

Case report



Crusted (Norwegian) Scabies and HTLV-1 Infection Association: A Case Report

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Received 27 January 2021;

Accepted 20 February 2021;

Published 01 March 2021

Abstract

Crusted scabies, formerly known as Norwegian scabies is an uncommon presentation of scabies that may occur in the in association with an immunosuppressive status. The article aims to present a case report in which a male patient with HTLV-1 carrier status admitted for investigation of eczematous and crusted chronic skin lesions and submitted to a dermatologic evaluation and a skin biopsy considering the hypothesis of a cutaneous form of lymphoma associated with HTLV-1 infection had the diagnosis of Crusted scabies instead. There is data regarding the association of crusted scabies and Human T-lymphotropic virus type 1 (HTLV-1) chronic infection. Therefore, this important diagnosis should always be accessed specially in HTLV-1 endemic regions.

Keywords: *Crusted scabies; Norwegian scabies; Human T-lymphotropic virus type 1; HTLV-1*

Introduction

Human T-lymphotropic virus type 1 is a type C retrovirus belonging to the Retroviridae family. It is an endemic infection in Japan, South and Central Americas, Middle East and some regions of Africa and Australia. It was the first human oncogenic retrovirus described on 1980. Recent estimation suggests that nearly 20 million people worldwide have been infected ^[1,2]. Transmission could occur by breastfeeding, transplacental, during labor, blood products transfusion, infected needles and sexually. The virus has a tropism to CD4 lymphocytes and the infection has its diagnosis done by serologic procedures such as ELISA and Western Blot technics ^[1-5].

The HTLV-1 infection can evolve to tropical spastic paraparesis and lymphoma/leukemia of T cells. However, since the infection could induce an immunosuppressive status, opportunistic diseases should have its occurrence also considered ^[1]. Crusted scabies, formerly known as Norwegian scabies is an uncommon presentation of scabies that may occur in the in association with an immunosuppressive status ^[6]. There is data regarding the association of crusted scabies and HTLV-1 chronic infection ^[4]. Therefore, this important diagnosis should always be accessed specially in HTLV-1 endemic regions.

The article aims to present a case report in which a male patient with HTLV-1 carrier status admitted at the hospital for

clinical investigation of eczematous and crusted chronic skin lesions, which was found to be caused by Crusted scabies. This highlights the importance of consider the possibility of chronic HTLV-1 infection in severe forms of scabies.

Case Report

A 66 year-old male patient was admitted in the hospital with a clinical history of crusted, mild pruritic skin rash especially in the face, scalp, abdomen and extensor faces of limbs for almost one year that worsened 20 days before admission. He had a chronic history of alcohol consumption but denied prescribed or over-the-counter medication, tobacco or illicit drugs use, as well as history of hemotransfusion or prior surgery.

He had the diagnosis of asymptomatic chronic HTLV-1 infection 3 years before when tried to perform a blood donation. His wife also had the diagnosis of HTLV-1 related transverse myelitis at that time. He complained of a 4Kg weight loss and fever for the past 3 days before admission. Laboratorial tests showed mild leukocytosis with preserved neutrophils and lymphocytes, normal kidney and hepatic function.

Antibiotics were introduced to cover a possible secondary bacterial skin infection, which cause the fever to cease, but without modification of the skin lesions. It was then performed a dermatologic evaluation and a skin biopsy considering the

hypothesis of a cutaneous form of lymphoma associated with HTLV-1 infection. Eggs and adult forms of *Sarcoptes scabiei* were found in the skin fragment confirming the diagnosis of Crusted scabies. Based on the diagnosis treatment with ivermectin

200mcg/kg once a day associated with sulfur based body lotion 5%. The patient experienced resolution of the skin lesions within 2 weeks of treatment, being discharged to complete another 2 weeks of treatment on an outpatient setting.



Figure 1: Crusted and exfoliated skin lesions involving face, scalp and trunk (A and B). Regression of lesions after 3 weeks of treatment with ivermectin (C and D).

Discussion

The CD4 lymphocytes are the main target of HTLV-1, resulting in a chronic infection with a long clinical latency [7]. The evidences of greater prevalence, morbidity and mortality of, *Pneumocystis jirovecii*, fungal and *Strongyloides* as well as severe forms of dermatologic infections in patients with chronic HTLV-1 infection suggest some degree of immunosuppression [8].

Researches trying to link the HTLV-1 infection to human diseases have been developed since the first description of the virus. Adult T cells leukemia/lymphoma (ATLL) was the first described condition related to the virus. The role of HTLV-1 was confirmed by demonstration of incorporation of proviral DNA to the neoplastic cells genome [5]. An etiologic role of HTLV-1 was further described in a subtype of spastic myelopathy, now known as HTLV-1 associated myelopathy or tropical spastic paraparesis (HAM/TSP) [9]. Terada et al in 1992 demonstrated causal

association of HTLV-1 with an ophthalmologic involvement known as HTLV-1 associated uveitis [10].

Amano et al described dermatologic lesions in HTLV-1 infected patients, especially those with ATLL or HAM/TSP [1]. However, it has been reports of asymptomatic HTLV-1 infected patients as well [11]. HTLV-1 infection has been associated with infective dermatitis, T cell cutaneous lymphoma, leprosy, stroglyoides infection and crusted scabies. Some of these conditions have biologic background to justify the association with HTLV-1 infection. Although, the association of HTLV-1 with clinical conditions, such as leprosy, lay on epidemiological database [12].

Verdonck et al had proposed grouping the HTLV-1 associated diseases into three categories (inflammatory, neoplastic and infectious complications) even though the exact pathophysiologic mechanisms were not clearly understood [7]. Crusted scabies is among the infectious complications and

considered a rare severe form of disseminated infestation by the *Sarcoptes scabiei* var *hominis* [12].

Boeck and Danielssen first described crusted scabies in 1848 on Norway in a group of patients with leprosy. It has strong association with low economic levels and before introduction of ivermectin as part of treatment the mortality rate of crusted scabies was around 50%. The natives from north Australia are among the most affected people worldwide [6]. Aside from the classic presentation, in which there is less than 20 sarcoptes per gram of skin, there is more than 4000 sarcoptes per gram of skin or about 2 million sarcoptes per person in the crusted scabies. This form of presentation is usually seen in patients with some underlying condition that promote an immunosuppressive state such as HIV infected patients, neoplastic disorders, especially hematologic ones, long term use of corticosteroids and transplant [6,13,14]. Secondary infections may occur because the sarcoptes activity in the epidermis can produce skin changes that favor the growth of *Staphylococcus* and *Streptococcus* genus bacteria instead of *Lactobacillus* species [6].

From an immunological point of view, the classical scabies develop a type IV hypersensitivity reaction after four weeks of infestation. The patient who develops crusted scabies has some defect on this form of hypersensitivity reaction, allowing the sarcoptes over proliferation. It means that these patients have an ineffective dermo-epidermal inflammatory response and develop a severe keratodermic reaction with thick yellowish crusts and extremely high parasitic load. Serum immunoglobulins titers of IgE, IgG, IgG1 and IgG4 are marked elevated but are not protective as well as the high eosinophil's count [6,15]. Walton et al compared the inflammatory reaction among patients with classic and hyperkeratotic/crusted scabies and concluded that the Norwegian scabies non-protective immunologic response has two main characteristics: a dermo-epidermal cell infiltration with CD8 lymphocyte predominance, instead of CD4 lymphocytes, and a Th2 immune response instead of Th1 [6].

Mounsey et al had demonstrated that those disrupted immune responses in the skin were associated with uncommon local hypersecretion of IL-17. This interleukin is known for its key role at the pathophysiology of psoriasis; it is responsible for an abnormal fast epidermal cells renewal, with epidermal hyperplasia and hyperkeratosis [16]. Assuming the IL-17 pathway in the crusted scabies, it would explain the gross aspect of the skin in this presentation of the disease in comparison with the classic scabies. The skin lesions of Norwegian scabies and psoriasis have histological similarities with acantosis, keratinocytes apoptosis, hyperkeratosis, dermal lymphocytic infiltration and basal mitosis. These findings demonstrate a common IL-17 activation pathway pathophysiology [6].

The Norwegian scabies clinically exhibits erythematous plaques, poorly defined that rapidly develops hyperkeratotic psoriasiform scales, crusts, erythrodermia and adenopathy [17]. In the disease severe forms, there is more than 30% of skin involvement, with extension to the scalp. Since there is an abnormal immune response in which CD8 lymphocytes are predominant, patients have mild or even no pruritus, a clinical finding that distinguishes the crusted scabies from the classical form known by its intense pruritus especially at night [6]. Superimposed bacterial infections and regional lymphadenopathy are frequently found [15].

An early diagnosis of Norwegian scabies is crucial for the disease treatment and control [14]. However, a diagnosis delay is the rule as seen on clinical reviews [6]. Frequently patients with crusted scabies receive treatment with topical or systemic corticosteroids because of a misdiagnosis with psoriasis, atopic dermatitis or

seboreic dermatitis. This would favor the development of severe presentations of the disease [15]. The identification of the sarcoptes, its eggs or feces, made by microscopic examination of scales obtained through skin scrapping establishes a definite diagnosis. In some non-satisfactory cases, more sensible and specific methods such as dermatoscopy and videodermatoscopy could be used [18].

The crusted scabies treatment is associated with high rates of resistance and relapses. Ivermectin is the only oral available treatment. It paralyzes the sarcoptes by a peripheral neurotoxicity but it does not affect the eggs neither the young sarcoptes. These forms have an incomplete nervous system development, which makes it insensible to ivermectin until 2 weeks. As a result single dose treatment is completely ineffective. Australian studies recommend weekly doses of ivermectin for at least 4 consecutive weeks in association with topical treatment such as permethrin, benzyl benzoate and keratolytic lotions as well as environment disinfection and contact isolation [6,15].

Since crusted scabies is a neglected disease, there are few cases reported on medical literature. On the Australian aborigine population in which the HTLV-1 is endemic, Norwegian scabies has been described as a viral infection marker [4,19]. Based on this data, a HTLV-1 serologic test in patients with a diagnosis of crusted scabies could be useful on endemic regions, especially when there is no other risk factor for a HTLV-1 infection.

Conclusion

Although the understanding of HTLV-1 pathophysiology has evolved, it still is an underdiagnosed disease with a great proportion of asymptomatic carriers. The dermatological are present and must be recognized especially in endemic regions. Among those dermatological complications, the crusted scabies, such as this case report, must be included on the differential diagnosis of exfoliative erythrodermia in HTLV-1 infected patients.

The dermatological finding of diffuse skin lesions on asymptomatic patients but with positive serology may have relevance on the diagnosis of HTLV-1 infection and on the management of refractory/relapsing lesions to conventional treatment. Thus, screening for HTLV-1 infection is imperative on patients with newly diagnosed Norwegian scabies.

Conflicts of Interests

All authors declare no conflicts of interests.

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