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Case presentation

Leser-Trélat Sign in Tumor-Stage Mycosis Fungoides

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Abstract

A 71-year-old man presented with numerous pruritic seborrheic keratoses, with an eruptive onset over the course of 3 months. At presentation, he was also found to have hypopigmented tumors diffusely scattered throughout his body that were found to be mycosis fungoides on histologic examination. A theory regarding the pathophysiology of the development of eruptive seborrheic keratoses in the presence of mycosis fungoides is briefly discussed and 10 previous case reports of the Leser-Trélat sign in the setting of mycosis fungoides are reviewed.

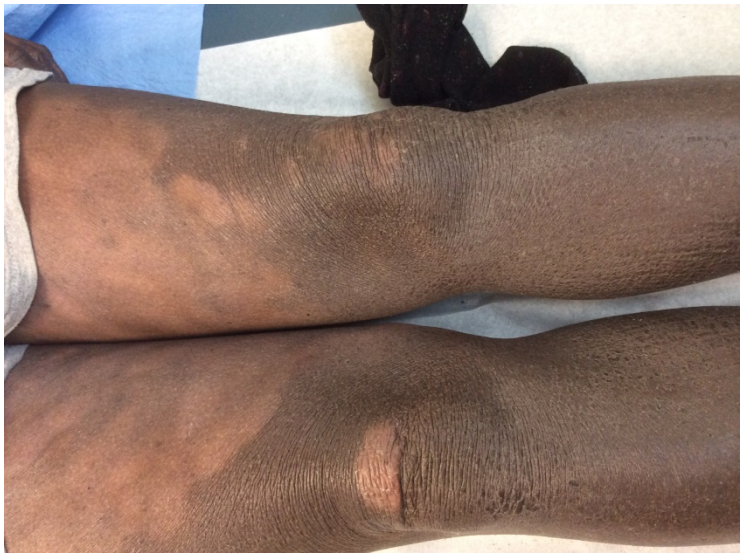
Keywords: leser-trélat sign, mycosis fungoides, egfr

Introduction

The Leser-Trélat (LT) sign is described as a sudden increase in size and number of seborrheic keratoses in the setting of an underlying malignancy [1]. The LT sign has been commonly reported as a paraneoplastic sign in association with gastric adenocarcinoma [2], but has also been found in acute leukemia [3], and mycosis fungoides (MF)[4]. We present an additional case report on the Leser-Trélat sign presenting concurrently with the diagnosis of MF, and review previous case reports as well as a theory on the pathophysiologic mechanism of this paraneoplastic process.

Case synopsis

A 71-year old man presented with numerous eruptive pruritic patches papules, and plaques on the neck, trunk, arms, and hands. He reported the rash began 3 months prior and had progressively expanded over time. He rated his itch severity as an eight on a 10-point visual analog scale (VAS). The patient also reported numerous lumps over his neck, truck, and legs that appeared a year prior. The patient reported a history of hypertension, as well as a family history of prostate cancer (brother), and kidney disease (father). There was no personal or family history of skin cancer.



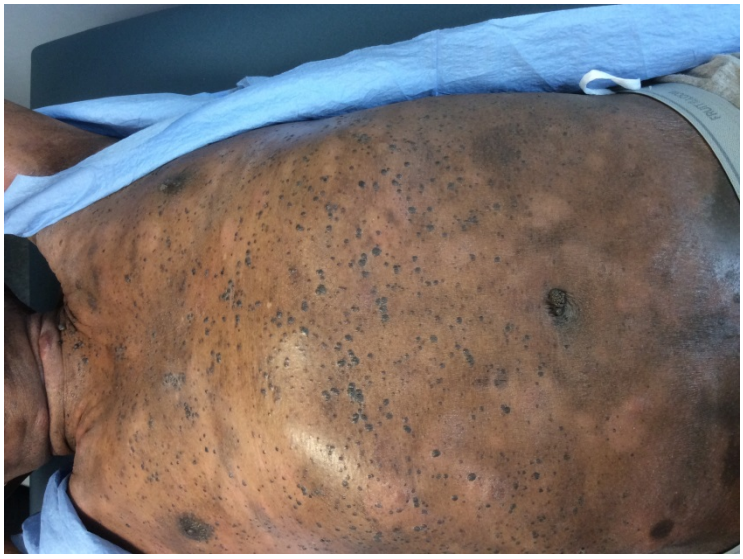
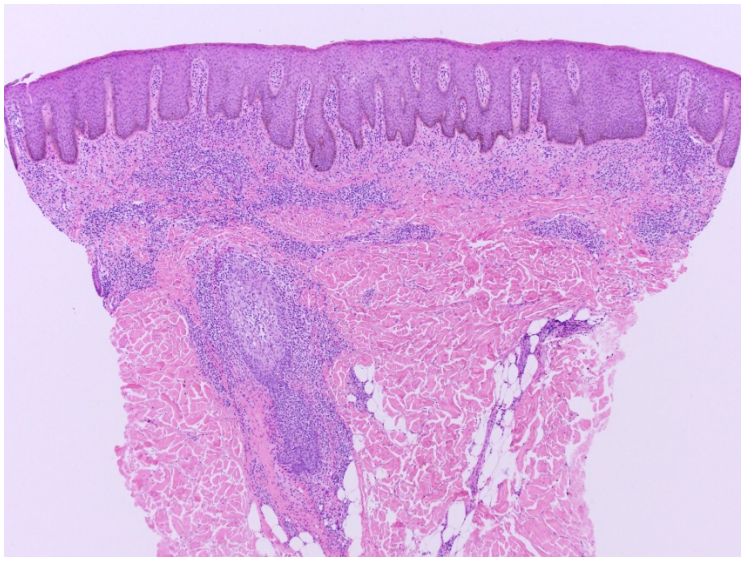


Figure 1. Hyperpigmented patches spread diffusely over legs. **Figure 2.** Seborrheic keratoses overlying the trunk in combination with hypopigmented tumors representing mycosis fungoides

On physical examination, there were numerous hyperpigmented patches diffusely over his trunk, back, and lower legs (Figure 1). Multiple hypopigmented tumors were found on the lower abdomen, back of the neck, left elbow, and central back. In addition, numerous keratotic papules were noted diffusely over the trunk and back (Figure 2). Icthyosiform changes , as well as keratoderma, were found on the lower legs. Lymphadenopathy was noted in right axilla and right inguinal area. Based on the presentation, tumor-stage mycosis fungoides and paraneoplastic eruptive seborrheic keratoses were suspected.



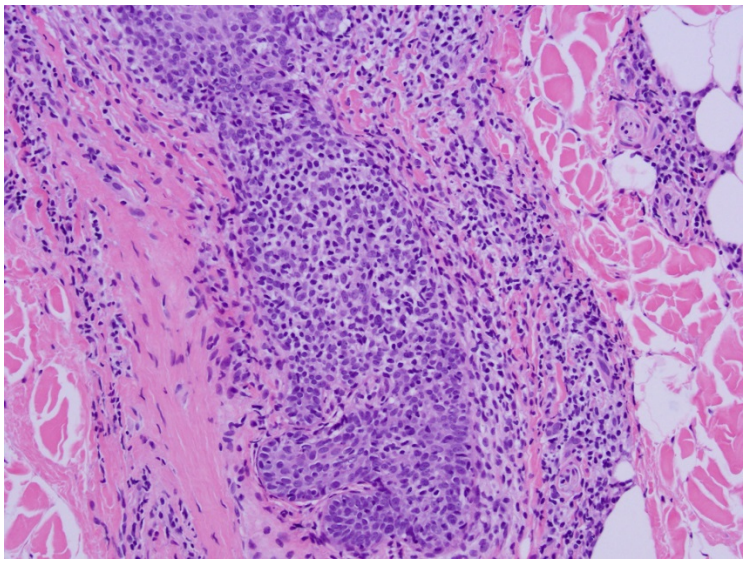


Figure 3a. Acanthosis and parakeratosis with a dense nodular and diffuse infiltrate of atypical lymphocytes. **Figure 3b.** 40x view of a nodular infiltrate of atypical lymphocytes

Two punch biopsies were performed; one was taken from a hyperpigmented patch on the left buttock and the second from a hypopigmented tumor on the right lower abdomen. Both biopsies revealed acanthosis and parakeratosis with a dense nodular and diffuse infiltrate of atypical lymphocytes (Figure 3), some of which were in mitosis. Prominent epidermotropism was noted. Immunohistochemistry displayed increased CD4 over CD8, and scattered CD20 positive cells. The biopsy from the right lower abdomen was consistent with nodular stage MF, whereas the biopsy from the right buttock displayed fulliculotropic MF.

Discussion

The case presented is consistent with the LT sign, the sudden onset (3 months) of the patient's seborrheic keratoses in conjunction with the new diagnosis of mycosis fungoides. Our patient experienced significant pruritus, which is the most commonly reported symptom in association with the LT sign, occurring in half of reported cases [7]. Pruritus is not frequently associated with cases of seborrheic keratoses that are unrelated to the LT sign. Thus, itch is an important symptom to evaluate in patients with the new onset of multiple seborrheic keratoses.

We have summarized the presence of itch, demographic information, and clinical characteristics of previous case reports of the LT sign in the setting of MF in Table 1. We performed a literature search on Pubmed and Google Scholar using the keywords 'Leser-Trélat' with 'mycosis fungoides', 'cutaneous t cell lymphoma', and '**Sézary** syndrome'. References from the extracted articles were also screened for additional case reports.

Table 1. Previous case reports of mycosis fungoides associated with the sign of Leser-Trélat.

Age	Sex	Race	MF Stage	SK Biopsy	Itch	Time to SK	Response to Treatment	First Author
63	M	Caucasian	Plaque	Yes	"Severe"	Concurrent	Remit to treatment	Martínez-Morán *et al.*[8]
76	F	Caucasian	Unknown	Yes	"Extreme"	4 years after MF	MF/SK unresponsive	McCrary *et al.*[9]
35	F	Asian	Plaque	Yes	"Severe"	3 weeks before MF	SKs remained after treatment of MF	Miyako *et al.*[10]
61	F	Unknown	Unknown	No	Yes	2 years after MF	Resolved with treatment	Toonstra *et al.*[11]
61	M	Caucasian	Unknown	No	No	2 months after MF		Safai *et al.*[4]
59	F	Unknown	Sézary syndrome	Unknown	Yes	Before Sézary syndrome	Treatment results in reduction of SKs	Bursztejn *et al.*[12]
57	M	Caucasian	Sézary syndrome	Yes	Yes	5 years after MF	Resolution with treatment	Cohen *et al.*[13]
58	M	Unknown	Sézary syndrome	Yes	Yes	7 months after MF	Resolution with treatment	Wieselthier *et al.*[14]
55	M	Caucasian	Sézary syndrome	Yes	"Increased"	4 months after MF		Dantzig *et al.*[15]
71	F	Asian	Sézary syndrome	No	"severe"	Concurrent	SKs regressed with SS therapy	*Horicuhi et al.*[16]
71	M	African American	Tumor Stage	No	Yes	9 months after MF	Unknown	Rowe *et al.*

We reviewed 10 previous case reports of the LT sign in the setting of MF. Our sample of 11 cases reveals an average age of 61 ± 11 years. The sample consists of five females and six males. The seborrehic keratoses were biopsy-proven in six case reports and itching was associated with the LT sign in 10 of the 11 cases.

The LT sign was reported to occur before, concurrently, or after the development of MF with a timeframe of weeks to years between the LT sign and MF. Of the seven cases of MF that responded to treatment, six resulted in a reduction in SKs or complete resolution. The high concordance of resolution of the LT sign with treatment of the underlying malignancy is highly suggestive that the LT sign is a true paraneoplastic phenomenon.

A concrete pathophysiologic explanation for the LT sign has yet to be determined. Seborrheic keratoses are most commonly associated with mutations in the fibroblast growth factor-3 gene (FGF-3). However, FGF-3 mutations have not been investigated in the setting of cutaneous T cell lymphoma (CTCL) or in association with the LT sign [5]. A number of findings have implicated mutations in the epidermal growth factor receptor (EGFR) gene as a potential mechanism behind the LT sign.

In one case study, a 54-year-old woman displaying the LT sign in the setting of gastric carcinoma was found to have elevated epidermal growth factor in a 24-hour urinary excretion radioreceptor assay [2]. Additionally, mutations of the EGFR gene have been found to be associated with seborrheic keratoses on genetic screenings [5]. EGFR has additional ties to CTCL. Researchers

found elevated epidermal levels of epidermal growth factor and EGFR in patients with CTCL that displayed pseudoepitheliomatous hyperplasia on histologic examination [6]. Additional investigation is needed in order to explore mutations in EGFR and additional factors in order to elucidate the pathophysiologic mechanism behind the LT sign.

Conclusion

We described a case of eruptive seborrheic keratoses in the setting of MF and summarized 10 previous cases of the LT sign associated with MF. The majority of patients from these reports suffer from pruritus related to their seborrheic keratoses and the majority of seborrheic keratoses resolved with treatment of MF. EGFR has shown promise in elucidating the pathophysiology of the LT sign in the setting of MF, but more work needs to be done to describe the mechanism of action.

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References

1. Kurzrock R, Cohen PR. Cutaneous paraneoplastic syndromes in solid tumors. Am J Med. 1995 Dec;99(6):662-71. [PMID:7503090]
2. Kameya S, Noda A, Isobe E, Watanabe T. The sign of leser-trelat associated with carcinoma of the stomach. Am J Gastroenterol [Internet]. 1988 Jun;83(6):664-6. [PMID:2837080]
3. Greer KE, Hawkins H, Hess C. Leser-trelat associated with acute leukemia. Arch Dermatol. 1978 Oct;114(10):1552. [PMID:152610]
4. Safai B, Grant JM, Good RA. Cutaneous manifestation of internal malignancies (II): The sign of leser-trelat. Int J Dermatol. 1978 Jul-Aug;17(6):494-5. [PMID:150408]
5. Hafner C, Toll A, Fernandez-Casado A, Earl J, Marques M, Acquadro F, Mendez-Pertuz M, Urioste M, Malats N, Burns JE, Knowles MA, Cigudosa JC, Hartmann A, Vogt T, Landthaler M, Pujol RM, Real FX. Multiple oncogenic mutations and clonal relationship in spatially distinct benign human epidermal tumors. Proc Natl Acad Sci U S A. 2010 Nov 30;107(48):20780-5. [PMID:24075223]
6. Courville P, Wechsler J, Thomine E, Vergier B, Fonck Y, Souteyrand P, Beylot-Barry M, Bagot M, Joly P. Pseudoepitheliomatous hyperplasia in cutaneous T-cell lymphoma. A clinical, histopathological and immunohistochemical study with particular interest in epithelial growth factor expression. the french study group on cutaneous lymphoma. Br J Dermatol. 1999 Mar;140(3):421-6. [PMID:10233260]
7. Husain Z, Ho JK, Hantash BM. Sign and pseudo-sign of leser-trelat: Case reports and a review of the literature. J Drugs Dermatol. 2013 May;12(5):e79-87. [PMID:23652964]
8. Martínez-Morán C, Sanz-Muñoz C, Miranda-Romero A. Leser-Trélat sign associated with Sézary syndrome and transitional cell carcinoma of the bladder. Actas Dermosifiliogr. 2007 Apr;98(3):214-5. [PMID:17504710]
9. McCrary ML, Davis LS. Sign of Leser-Trélat and mycosis fungoides. J Am Acad Dermatol. 1998 Apr;38(4):644. [PMID:9555814]
10. Miyako F, Dekio S, Tamura H, Yamada Y, Miyata N, Jidoi J, Tohgi K. Mycosis fungoides with Leser-Trélat sign: the first report of a patient from Japan. J Dermatol. 1994 Mar;21(3):189-93. [PMID:8014273]
11. Toonstra J, Ramselaar CG, van der Putte SC. Leser-Trélat sign in mycosis fungoides. A further case report. Dermatologica. 1985;171(4):247-9. [PMID:2934280]
12. Bursztejn AC, Doumat-Batch F, Granel-Brocard F, Perrin A, Cuny JF, Barbaud A, Schmutz JL. Sézary syndrome and Leser-Trélat sign: a chance association?. Ann Dermatol Venereol. 2008 Apr;135(4):287-90. [PMID:18420075]
13. Cohen JH, Lessin SR, Vowels BR, Benoit B, Witmer WK, Rook AH. The sign of Leser-Trélat in association with Sézary syndrome: simultaneous disappearance of seborrheic keratoses and malignant T-cell clone during combined therapy with photopheresis and interferon alfa. Arch Dermatol. 1993 Sep;129(9):1213-5. [PMID:8395792]
14. Wieselthier JS, Bhawan J, Koh HK. Transformation of Sézary syndrome and the sign of Leser-Trélat: a histopathologic study. J Am Acad Dermatol. 1990 Sep;23(3 Pt 1):520-2. [PMID:2145329]
15. Dantzig PI. Sign of Leser-Trélat. Arch Dermatol. 1973 Nov;108(5):700-1. [PMID:4270762]
16. Horiuchi Y, Katsuoka K, Tsukamoto K, Takezaki S. Leser-trelat sign associated with sezary syndrome. Cutis [Internet]. 1985 Nov;36(5):409-10. [PMID: 2933229]