Leser-Trélat Sign Presentation with Mediastinal Squamous Cell Carcinoma

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Abstract

The sign of Leser-Trélat is a rare dermatological manifestation of a paraneoplastic syndrome. It is characterized by an abrupt onset of numerous seborrheic keratoses in association with adenocarcinomas and lymphoproliferative disorders. Herein, we review a case of a 59-year-old female with the classic cutaneous presentation of the sign Leser-Trélat. Our patient's cutaneous expression coincided with a mediastinal squamous cell carcinoma.

Introduction

European surgeons Edmund Leser and Ulysse Trélat first independently associated internal malignancies with these skin lesions in 1890. In addition, Eugen Holländer first associated “verrucae seborrhoeicae” with internal malignancy in 1901. Leser-Trélat sign is a rare dermatological manifestation of a paraneoplastic syndrome characterized by an abrupt onset of numerous seborrheic keratoses. Associated symptoms often include pruritus and velvety, lichenified skin characteristic of acanthosis nigricans. Typically, the sign of Leser-Trélat presents in the elderly, and it has been associated with adenocarcinoma as well as lymphoproliferative disorders. The adenocarcinoma most frequently originates from the colon, breast, or stomach. Although potentially paraneoplastic, the eruptive lesions of Leser-Trélat occur in malignancies of other organs and in non-malignant ailments. The validity of this dermatological phenomena has been challenged due to the fact that seborrheic keratoses and neoplasms are both common in the elderly population.

The exact pathogenesis of Leser-Trélat sign is unknown; however, it is theorized that it may be related to an overproduction of growth hormone, epidermal growth factor (EGF) and transforming growth factor alpha (α-TGF). The latter is not found in normal adult cells, but in fetal cells and transformed cell lines. Both EGF and α-TGF bind to the EGF receptor found in keratinocytes, especially in actively proliferating cells of the basal layer of normal epidermis. Normally EGF receptors are present mainly on basal keratinocytes and decrease as keratinocytes differentiate in the upper epidermal layers. However, acanthosis nigricans, seborrheic keratoses, and acrochordons contain a dense population of receptors in all layers of the epidermis except for the stratum corneum. The similarity in hyperactivity of these growth factors during cutaneous malignancies and cutaneous paraneoplastic syndromes could provide the link between the expression of Leser-Trélat sign and squamous cell carcinoma. In many reported cases, the removal of the malignancy greatly reduced the appearance of the Leser-Trélat sign.

Case Presentation

A 59-year-old Caucasian woman, Fitzpatrick type III, with history of mediastinal squamous cell carcinoma, Ehlers-Danlos syndrome, molar pregnancy, COPD, osteoarthritis, chronic fatigue and smoking, presented with several lesions of concern on her back and submammary region. The lesions were numerous, stuck-on plaques that were waxy brown to dark brown in coloration (Figures 1, 2). Dermoscopically, they presented with comedone-like openings, milia-like cysts, and bulbous projections. The lesions were first noted nine years prior and appeared rapidly, but the patient became concerned with a more recent development of plaques. The patient could not correlate the exact onset of her seborrheic keratoses with her malignancy, although she denied significant keratotic lesions prior to her diagnosis. The patient denied change in size and color but admitted to intermittent pruritus. In addition, she displayed generalized hair thinning and non-scarring alopecia of the scalp. On remaining physical exam, the patient appeared generally thin, with aphasia, but no palpable lymphadenopathy was appreciated.

Two lesions suspicious for atypical processes were biopsied, by shave removal, from the mid back and left submammary regions. The biopsy revealed findings characteristic of seborrheic keratoses. Several other lesions on the back and submammary region suspicious for irritated benign growths were treated with cryotherapy.

The patient initially sought medical assistance in September 2012 for aphasia. A CT of the neck and chest noted a hypodense 0.8 cm nodule in the lower left lobe of the thyroid and a 3.8 cm left anterosuperior mediastinal mass and adenopathy. Biopsies of both lesions determined that the thyroid nodule was benign; however, the mediastinal mass was consistent with squamous cell carcinoma (TxN2M0, stage IIIA). Mass effect caused aphasia secondary to left vocal cord paralysis resulting from recurrent laryngeal nerve involvement.

The patient was treated with stereotactic body radiation therapy (SBRT), and the patient underwent CyberKnife radiosurgery in five fractions. The patient was not offered chemoradiation therapy nor neoadjuvant chemotherapy. In May 2013, a PET scan showed the mediastinal mass had reduced to 2.5 cm in size.

The follow-up PET scan on November 2013 noted a hypermetabolic lesion in the region of the aortic arch on the mediastinal mass, with no change from prior imaging. In addition, the patient had an elevated CEA of 11.52 ng/mL. CT of the chest in February 2014 demonstrated a gradual increase of the mediastinal mass in the left mid lung zone that measured 3.5 cm x 2.5 cm. A stable subcentimetric nodular density along the lateral aspect of the left major fissure was noted, as well. No abnormal hilar or mediastinal adenopathy were noted, but it was subsequently determined that the malignancy was unresectable.

A CT-guided biopsy and Theros CancerType ID noted a persistent primary keratinizing squamous cell carcinoma of the lung, with necrosis and calcifications. Further evaluation included whole-body radiological imaging, and results showed no additional areas of focus or abnormality. The patient denied palliative chemotherapy and elected to be closely monitored.

Discussion

We report a case with a characteristic presentation of Leser-Trélat sign associated with mediastinal squamous cell carcinoma. Although our patient's case has an unusual origin, there are several cases of Leser-Trélat sign in the literature with similar features. Heaphy et al. presented a case of a 58-year-old woman who was not only similar in age to our patient but also experienced fatigue and had a smoking history. However, in their case, the Leser-Trélat sign was caused by adenocarcinoma of the lung, which is commonly associated with...
this cutaneous manifestation. The similarities in presentation support our conclusion that our patient’s dermatologic manifestation is the sign of Leser-Trélat. In both cases, the patients are not elderly, and therefore the onset of seborrheic keratosis and malignancy cannot be attributed to age alone. In addition, Mukherjee et al. described a case of squamous cell carcinoma of the lung with a paraneoplastic presentation. However, in that case, the paraneoplastic type was acanthosis nigricans.

The variation in ailments that present with eruptive seborrheic keratosis makes the criteria for Leser-Trélat sign a controversial topic in the medical community. Several studies have been conducted that analyze the ailments of patients who present with eruptive seborrheic keratosis and compare them with a control group. These case-control studies reveal no significant association of specific internal malignancies with eruptive seborrheic keratosis versus other ailments. Conclusion

Although widely debated and disputed in multiple studies, there continues to be a large database of literature validating the sign of Leser-Trélat as a paraneoplastic syndrome. In order to gain a better understanding of this condition, it is essential to continue documenting all possible presentations. Regardless of cause, it is critical to be aware of the presentation of the sign of Leser-Trélat and its implication of malignancies, internal or cutaneous.

References