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Eruptive seborrheic keratoses associated with adalimumab use

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Abstract

Background: Seborrheic keratoses are common, benign cutaneous growths, however in rare situations they can acutely erupt in large numbers. Eruptive seborrheic keratoses can be associated with internal malignancy (sign of Leser-Trelat), but may also appear in conjunction with inflammatory dermatoses and adverse drug reactions.

Main observation: A 71-year-old Caucasian man presented with acute onset of a pruritic, burning papular erythematous rash on his chest, upper extremities and lower extremities after a routine adalimumab injection for rheumatoid arthritis. Two skin biopsies obtained showed findings diagnostic of seborrheic keratoses. Spontaneous resolution of the diffuse eruptive seborrheic keratoses was achieved within 3 months of discontinuing adalimumab therapy.

Conclusions: We believe the development of eruptive seborrheic keratoses due to adalimumab therapy is rare, and because our patient responded promptly to discontinuation of the drug we suggest this should be the preferred course of action in future cases. (*J Dermatol Case Rep.* 2013; 7(2): 60-63)

Introduction

Seborrheic keratoses are common, benign cutaneous growths that generally increase in frequency with age and sun exposure.[1] In certain situations, however, they can acutely erupt in large numbers, a condition known as eruptive seborrheic keratoses. Eruptive seborrheic keratoses can be a sign of internal malignancy (sign of Leser-Trelat), or associated with noncancerous conditions such as inflammatory dermatoses and drug reactions.[2-7] We present an unusual case of eruptive seborrheic keratoses associated with adalimumab (Humira) use, which to our knowledge, has not been reported before.

Case Report

A 71-year-old Caucasian man with a history of rheumatoid arthritis was seen in the dermatology department complaining of acute onset of a pruritic rash on his chest, upper extremities and lower extremities. The patient had been receiving biweekly adalimumab injections for approximately 2 months without complication until shortly after his 5th injection when he developed a papular erythematous rash on his chest with satellite patches on his extremities. He complained of itching and burning at the sites of the rash, but denied fever, chills, night sweats, weight loss, previous occurrences of a similar rash, or recent medication changes other than the initiation of adalimumab.

On physical examination, there were numerous skin colored waxy, stuck-on appearing papules with halos of erythema. These newly developed lesions covered his torso, bilateral lower extremities all the way to the dorsum of both feet, and bilateral upper extremities, but spared the head, buttocks, groin, and hands. The few larger, pigmented, previously established seborrheic keratoses were uninvolved.

A full work-up revealed no obvious cause for the outbreak. The following investigations were performed and found to be within normal limits: complete blood count, urea and electrolytes, liver function tests, C reactive protein, extractable nuclear antigen antibodies (ENA) panel, C3 and C4 complement, double stranded DNA antibodies, chest X-ray, colonoscopy, and chest/abdomen/pelvis CT. The rheumatoid factor was only slightly above normal limits at 17.0 IU/mL

and antinuclear antibody elevated to 15 IU/mL at their respective peaks. Two skin biopsies obtained showed findings diagnostic of seborrheic keratoses (Fig. 2). Though wart was considered in the differential diagnosis, other than the papillomatous surface, no other diagnostic features were identified. During the course of treatment, the patient developed erythroderma and the possibility of mycosis fungoides was raised, however definitive histologic features were not identified. Only one of three biopsies submitted for T-cell receptor clonality studies by PCR showed a clonal T cell population, which was insufficient for a diagnosis of mycosis fungoides.[8]

A short course of oral prednisone and topical clobetasol ointment provided little relief. The patient developed more confluent and intense erythema, and extensive flaking over the areas of erythema. One month after presentation, the adalimumab was discontinued (after a total treatment course of approximately 3 months). The eruptive seborrheic keratoses slowly receded and within 3 months of medication cessation (4 months after onset) they completely involuted and the condition was resolved. The evolution of the patient's lesions is displayed in Figure 1.

Discussion

The phenomenon of eruptive seborrheic keratoses was first described in literature by Dr. Murray Williams in 1956, who documented four cases of multiple seborrheic keratosis-like lesions appearing on patients with erythroderma secondary to eczematous dermatoses.[2] The lesions were deemed "acanthomata" and similar to classic seborrheic keratoses in almost every aspect except their transient nature. In all four cases, the lesions spontaneously resolved within six months of the erythroderma resolution.

Since that time, other cases documenting eruptive seborrheic keratoses in connection with erythroderma have been published, with associated inflammatory dermatoses such as

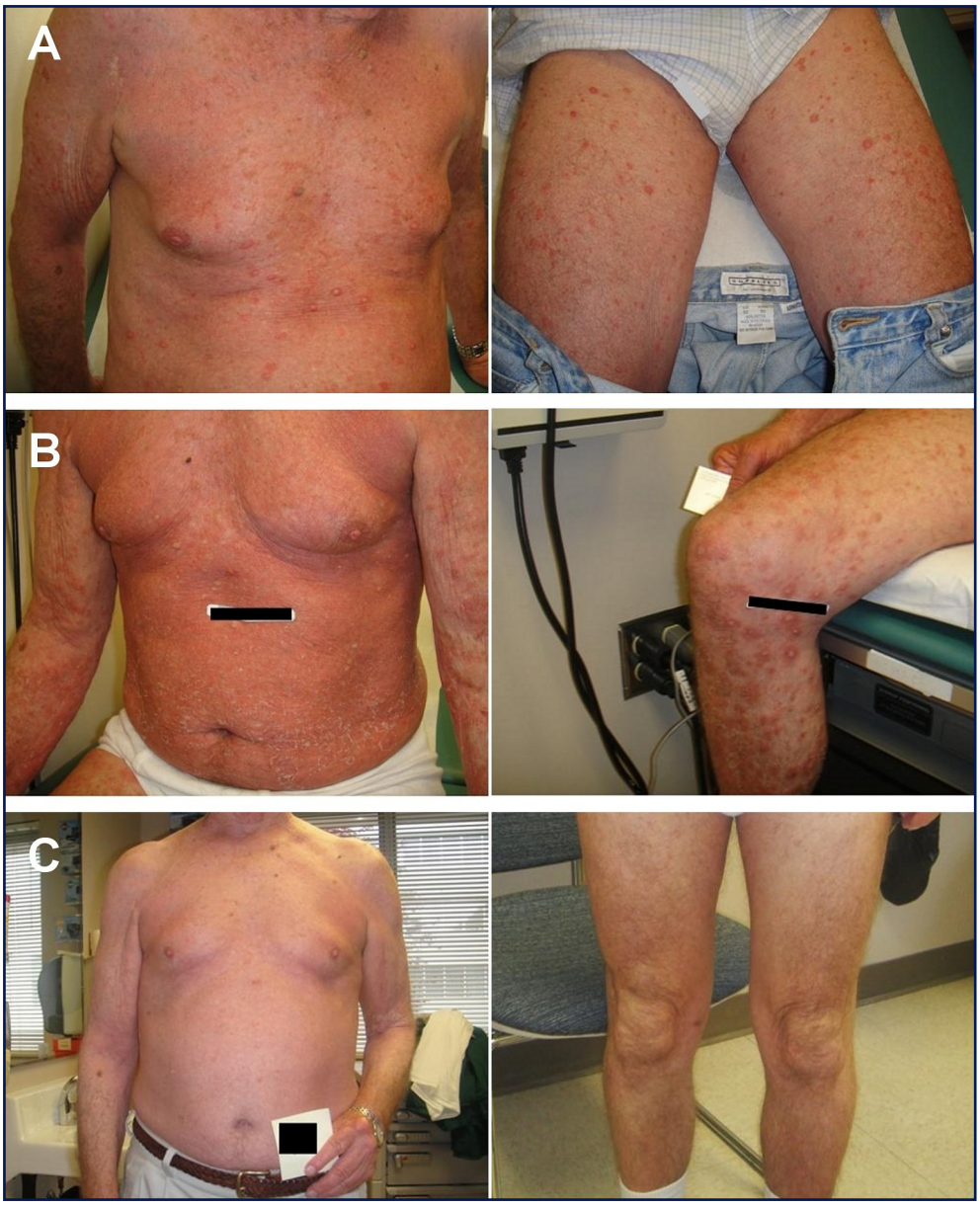

Figure 1

Evolution of eruptive seborrheic keratoses due to adalimumab use. (A) Initial eruption, (B) 2 months after initial eruption, (C) 4 months after initial eruption (3 months after discontinuation of adalimumab).

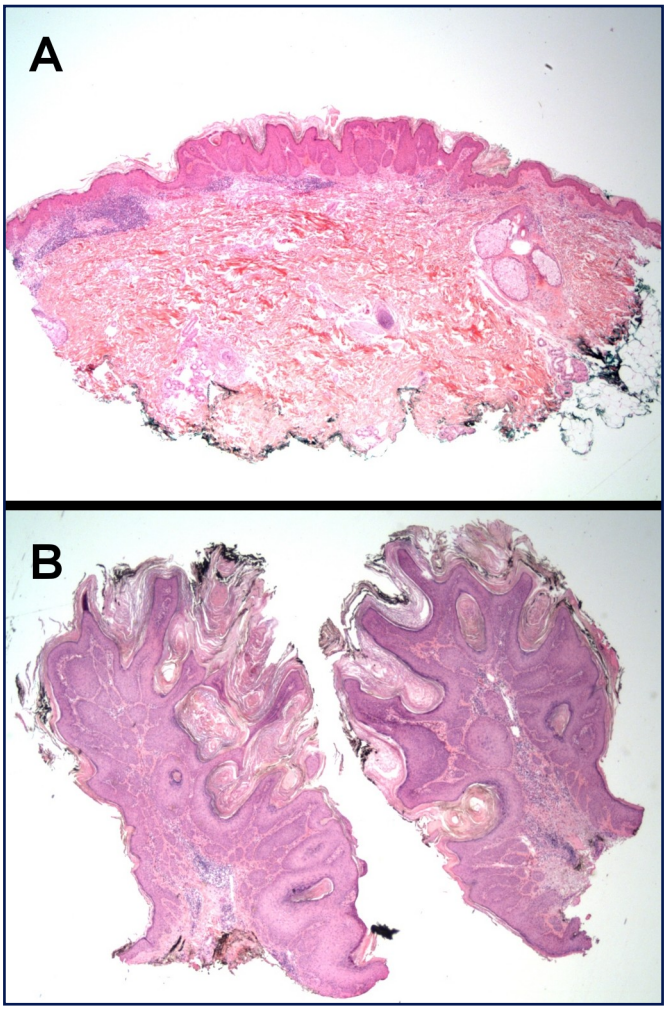

Figure 2

Seborrheic keratoses. Hematoxylin-eosin stained sections showing a papillomatous epidermis with irregular acanthosis and overlying hyperkeratosis. Pseudo-horn cysts are rare. The superficial dermis shows a predominantly perivascular infiltrate composed of lymphocytes, histiocytes and rare mast cells. Eosinophils are not identified. Example of a flatter lesion (A) and one that was more polypoid (B).

pityriasis rubra pilaris,[3,4] psoriasis,[5] eczema,[2,9] and drug eruptions.[6] In these cases, the eruptive seborrheic keratoses developed either in the presence of erythroderma or after its appearance. Resolution of the seborrheic keratoses was often achieved with treatment of the underlying condition rather than any specific treatment for the keratoses.[3,4,6]

The case presented here is unique because this patient's eruption began as discrete eruptive seborrheic keratoses surrounded by a halo of erythema. The erythema progressed after the initial eruptions to later become confluent in areas, especially his torso. This presentation differs from published literature in that the appearance of the eruptive seborrheic keratoses preceded the erthroderma instead of developing in parallel or after its appearance. However, similar to previous reports, the eruption spontaneously resolved without any specific treatment when the causative agent, adalimumab, was discontinued.

The eruption of multiple seborrheic keratoses has also been associated with internal malignancy, a phenomenon known as the sign of Leser-Trelat. However, the validity of this paraneoplastic sign has been questioned in literature and still remains a matter of debate.[10] In the case of our patient, we conducted an extensive laboratory and imaging work up and ruled out malignancy as a cause of the eruption.

Conclusions

We report this case as a possible adverse reaction to adalimumab. To the best of our knowledge, this is the first documented case in literature of eruptive seborrheic keratoses associated with adalimumab use. A previous publication reported 3 incidents of seborrheic keratoses associated with TNF alpha blocking therapy, however details regarding the associated drug (infliximab, etanercept or adalimumab), temporal association, and clinical course were not published.[7] We believe the development of eruptive seborrheic keratoses due to adalimumab therapy is rare. Our patient responded promptly to discontinuation of the drug and we suggest this should be the preferred course of action in future cases.

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References

1. Yeatman JM, Kilkenny M, Marks R. The prevalence of seborrhoeic keratoses in an Australian population: does exposure to sunlight play a part in the frequency? *Br J Dermatol.* 1997; 137: 411-414. PMID: 9349339.
2. Williams MG. Acanthomata appearing after eczema. *Br J Dermatol.* 1956; 68: 268-271. PMID: 13342345.
3. Gleeson CM, Chan I, Griffiths WA, Bunker CB. Eruptive seborrhoeic keratoses associated with erythrodermic pityriasis rubra pilaris. *J Eur Acad Dermatol Venereol.* 2009; 23: 217-218. PMID: 18482315.
4. Schwengle LE, Rampen FH. Eruptive seborrheic keratoses associated with erythrodermic pityriasis rubra pilaris. *Acta Derm Venereol.* 1988; 68: 443-445. PMID: 2461032.
5. Vestergaard ME, Kossard S, Murrell DF. Seborrhoeic keratoses appearing in sites of previous psoriasis plaques during treatment with efalizumab. *Clin Exp Dermatol.* 2009; 34: e564-e566. PMID: 19508488.
6. Flugman SL, McClain SA, Clark RA. Transient eruptive seborrheic keratoses associated with erythrodermic psoriasis and erythrodermic drug eruption: report of two cases. *J Am Acad Dermatol.* 2001; 45: S212-S214. PMID: 11712062.
7. Flendrie M, Vissers WH, Creemers MC, de Jong EM, van de Kerkhof PC, van Riel PL. Dermatological conditions during TNF-alpha blocking therapy in patients with rheumatoid arthritis: a prospective study. *Arthritis Res Ther.* 2005; 7: R666-R676. PMID: 15899052.

8. Thurber SE, Zhang B, Kim YH, Schrijver I, Zehnder J, Kohler S. T-cell clonality analysis in biopsy specimens from two different skin sites shows high specificity in the diagnosis of patients with suggested mycosis fungoides. *J Am Acad Dermatol*. 2007; 57: 782-790. PMID: 17646032.

9. Barrière H, Litoux P, Bureau B, Welin J. Acanthomes post-eczema. *Bull Soc Fr Dermatol Syphiligr*. 1972; 79: 555-557. PMID: 4267686.

10. Fink AM, Filz D, Krajnik G, Jurecka W, Ludwig H, Steiner A. Seborrheic keratoses in patients with internal malignancies: a case-control study with prospective accrual of patients. *J Eur Acad Dermatol Venereol*. 2009; 23: 1316-1319. PMID: 19309432.