Paget's disease of the vulva in a patient with scleroderma and underlying adenocarcinoma: case report

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Summary

Systemic sclerosis (SSc) is a multisystem connective tissue disease characterized by fibrosis of the skin and internal organs. Several studies have demonstrated an increased frequency of cancer in patients with SSc. We report a case of a 71-year-old woman with SSc, who presented with an eczematous lesion of the vulva. The diagnosis of Paget's disease of the vulva (PVD) was established. The patient underwent radical vulvectomy, but 18 months later died due to adenocarcinoma of unknown primary origin. SSc and PVD are associated with various types of malignancies and patients suffering from these diseases should be under surveillance in order for any suspicious symptoms of malignancy to be early detected and investigated.

Key words: Paget's disease of the vulva; Scleroderma; Malignancy.

Introduction

Systemic sclerosis (SSc) is a multisystem connective tissue disease characterized by fibrosis of the skin and internal organs. Several studies have demonstrated an increased frequency of cancer in patients with SSc [1, 2]. We report a case of a 71-year-old woman with SSc, who presented with an eczematous lesion of the vulva. The diagnosis of Paget's disease of the vulva (PVD) was established. The patient underwent radical vulvectomy, but 18 months later died due to adenocarcinoma of unknown primary origin.

Case Report

A 71-year-old woman was referred to the Gynecological Department with an eczematous and reddish lesion of the vulva. She had a 25-year history of limited scleroderma, with Raynaud phenomenon, interstitial pulmonary fibrosis, digital ulcers and mild pulmonary hypertension. She also had severe osteoporosis under treatment with biphosphonates.

The patient underwent radical vulvectomy with groin and femoral node dissection. The biopsy of the tissue showed Paget's disease of the vulva without extension beyond the basement membrane. The nodes and the margins were clear.

Three months after surgery the patient experienced sudden dyspnea and was admitted to the hospital. The diagnosis was right pleural effusion. A Bulleau tube was placed and chest fluid was removed. Many malignant cells of unknown origin were detected in the fluid analysis. Computed tomography (CT) of the lungs showed pleural effusion with atelectasia of the right lung with no lymph node involvement and no neoplastic lesions. CTs of the abdomen and the brain were normal.

The pleural effusion reappeared two weeks later and the patient was referred to the Department of Cardiosurgery, where she underwent pleurectomy of the right thorax, decortication of the pleura and aspiration of the pleural fluid. The biopsy of the pleura showed adenocarcinoma of unknown primary origin. The patient was referred to us in order to investigate the origin of the adenocarcinoma. All blood tests, including tumor markers, were normal. The patient underwent a new CT of the brain, lungs and abdomen, mammography, gastroscopy, colonoscopy, bone scan, magnetic resonance imaging, of the abdomen and ECHO exam of the lower abdomen. No primary origin was found. She refused chemotherapy. As a result she was discharged and she was in very good clinical condition, without symptoms of any malignancy or local recurrence of the disease for about one year.

One year later the patient was referred to us with severe low back pain and dyspnea. The X-ray exams showed fracture of Th_{10} and large pleural effusion of the right thorax. The bone scan showed osteolytic lesions of the spine and the CT of the lungs showed pleural effusion with a metastic lesion in the liver. The patient and her relatives refused any further diagnostic or therapeutic evaluation. A few days later the patient died and the diagnosis was adenocarcinoma of unknown primary origin.

Discussion

PDV is a rare condition that accounts for < 1% of vulvar neoplasms [3], and affects mainly postmenopausal white women with a mean age of diagnosis at 64 years [4]. After treatment about one-third of women experience local recurrences over many years [5, 6]. Underlying adenocarcinoma is found to 10% to 20% of the cases [7]. Commonly associated malignancies are breast, basal cell, rectal, genitourinary and cervical carcinoma [5].

In our case a 71-year-old woman with a history of scleroderma experienced itching and burning of the vulva with a reddish lesion which proved to be PDV. Population-based surveys reveal a higher incidence of malignancy in scleroderma patients [1, 2]. The types of cancer reported include lung cancer, non-melanoma skin cancer and liver cancer [1]. Possible reasons for this includes fundamental aspects of scleroderma biology – a number of cellular oncogenes are overexpressed, and there are reports of a reduction in the level of tumor suppressor genes [8]. Other relevant factors may be the use of potentionally carcinogenic chemotherapies like cyclophosphamide and the possible effects of long-term immunomodulation treatment [9].

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At the time of diagnosis, the patient was under therapy with low-dose prednizolone (10 mg/day) and nifedipine (30 mg/day). She also had received azathioprine (100 mg/day) for pulmonary fibrosis, bosentan (125 mg/day) for pulmonary hypertension and intravenous pulses with iloprost for digital ulcers and the Raynaud's phenomenon. She had never received cyclophosphamide.

Despite the detailed investigation and search, no origin of the malignancy was found. To the best of our knowledge this is the first report of PDV co-existing with scleroderma in the same patient. PDV may be a longstanding problem but few patients die of this condition. On the other hand systemic sclerosis is a multisystem disease that is often fatal due to respiratory involvement (pulmonary fibrosis and pulmonary arterial hypertension) [10] and other complications. In our case the cause of death was adenocarcinoma, which may be related to both diseases.

In conclusion, PDV and scleroderma are two rare conditions associated with various types of malignancies. Patients suffering from these diseases should be under diligent surveillance and any suspicious symptoms of malignancy should make this more intensive.

References

[1] Abu-Shakra M., Guillemin F., Lee P.: "Cancer in systemic sclerosis". *Arthritis. Rheum.,* 1993, *36,* 460.

[2] Rosenthal A.K., McLaughlin J.K., Gridley G., Nyren O.: "Incidence of cancer among patients with systemic sclerosis". *Cancer,* 1995, *76,* 910.

[3] Tebes S., Cardosi R., Hoffman M.: "Paget's disease of the vulva". *Am. J. Obstet. Gynecol.*, 2002, *187*, 281.

[4] Petkovic S., Jeremic K., Vidakovic S., Jeremic J., Lazovic G.: "Paget's disease of the vulva: a review of our experience". *Eur. J. Gynaecol. Oncol.,* 2006, *27,* 611.

[5] Curtin J.P., Rubin S.C., Jones W.B., Hoskins W.J., Lewis J.L.: "Paget's disease of the vulva". *Gynecol. Oncol.*, 1990, *39,* 374.

[6] Tsukada Y., Lopez R.G., Pickren J.W., Piver M.S., Barlow J.J.: "Paget's disease of the vulva: a clinicopathologic study of eight cases". *Obstet. Gynecol.,* 1975, *45*, 73.

[7] Gunn R.A., Gallager H.S.: "Vulvar Paget's disease: a topographic study". *Cancer*, 1980, *46*, 590.

[8] Denton C.P., Black C.M.: "Scleroderma clinical and pathological advances". *Best. Pract. Res. Clin. Rheumatol.*, 2004, *18,* 271.

[9] Hesselstrand R., Scheza A., Akesson A.: "Mortality and causes of death in a Swedish series of systemic sclerosis patients". *Ann. Rheum. Dis.*, 2003, *57*, 682.

[10] Steen V.D., Medsger T.A.: "Changes in causes of death in systemic sclerosis, 1972-2002". *Ann. Rheum. Dis.*, 2007, *66,* 940.

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