A Rare Case of Acquired Ichthyosis Related to Pulmonary Tuberculosis

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ABSTRACT Acquired ichthyosis (AI) is a clinical condition associated with keratinization defects, characterized by accumulation of cutaneous scales, with or without epidermal proliferation and inflammation of the dermis. With this report, we want to present the case of a 58-year-old man who referred to our clinic with severe and diffuse scaling of the skin associated with irrepressible itching, unresponsive to oral antihistamines. After our diagnosis of acquired ichthyosis, we subjected him to diagnostic investigations aimed at identifying the triggering cause. After performing laboratory tests and radiographic investigations, the diagnosis of pulmonary tuberculosis (TBC) emerged. The treatment of the underlying TBC initially did not improve the patient's clinical condition, but after the interruption of treatment with isoniazid, the cutaneous involvement resolved. In literature, to date, there is poor scientific evidence of tuberculosis-related and isoniazid-related ichthyosis; moreover, some of those patients had a concomitant history of solid tumors (long associated with acquired ichthyosis), which makes it more difficult to identify the triggering cause among many.

KEYWORDS: acquired ichthyosis, tuberculosis, pulmonary

INTRODUCTION

Acquired ichthyosis is clinically and histologically indistinguishable from ichthyosis vulgaris (IV), a hereditary monogenic disease that occurs in the first years of life, associated with mutations in the profilaggrin gene (FLG). The cause of the clinical manifestation of ichthyosis (both acquired and hereditary) is the reduction of the cohesion of epidermal cells, altering the integrity and therefore the function of the epidermal barrier. Diagnosis is clinical, with careful examination of the skin, analysis of the period of onset (in childhood for the hereditary form, in adulthood for the acquired one), and collection of personal and family history. Skin biopsy is not an essential diagnostic test, but it highlights the characteristics of ichthyotic skin, with the presence of mild orthokeratotic hyperkeratosis with or without hypogranulosis or agranulosis [1]. In the clinical suspicion of acquired ichthyosis, more in-depth investigations are needed to identify a possible trigger and to set up a correct diagnostic-therapeutic procedure. There is scientific evidence in literature that acquired ichthyosis can often be the clinical manifestation of a systemic condition. It can represent a paraneoplastic manifestation, a reaction to drugs or, less frequently, be related to malnutrition or systemic diseases. This form of ichthyosis undergoes clinical improvement only after treatment of the underlying cause [2].

CASE PRESENTATION

A 58-year-old patient was referred to our Dermatological Unit for the presence of extensive cutaneous xerosis lasting three months, for which he had never performed any topical or oral therapy, except antihistamines, without benefit. On physical examination, he presented fine scaling of the skin diffusely involving the entire body surface (including the scalp), especially on the lower limbs, associated with irrepressible itching mainly at night. Given the suspicion of acquired ichthyosis, a skin biopsy, blood tests with infectious disease screening, and radiological examina-

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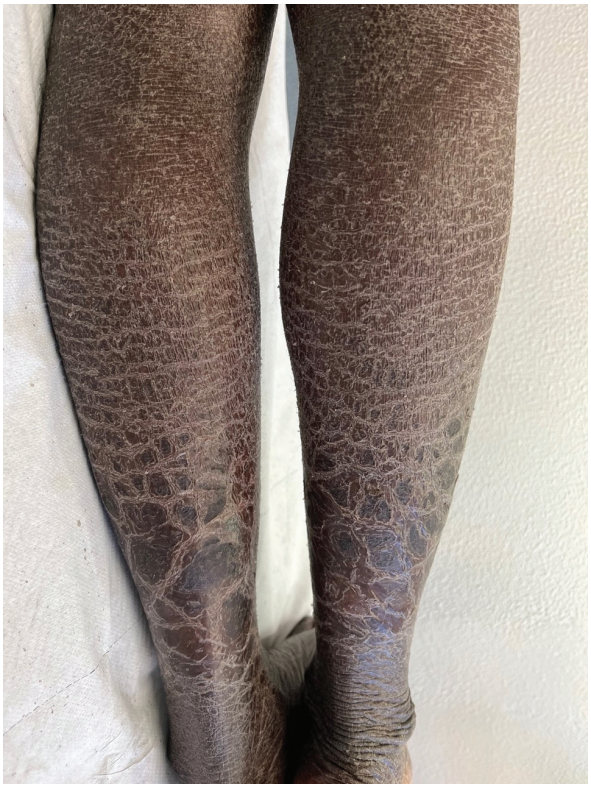

Figure 1. Detail of an ichthyotic skin, with large, fish-like scales of lower limbs

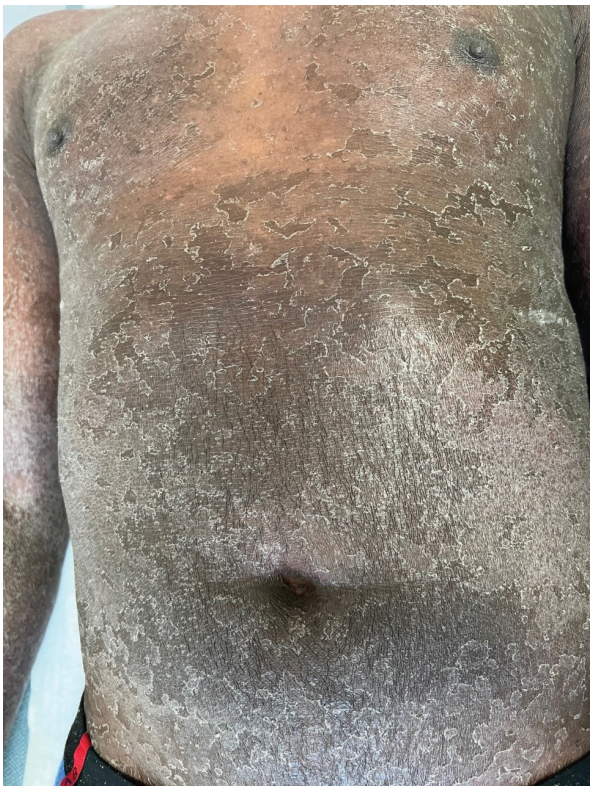

Figure 2. Ichthyotic skin before treatment, with skin scales of the chest and abdomen

tions were performed. Screening was positive for HBV reactivation and negative for HCV and HIV; Quantiferon was uninterpretable, and histological examination showed mild epidermal acanthosis with alternating parakeratosis. Tomoscintigraphy demonstrated multiple volumetrically increased lymph nodes in the laterocervical, supraclavicular, axillary, inguinal, and abdominal areas, characterized by thickened cortex and poor representation of the adipose hilum. Positron Emission Tomography (PET) showed increased glucose metabolism in lymph nodes. At that time, the suspicion of a hematological malignancy (particularly Hodgkin or non-Hodgkin lymphoma) was very high. Axillary lymphadenectomy was performed, with the outcome of dermatopathic lymphadenitis, negative for neoplastic cells of B and T lymphocyte populations and with regular germinal centers, Bcl-2 negative, orienting more towards an infectious cause rather than the initial neoplastic suspicion. Therapy with lamivudine was initiated (for HBcAb positivity), and Quantiferon was requested again, with a positive result; therefore, the patient started triple therapy according to the following scheme: isoniazid + rifampicin + pyridoxine for three months. Due to clinical worsening following initiation of triple therapy, with increasing pruritic symptoms, treatment was changed to a dual regimen of rifampicin + pyridoxine for four months. Already one month after the patient started anti- tuberculosis therapy, pruritic symptoms resolved, and there was a significant improvement of the skin, with persistence of mild cutaneous xerosis.

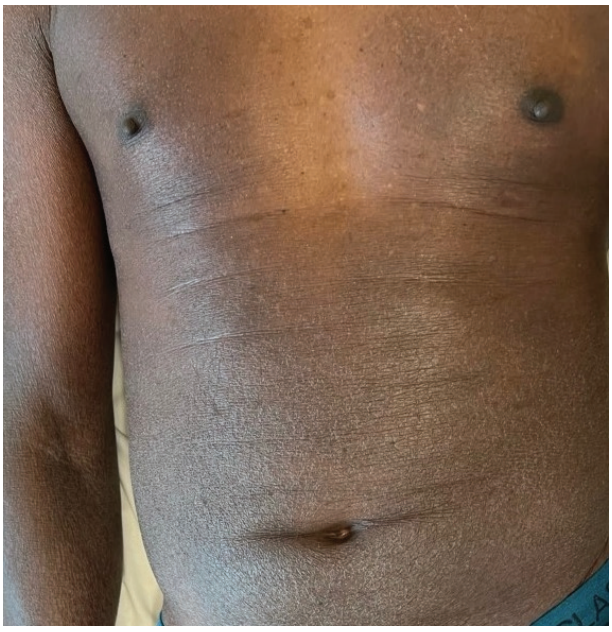

Figure 3. Skin of the chest and abdomen after three months of anti-tuberculosis therapy

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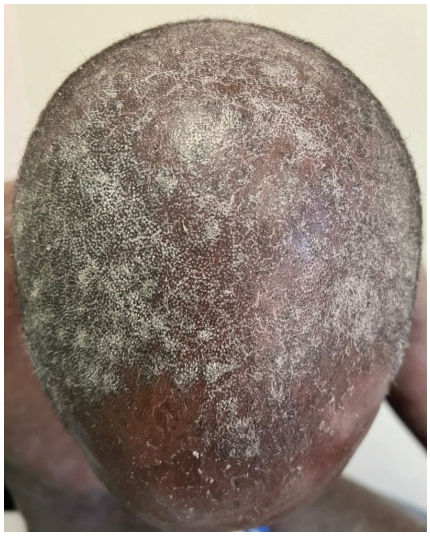

Figure 4. Ichthyotic skin before treatment, with skin scales of the scalp

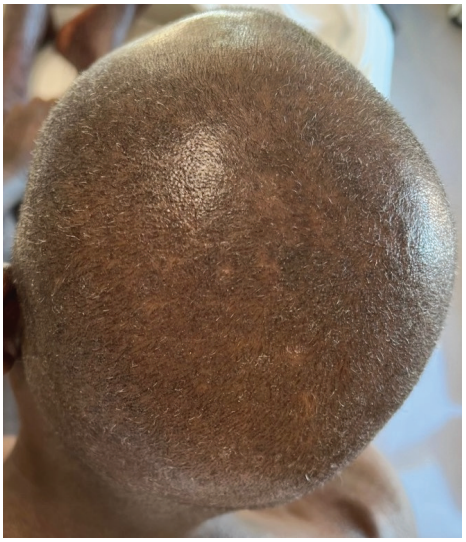

Figure 5. Skin of the scalp after three months of anti-tuberculosis therapy

DISCUSSION

Acquired ichthyosis is a nonhereditary cutaneous disorder, more frequent in adulthood, and associated with abnormal cornification of the skin. AI can frequently represent a cutaneous manifestation of underlying neoplastic diseases, in particular non-solid hematologic tumors (non- Hodgkin's and Hodgkin's lymphomas, leukemia, multiple myeloma), and solid tumors (most commonly breast and lung cancer and sarcomas) [3]. Less frequently, it can be a reaction to drugs (including isoniazid, cholesterol-lowering agents, allopurinol, targeted cancer therapies such as EGFR inhibitors and BRAF inhibitors, nicotinic acid and antipsychotic drugs) or a manifestation of systemic disorders (i.e. systemic lupus erythematosus, leprosy, AIDS, renal insufficiency, sarcoidosis, hypo- and hyperthyroidism) [4]. Cases of ichthyosis related to tuberculosis are rarely described in the literature [5–7], and a few cases of worsening or induction of ichthyosis after treatment with isoniazid have been reported [8,9]. Tuberculosis has been largely associated with specific cutaneous manifestations such as scrofuloderma, lupus vulgaris, and tuberculosis verrucosa cutis [10], but there is still poor evidence to classify acquired ichthyosis as a nonspecific cutaneous manifestation in patients with active tuberculosis. Furthermore, these specific skin manifestations of tuberculosis allow direct detection of mycobacteria through Ziehl–Neelsen staining and isolation of skin material in Löwenstein–Jensen medium; conversely, no direct evidence is available in literature for nonspecific cutaneous manifestations of TBC. Keratolytic agents are useful to remove skin scales, and hydration with lipid-rich emollients helps restore the cutaneous barrier and prevent penetration of microbial agents through damaged skin; however, these measures are not sufficient to treat the manifestation. What is necessary is to associate appropriate therapy targeting the underlying disorder. Based on increasing evidence of patients treated for tuberculosis who recovered from ichthyosis, acquired ichthyosis should be considered, among others, a possible manifestation related to TBC, although rare.

CONCLUSION

Management of patients with acquired ichthyosis involves multidisciplinary care. It is important for the clinician to perform accurate anamnesis and specific diagnostic investigations to identify the possible underlying cause. With this case report, we aim to provide further scientific evidence of the correlation between pulmonary tuberculosis and acquired ichthyosis, as well as evidence supporting isoniazid as a drug associated with worsening of the clinical condition and potentially acting as a triggering cause of AI.

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