

Extramammary Paget's Disease Associated with Autoimmune Hemolytic Anemia

Sir,

Extramammary Paget's disease (EMPD) usually affects elderly patients. The tumors often recur locally even if the patients are treated sufficiently with surgery and/or irradiation (1-4). We here report a patient suffering from local recurrence of EMPD, who later developed autoimmune hemolytic anemia due to warm-acting antibodies.

CASE REPORT

A 79-year-old man was referred to us in April 1989 with a 10-year history of a red rash affecting his genitalia. On examination, there was a well-defined erythematous plaque on the shaft of the penis and the adjacent scrotum. Histology of skin biopsies showed that the epidermis was colonized by large, pale cells with a voluminous cytoplasm, which was consistent with the features of EMPD. The adjacent skin did not show any pagetoid dermal invasion, and there was no evidence of a cutaneous adnexal carcinoma. Other investigations excluded the presence of internal malignancy. Laboratory evaluations showed a slight degree of anemia (erythrocytes, 366×10^4 ; hemoglobin, 11.3 g/dl; and hematocrit, 34.8%). The results of the following studies were normal: antinuclear antibody, rheumatoid factor, erythrocyte sedimentation rate, and C-reactive protein. He received radiotherapy using electrons (total 50 Gy) for EMPD, because he was judged to be a high-risk case for general anesthesia due to his severe arrhythmia. However, EMPD recurred 7 months later. The erythematous lesion remained stationary even after the following treatments: additional radiation of 20 Gy, repeated topical applications of 5-fluorouracil under occlusion, repeated local injections of 3×10^6 IU of beta-interferon and repeated cryotherapy using liquid nitrogen.

From December 1994, his erythrocyte count decreased rapidly, and he became increasingly pale and fatigued. In July 1995, examination of the blood revealed an erythrocyte count of 190×10^4 , a hemoglobin count of 6.3 g/dl, and a hematocrit count of 18.9%. The myelogram showed erythroid hyperplasia with a granulocytic erythroid ratio of 54/46, and no atypical cells were observed. Both direct and indirect Coombs' tests were found to be positive. Deposition of immunoglobulin G and complement was found on the red cell surface, and the patient's serum was found to agglutinate all cells in a red cell panel at 37°C. However, anti-nuclear antibody and rheumatoid factor remained negative, and we could not find any sign of collagen diseases. We made a diagnosis of autoimmune hemolytic anemia due to the presence of autoantibodies exhibiting great affinity for erythrocytes at 37°C (warm-acting antibodies), associated with EMPD. Therapy with prednisone 20 mg daily for 6 weeks produced a good response for the anemia, followed by improvement of the laboratory data, which showed an erythrocyte count of 279×10^4 , a hemoglobin count of 9.3 g/dl, and a hematocrit count of 29.3%.

DISCUSSION

The treatment of EMPD is always problematic. Although EMPD is mainly treated by surgical excision, with safety margin control and/or radiation, there is often local recurrence after these therapies (1-4). However, EMPD remains indolent unless this disorder has an underlying adnexal adenocarcinoma

or an underlying internal malignancy. Since Paget's disease in our patient was carcinoma in situ at the time of radiation, the lesions of local recurrence were also confined to the epidermis only.

Autoimmune hemolytic anemia (AIHA) is caused by autoantibodies, mostly consisting of warm-reacting antibodies specific for red blood cells (5, 6). Although many patients belong to the idiopathic variety of AIHA, some cases showed associated disorders. The most common underlying disease is a reticuloendothelial neoplasia, followed in frequency by collagen diseases, and less commonly by infections, drug reactions, and carcinomas. Carcinomas with secondary AIHA include squamous cell carcinomas, adenocarcinomas, hypernephromas, oat cell carcinomas and seminomas (7). It is highly likely that EMPD induced AIHA in our case. Successful control of carcinomas by extirpation, irradiation and chemotherapy improves AIHA. However, as we could not totally eradicate the EMPD in our case, it was impossible to judge the effect of such a therapy. Our patient showed improvement of anemia by systemic corticosteroid treatment, which has been reported to be often less effective in AIHA associated with carcinomas than in idiopathic AIHA. When anemia occurs in patients with carcinomas including EMPD, it is advisable to examine the presence of autoantibodies specifically reactive for red blood cells by means of Coombs' tests.

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