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Eruptive inflamed seborrheic keratoses in the setting of endometrial adenocarcinoma☆

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ABSTRACT

Eruptive seborrheic keratoses have been reported as a rare paraneoplastic dermatosis in the setting of internal malignancy, particularly that of the digestive tract. This case illustrates a patient with a family history of gastric cancer who presented with an acute eruption of inflamed pruritic seborrheic keratoses with annular and gyrate erythema, and was found to have endometrial adenocarcinoma. The inflammatory cutaneous eruption resolved shortly after surgical removal of the dysplastic uterine tissue. This case demonstrates an example of a common gynecological malignancy presenting in an uncommon way; in the absence of uterine bleeding, the patient's skin manifestations in the form of a paraneoplastic dermatosis prompted timely diagnosis. Thus this case serves to raise awareness of cutaneous manifestations of a women's health issue, in which early detection can impact health outcomes.

Introduction

The Sign of Leser-Trelat historically has been characterized as the sudden eruption of numerous seborrheic keratoses and considered an ominous sign of internal malignancy, as it is classically described before the diagnosis of malignancy. However, eruptions have also been reported concurrently with and after diagnosis. The seborrheic keratoses themselves are benign and, in some cases, have been reported to resolve with treatment of the underlying malignancy. The mechanism of this phenomenon has been ascribed to secreted cytokines and growth factors from tumors (e.g., elevated epidermal growth factor receptor [EGF-R]-mediated signaling) leading to development of seborrheic keratoses (Yamamoto, 2013). The malignancies classically implicated in the setting of Sign of Leser-Trelat are gastric adenocarcinoma and other tumors of the digestive tract; additionally, other classes of malignant tumors, such as lymphoma and breast cancers, have been cited in association with the condition (Husain et al., 2013). Rare cases of gynecologic cancers (e.g., uterine leiomyosarcoma and ovarian adenocarcinoma) have been associated with the Sign of Leser-Trelat (Abakka et al., 2013; Holguin et al., 1986). In general, with the exception of hypercalcemia and disseminated intravascular coagulation, paraneoplastic syndromes are not classically associated with gynecologic cancer (Ashour et al., 1997). This case illustrates eruptive seborrheic keratoses with atypical annular and gyrate erythema that occurred in the setting of endometrial adenocarcinoma, which resolved upon surgical removal of the malignant uterine tissue (Lacey and Chia, 2009).

Case report

A 61-year-old post-menopausal Caucasian female presented for an initial evaluation of numerous intensely pruritic scaly spots on her trunk. She reported that similar lesions had been diagnosed as seborrheic keratoses by another dermatologist; however, in the month before presentation in our clinic, the number of lesions on her trunk had dramatically increased. The patient was able to distinguish new lesions from her existing seborrheic keratoses because they were constantly pruritic and many had coalescing and concentric rings of erythema around them. The patient denied the application of any potential irritants to the pigmented plaques. She denied any history of cancer, but upon inquiry regarding her family history, she reported that her father had died of gastric cancer. The patient denied any constitutional symptoms or any uterine bleeding, and complete review of symptoms was significant only for depression. Her past medical history was significant for squamous cell carcinoma, uterine fibroids, dysmenorrhea, granuloma annulare (GA), and benign pulmonary nodules. Notably, she previously denied active GA lesions for years. She was a previous smoker, but had quit 3 years previously. Total body skin examination was notable for numerous brown papules that appeared to be attached to the surface of her skin as well as plaques consistent with inflamed seborrheic keratoses with surrounding annular and gyrate erythema with scaling at edges of rings—some of which were concentric and had the appearance of targets—on the face, neck, and trunk. There were no signs of acanthosis nigricans. Biopsy of an erythematous lesions surrounding a seborrheic

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keratosis on her trunk revealed multifocal intraepidermal Langerhans cell microabscesses with eczematous dermatitis and superficial perivascular infiltrate containing scattered histiocytes and without granulomatous inflammation.

This presentation of atypical, acute eruption of seborrheic keratoses and family history of gastric cancer, as well as the fact the patient had not yet had her age-appropriate cancer screenings, prompted concern that the eruption was a marker of internal malignancy, and screenings for malignancy were recommended. She initially declined colonoscopy and other first-line screenings and insisted that she would only accept a positron emission tomography scan, which highlighted focal intense uptake in the uterus; based on this, transvaginal ultrasound was recommended and revealed abnormally thickened endometrium. The patient later consented to gastrointestinal screenings. Endoscopy revealed no signs of malignancy in the esophagus, stomach, or duodenum. Colonoscopy revealed two benign polyps in the sigmoid colon. Pancreatic screening labs were negative. She then underwent endometrial biopsy, which revealed focal complex atypical hyperplasia. Dilatation and curettage also revealed complex focal atypical hyperplasia, which prompted the gynecology team to perform a hysterectomy, and the postoperative diagnosis was endometrial adenocarcinoma. Because of the significant, distressing pruritus associated with the lesions, the patient was treated symptomatically during the work-up period. Symptomatic treatment with cryotherapy, phototherapy, and topical steroids yielded some partial improvement; however, the patient experienced dramatic clearance of the erythematous skin lesions and marked improvement in her pruritus after surgical removal of the abnormal uterine tissue. At present, after the hysterectomy, she has developed no new seborrheic keratoses and is asymptomatic.

Discussion

Although seborrheic keratoses are a common benign skin finding in elderly people, a rapid and intensely pruritic eruption warrants suspicion for occult internal malignancy. Special care should be taken for patients with first-degree relatives of gastric cancer because it is the most commonly implicated cancer in paraneoplastic dermatoses (e.g., the Sign of Leser-Trelat). The marked annular, gyrate, and targetoid erythema associated with seborrheic keratoses seen in our patient is not typical for the classic sign of Leser-Trelat. The cause of annular erythema remains unclear. It is possible that this unusual morphology represents two coexistant paraneoplastic dermatoses similar to those seen in cases of prostate cancer and renal angiosarcoma (Da Rosa et al., 2009; Rubegni et al., 2014) The possibility that the annular erythematous plaques could be a reactive granulomatous process was also considered, given the patient's history of GA. However, upon consultation with the pathologist, it was clarified that no granulomatous inflammation was seen. The notable presence of high numbers of Langerhans cells seen on microscopy may have signified abnormal antigen presentation in these lesions, which also supports a paraneoplastic process. It was suspected that cytokines and hormone stimuli associated with the endometrial adenocarcinoma might have triggered the paraneoplastic dermatosis. As in this patient's case, cutaneous symptoms may resolve with treatment of the underlying condition.

This case demonstrates a common gynecological cancer presenting with a paraneoplastic dermatosis rather than the classical signs of uterine bleeding, and serves to raise awareness of cutaneous manifestations as markers of malignancy in a women's health issue in which early detection can affect health outcomes.

Clinical pearls

- A sudden eruption of numerous seborrheic keratoses should prompt a malignancy work-up in patients with risk factors and those who have not undergone age-appropriate cancer screenings.
- Although gastric adenocarcinoma is the malignancy most commonly associated with the Sign of Leser-Trelat, the possible association of other malignancies may necessitate a thorough work-up for internal malignancy.

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