

Leser-Trélat sign as a rare manifestation of cutaneous melanoma

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Abstract

Leser-Trélat Sign (LTS) is a rare paraneoplastic syndrome characterized by the sudden eruption of multiple seborrheic keratoses in patients with internal malignancy, commonly localized in the gastrointestinal tract. We report an 80-year-old female patient showing a rapid increase in the number and size of seborrheic keratosis associated with the diagnosis of a cutaneous nodular melanoma (Breslow thickness: 4.5 mm) located on the right flank. After the excision of melanoma, subsequent staging procedures resulted negative, moreover no evidence of melanoma recurrence and no changes of the seborrheic keratoses was detected after a follow-up of 52 months. Although the association between melanoma and Leser Trelat sign is rare, an accurate skin examination with the aid of dermatoscopy searching for undiagnosed skin cancers, should be suggested in patient with sudden eruption of keratosis seborrheic to early diagnose and treat a possible melanoma.

Introduction

Leser-Trélat Sign (LTS) is a rare paraneoplastic syndrome characterized by the sudden eruption of multiple seborrheic keratoses in patients with internal malignancy, commonly localized in the gastrointestinal tract.¹⁻³

We report one patient with a rapid increase in the number and size of seborrheic keratosis, associated with the development of a cutaneous melanoma.

Clinical Case

An 80-year-old female was examined for the treatment of multiple, itchy verrucous papules and plaques located on the

trunk, which had rapidly increased in number and size during the last year. Physical examination showed hundreds of seborrheic keratoses, with variegated colours ranging from yellowish to brown, located on neck, face, upper chest and back (Figure 1a). In addition, a brown to red plaque with an overlying red pink nodule was observed on the right flank (Figure 1b). The patient was otherwise asymptomatic and in good general health. Dermatoscopy of the lesion on the right flank showed a polymorphous vascular pattern and white streaks at the periphery of the plaque, and irregular blotches of pigmentation and atypical vessels as features of the nodular area (Figure 1c). Histological examination of the excised lesion showed irregular nests of atypical melanocytes located in the dermis with the presence of focal intraepidermal spreading, leading to the diagnosis of invasive melanoma (Breslow thickness: 4.5 mm) (Figure 1d). Subsequent staging procedures including sentinel lymph node biopsy, total body CT scan, tumour markers (CEA, CA 19.9, CA 15.3), mammography, Pap smear, gastroscopy and colonoscopy were all negative. After a follow-up of 52 months, no evidence of melanoma recurrence and no changes of the seborrheic keratoses was detected.

Discussion

LTS was initially described in the 1800s by Leser and Trélat as a cutaneous sign associated with the onset of multiple eruptive cherry angiomas in oncologic patients, and subsequently by Hollander as associated with seborrheic keratoses in 1900.¹⁻³ The lesions are often pruritic and are preferentially located on the trunk with a "Christmas tree" or "rain drop" pattern.¹⁻³ LTS is more common in elderly people, with an average age of 61 years and no sex prevalence, and in approximately half of the cases it is associated with adenocarcinomas (gastrointestinal in 32%) followed by lymphoproliferative disorders in 20% and more rarely with breast, lung, bladder, kidney, prostate, ovary or nasopharyngeal carcinoma.³ Pathogenesis of the LTS is still unclear, although a correlation between the release of EGF and TGF-alpha from malignant cells and keratinocyte proliferation has been proposed.^{2,3} Since the presence of numerous seborrheic keratoses is a common finding in elderly individuals who have, at the same time, a high prevalence of malignancies, some authors questioned the existence of LTS as an entity *per se*.³ However, the finding of the LTS also in young oncologic

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Key words: Leser-Trélat sign; melanoma; oncologic patient; paraneoplastic syndrome; seborrheic keratosis.

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patients, and its association in more than 20% of cases with other cutaneous paraneoplastic syndromes as acanthosis nigricans, support the reliability of this condition as a marker of malignancies.³

The patient we described is, to our knowledge, the fifth case-report of LTS associated with cutaneous melanoma (Table 1). Diagnosis of nodular melanoma in our patient was made accidentally when the patient come to the outpatient clinic requiring treatment of seborrheic keratoses.

In 1987, Ellis and coworkers,⁴ described the first case of LTS in a 54-year-old man displaying multiple seborrheic keratoses on the upper chest and back, acanthosis nigricans and acrochordons of inguinal, axillary folds and neck, concomitant to a 0.75 mm thick superficial spreading melanoma of the back. The authors also demonstrated that EGF-receptor expression was initially increased in specimens of seborrheic keratosis and acanthosis nigricans, but decreased after melanoma resection.⁴ Moreover, the level of TGF-alpha in patient's urine also declined markedly after surgery, suggesting the probable etiopathogenetic role of growth factors released from the neoplastic melanocytes.⁴

A second case of LTS associated to a nodular melanoma (Breslow thickness: 2.16 mm) with regional lymph node involvement was reported in a 69-year-old man displaying a typical Christmas-tree pattern.⁵ Recently, the occurrence of LTS has been described in a 82-year-old male with multiple melanoma metastasis, in whom the

occult primary melanoma was supposed to be a pigmented lesion of right ear treated with curettage without histological examination.⁶ A further association of LTS with a metastatic melanoma of unknown primary was reported in a 71-years-old women as the onset of maculopapular lesions of violet-brown colour, pruritic, located on the right posterior thoracic region diagnosed clinically as seborrheic keratosis.⁷ However, in such patient those lesions seem to be disposed in a dermatomeric fashion

and do not exhibit the typical clinical hyperkeratotic surface and stuck on waxy aspect,^{2,7} thus in our view, the lesions should be more likely reinterpreted as zosteriform skin metastasis from melanoma.⁸

In this brief literature review of melanoma-associated LTS, the median age of patients (71 years-old, 3 males and 2 females) is in line with previous data of LTS with internal malignancy.³ Remarkably, median Breslow thickness resulted 2.45 mm, two cases were of unknown primary

and 3/5 patients had metastasis at the time of diagnosis (Table 1). Although the number of cases reported so far is very low, we observed a tendency to thick tumors and advanced diseases. In our case, the diagnosis of a thick nodular melanoma was incidentally made as well. The clinical scenario of LTS may be particularly challenging leading to a diagnostic delay of melanoma for two main reasons: i) multiple and large seborrheic keratoses may hide the melanocytic neoplasm beneath; and ii) a melanoma may sometimes clinically mimic a seborrheic keratosis. Recently it has been demonstrated that dermatoscopy improves the detection of seborrheic keratosis-like melanomas, increasing significantly the sensitivity.⁹ In our patient, the identification of atypical dermatoscopic features reinforced the clinical diagnosis of melanoma, which was further confirmed by characteristic histopathologic findings.

In conclusion, we highlight that physicians should be aware of the LTS sign for its significant clinical value. Although the association between melanoma and LTS is very rare, an accurate total body skin examination with the aid of dermatoscopy should be recommended in patients with sudden onset or increase in number and size of seborrheic keratoses, in order to early diagnose and treat a melanoma that is hiding among them.

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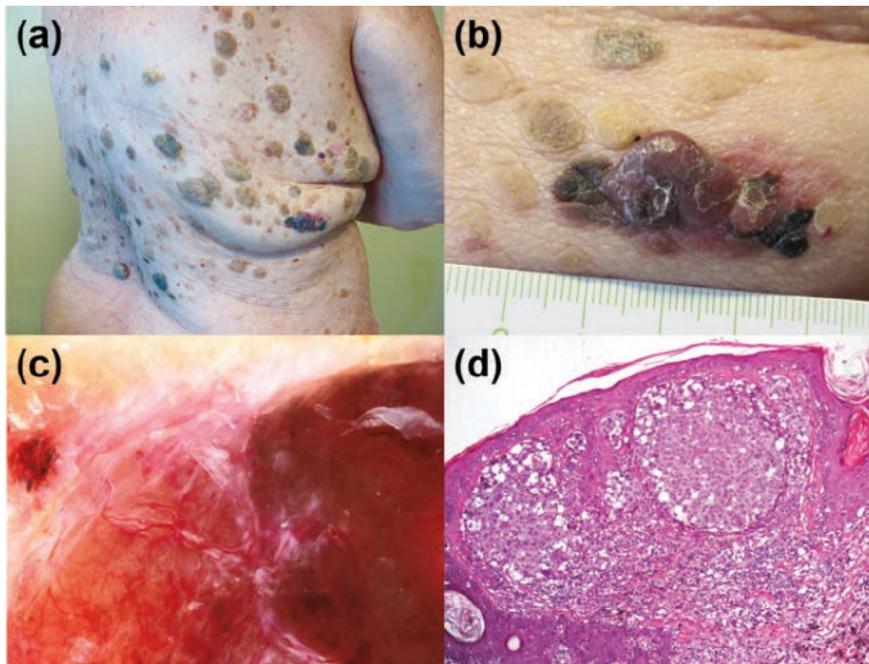


Figure 1. a) Multiple seborrheic keratoses with a Christmas tree pattern located on the trunk of 80 years-old women. b) Clinical detail of a nodular lesion on the right flank partly pigmented and intermingled between seborrheic keratoses. c) Dermatoscopy disclosing polymorphous vessels and irregular blotches. d) Histology showing a detail of the invasive melanoma and seborrheic keratosis-like features of the epidermis. (Hematoxylin and eosin stain; original magnification x100).

Table 1. Cases reporting an association between melanoma and Leser-Trélat Sign (LTS).

Author	Age, sex	Primary melanoma (Breslow thickness and site)	Metastatic involvement	Leser-Trélat Sign (site, pattern)	Other paraneoplastic signs
Ellis DL <i>et al.</i> (1987) ⁴	454 years old man	Superficial spreading melanoma, 0.75 mm, lower back	No evidence after 16 months of follow-up	Upper chest and back,	Acanthosis nigricans, multiple acrochordons
Fanti PA <i>et al.</i> (1989) ⁵	69 years old man	Nodular melanoma, 2.16 mm, left thigh	Regional (inguinal) lymph nodes	Trunk, thighs, Christmas tree pattern	-
Siedek V <i>et al.</i> (2009) ⁶	82 years old man	Unknown	Parotid gland, skin (forehead) and cervical lymph nodes	Head and trunk, Christmas tree pattern	-
Pereira R. <i>et al.</i> (2019) ⁷	71 years old Women	Unknown	Pleura, lymph nodes (axilla), skin (?)	Right posterior thoracic region (zosteriform?)	-
Our case	80 years old women	Superficial spreading melanoma, 4,5 mm, right flank	No evidence after 52 months of follow up	Trunk (Christmas tree pattern), head and neck	-

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