malformation can be described as a "hair of snakes" secondary to the twisting and dilatation of the underlying veins. Sometimes there is overlying alopecia (1). The mass tends to increase in size with crying or the Valsalva maneuver and decreases in size with standing. Congenital sinus pericranii is usually located in the midline frontal region of the scalp (40%)

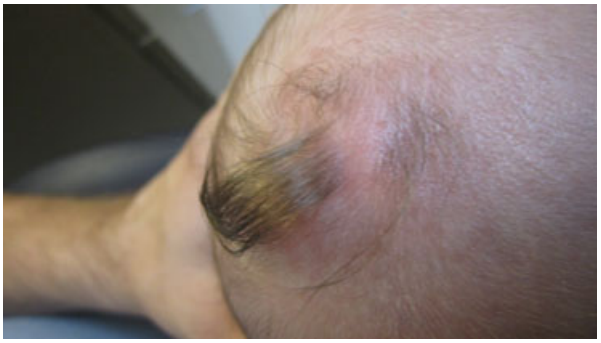

Figure 1. A soft nodule with an irregular hair collar of dark terminal hairs.