# Spontaneous Apparent Clinical Resolution with Histologic Persistence of a Case of Extramammary Paget's Disease: Response to Topical 5-Fluorouracil

L.F. Del Castillo, MD, Toledo, Spain
C. Garcia, MD, Toledo, Spain
C. Schoendorff, MD, Toledo, Spain
J.F. Garcia, MD, Toledo, Spain
L.M. Torres, MD, Toledo, Spain
D. Garcia Almagro, MD, Toledo, Spain

*An 86-year-old woman presented with a 3-year history of an erythematous axillary lesion, which was histologically confirmed to be extramammary Paget's disease (EMPD) confined to the epidermis and adnexa. Surprisingly, spontaneous clinical regression occurred in the lesion, but Paget's cells persisted within the epidermis and adnexa on histologic examination. One year of intermittent topical chemotherapy with 5-fluorouracil resulted in ulcers that were interpreted as EMPD and completely excised. Histologic examination showed a complete absence of Paget's cells. To our knowledge, only one previous report investigated apparent spontaneous clinical resolution with histologic persistence of EMPD. We emphasize that topical 5-fluorouracil cannot be considered a safe treatment modality for EMPD, but it may be useful in certain cases in which the extent of the lesions, or the general condition of the patient, advise against surgery or radiotherapy.*

Extramammary Paget's disease (EMPD) is a relatively rare disorder usually found in cutaneous apocrine gland-bearing regions. The majority of cases reflect a primary intraepithelial adenocarcinoma. Some cases reflect epidermotropic spread from a sweat gland neoplasm or carcinoma of an adjacent organ.[1]

From the Dermatology and Pathology Departments, "Virgen de la Salud" Hospital, Toledo, Spain.
REPRINT REQUESTS to C/Alameda, 21, 45400, Mora, Toledo, Spain (Dr. Del Castillo).

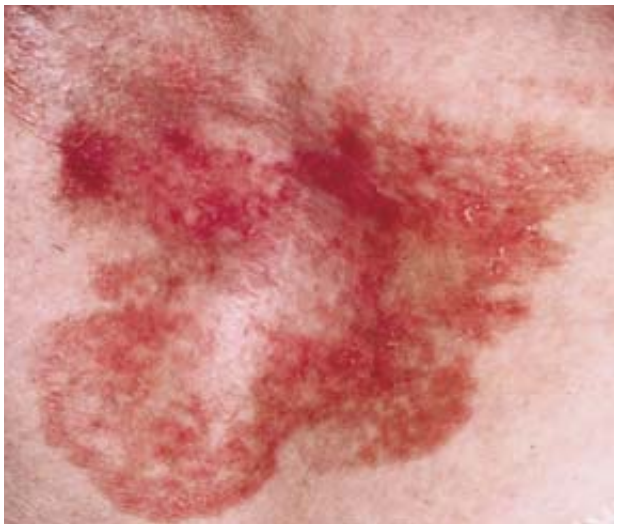

**FIGURE 1.** Initial clinical aspect of the lesion.

## Case Report

An 86-year-old woman had an erythematous and pruriginous plaque on her right axilla for 3 years. She had applied multiple creams containing corticosteroids, but no improvement was observed. The plaque was erythematous, slightly scaly, and delineated by lobulated margins (Figure 1). Complete anamnesis and physical examination did not reveal remarkable findings. Fungal cultures gave negative results.

Histologic examination of a cutaneous biopsy specimen permitted the diagnosis of EMPD; abundant large cells with pale cytoplasm, distributed singly and

in groups throughout the epidermis and epithelia of the adnexa, were noted. The upper dermis showed a dense inflammatory infiltration consisting of small round cells and plasma cells (Figure 2). The cytoplasm of the large cells was positive on periodic acid–Schiff stain and, on immunohistochemical investigation, stained positive for carcinoembryonic antigen and negative for S-100.

The patient was then referred for complete excision of the lesion. Excision was not performed, however, because the lesion was clinically undetectable when the surgeon saw the patient 1 month after the diagnosis.

The patient returned 4 months later. Only mild hypopigmentation was remarkable in the aspect of the axilla (Figure 3). Four additional biopsies of the margins of the lesion were obtained at that time. In two specimens, hematoxylin-eosin staining showed the persistence of Paget's cells within the epidermis and adnexa.

Treatment with topical 5-fluorouracil (5-FU) was begun to highlight the EMPD area. The patient then irregularly applied this treatment, with irregular frequency and without occlusion, during 1 year. At this time, evident ulcers could be seen at the treated area (Figure 4). Such ulcers were suspected to represent clinical highlights of EMPD and the patient was sent for complete excision of the ulcerated area, without previous confirmatory biopsy.

Histologic examination of the excised area revealed only ulceration (granulation tissue and chronic inflammation), without evidence of Paget's cells in either the epidermis or the adnexa. The patient has refused follow-up.

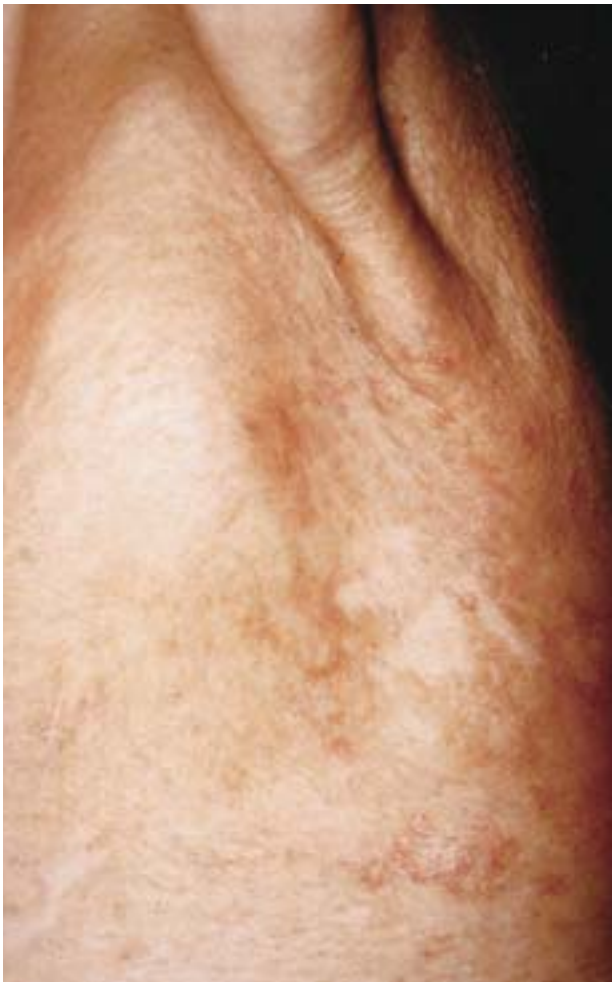

**FIGURE 2.** EMPD (H&E; original magnification, × 400).

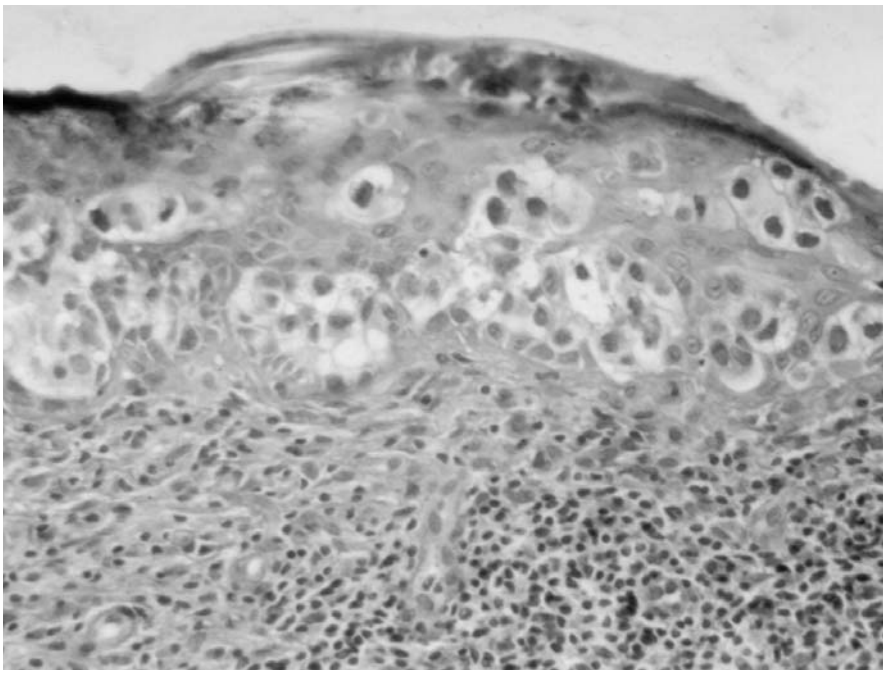

**FIGURE 3.** Spontaneous clinical regression (5 months later).

**FIGURE 4.** Ulcers after topical chemotherapy with 5-FU.

## Comments

The unusual feature of this case of EMPD was the spontaneous clinical change in the aspect of the lesion, simulating normal skin, but with histologic persistence of Paget's cells. As far as we know, such behavior has been described for EMPD in only one previous report.[2] Imakado *et al*[2] reported two cases of genital Paget's disease with bilateral axillary involvement in two men. In both cases, the axillary lesions changed day by day, becoming less pronounced and simulating normal skin. It was, according to the authors, a confusing phenomenon not previously reported and of unknown cause, probably related to the instability of the inflammatory cell infiltration. Both patients were surgically treated and were found free of disease, with no evidence of recurrence or metastasis 4 years after surgery.

Topical 5-FU has been shown to have a selective toxicity in premalignant and malignant epithelial lesions. The inflammatory response produced by 5-FU can help to delineate the extent of cutaneous involvement with EMPD as described by Eliezri *et al*.[3] However, topical 5-FU is not generally recommended as a unique therapy for EMPD. Theoretically, it should not eliminate Paget's cells of the adnexa, and persistence or recurrence would be the rule.[4] Arensmeier *et al*[5] reported a case of genital and perigenital EMPD in an 84-year-old man, in which topical chemotherapy with 5-FU, twice daily for 1 month, maintained the patient free of lesions, clinically and histologically, for 1 year. At that moment, a local recurrence was again treated with topical 5-FU. The patient died later of a myocardial infarction, and postmortem examination detected neither malignancy in internal organs nor Paget's cells at the area treated with 5-FU.

In our case, topical 5-FU was utilized to highlight EMPD, and the patient intermittently applied it during 1 year. The resulting ulcers were interpreted as a clinical highlight of EMPD, and the area was surgically removed without previous confirmatory biopsy. There were no signs of EMPD on postsurgical histologic examination.

We emphasize that, although topical 5-FU is a hazardous treatment modality since it can give the false impression that the lesion has resolved completely, it can be useful in cases of EMPD in which the extent of the lesions, or the general condition of the patient, advise against surgery or radiotherapy.

## REFERENCES


1. Heymann WR: Extramammary Paget's disease. *Clin Dermatol* 11: 83-87, 1993.
2. Imakado S, Abe M, Okuno T, *et al*: Two cases of genital Paget's disease with bilateral axillary involvement: mutability of axillary lesions. *Arch Dermatol* 127: 1243, 1991.
3. Eliezri YD, Silvers DN, Horan DB: Role of preoperative topical 5-fluorouracil in preparation for Mohs micrographic surgery of extramammary Paget's disease. *J Am Acad Dermatol* 17: 497-505, 1987.
4. Goette DK: Topical chemotherapy with 5-fluorouracil. A review. *J Am Acad Dermatol* 4: 633-649, 1981.
5. Arensmeier M, Theuring U, Franke I, *et al*: Topisch Therapie des extramammõren morbus Paget. *Hautarzt* 45: 780-782, 1994.