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Case Report

Primary Cutaneous Plasmacytoma after Rejection of a Transplanted Kidney: Case Report and Review of the Literature

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Abstract

Immunosuppressed organ allograft recipients are at risk of developing lymphomas and lymphoproliferative disorders as a consequence of immunosuppressive therapy and long-term antigenic stimulation from both the graft and possible viral infections. No more than 4% of the malignant tumors detected in organ recipients are plasmacytomas. Primary cutaneous plasmacytoma is a rare type of cutaneous B-cell lymphoma arising primarily in the skin. It is derived from clonally expanded plasma cells with various degrees of maturation and atypia. We report the occurrence of a solitary cutaneous plasmacytoma in a 56-year-old male patient undergoing hemodialysis after rejection of a grafted kidney. The diagnosis was made a few months after the kidney had been surgically removed. A thorough examination showed no evidence of systemic disease. Skin lesions were successfully treated with local radiotherapy. After 2 years of follow-up there were no local or systemic recurrences.
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1. Introduction

Organ transplant recipients are at high risk of posttransplantation lymphoproliferative disorders (PTLD) because of immunosuppression and chronic immune stimulation by both the grafted organ and possible viral infections such as that by Epstein Barr virus (EBV). Plasma cell tumors are rare, constituting 4% of all lymphomas observed in transplant recipients [1-3]. We report the onset of a primary cutaneous plasmacytoma (PCP) in a dialysis patient. The tumor was detected 1 year after chronic graft rejection.

2. Case Report

A 50-year-old white man developed chronic renal failure due to focal segmental glomerulosclerosis. In 1986 he began hemodialysis. In 1995 he underwent coronary artery bypass surgery after acute myocardial infarction. In January 1998 the patient received a cadaveric renal transplant and thereafter was maintained on immunosuppressive treatment (cyclosporine 225 mg 3 times a day, mycophenolate mofetil 500 mg 3 times a day, and methylprednisolone 16 mg once a day). Two episodes of acute rejection were treated with steroids. At discharge from the transplantation center, the patient's serum creatinine concentration was 300 μmol/L (3.3 mg/dL).

In November 1998, mycophenolate mofetil was replaced by azathioprine because of gastrointestinal discomfort attributed to the former drug. In January 1999 the serum creatinine concentration was 425 μmol/L (4.8 mg/dL).

In December 2000 the patient was admitted to the nephrology department because of chronic graft rejection with fluid overload and heart failure. The serum creatinine concentration was 665 μmol/L (7.5 mg/dL). A few days after the admission, all the immunosuppressive drugs were stopped. Hemodialysis was restarted.

In August 2001 surgical nephrectomy was performed. In September 2001 and in February 2002 the patient underwent percutaneous transluminal coronary angioplasty. In March 2002 he presented at the Department of Dermatology with an erythematous plaque 10 cm in diameter on the right leg (Figure 1). The lesion was not painful. The patient reported that the lesion had developed on his leg 1 year earlier and had grown slowly. He denied any previous trauma or insect bite at the site. A physician had prescribed oral antibiotics

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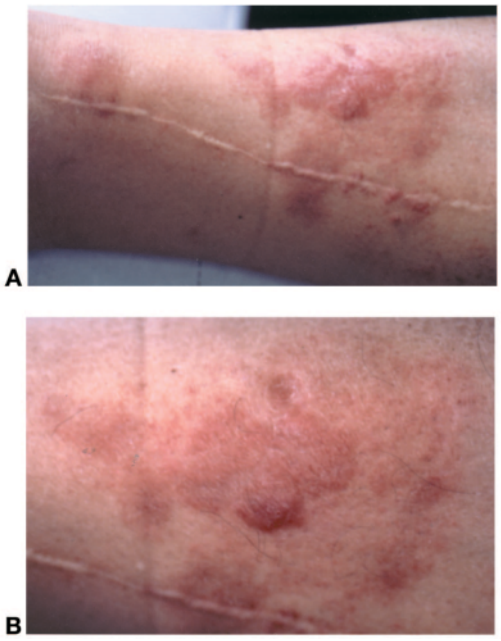

Figure 1. A, Skin lesions on the lower part of the right leg. B, Detail of the skin lesions on the lower part of the right leg.

with no benefit. The patient had not sought any other medical advice.

Skin biopsy revealed a dense, nodular infiltrate of mononuclear cells within the superficial and intermediate layers of the dermis. Cytomorphologic examination showed predominance of plasma cells with B- and T-lymphocytes. Immunohistologic examination demonstrated monoclonal expression of immunoglobulin κ light chains by the plasma cells (Figure 2). Anti–latent membrane protein monoclonal autoantibodies (Dako, Glostrup, Denmark) were used in a search for EBV in tumor cells, and the results were negative [4].

The diagnostic work-up included a full blood cell count, serum electrophoresis, serum and urine immunofixation, bone marrow biopsy, total body computed tomographic scan, and bone scintigraphy. All findings were within normal limits. The T-cell panel was normal. The results for immunoglobulin G (IgG) against EBV capsid and nuclear antigens were positive, but those for IgM were negative.

In August 2002 the patient underwent local radiotherapy and had a complete response. At the time of this writing, the patient was alive and well with no signs of cutaneous or systemic involvement.

3. Discussion

Malignant plasma cell tumors present in several forms, ranging from small localized lesions to widely disseminated disease. Localized forms include solitary plasmacytoma of the bone and extramedullary plasmacytoma, which are considered separate entities with different clinicopathological and prognostic features. Both forms can evolve into systemic disease. Lesions arising primarily in the skin are rare [5-8].

PCP is a rare disease described for the first time in 1949 [8]. Since then approximately 32 cases have been reported. PCP predominantly affects elderly or middle-aged men (mean age, 60 years; male to female ratio, 4:1). Clinically there may be as many as 50 cutaneous reddish to purple nodules, nodes, and plaques with no predilection for a particular site [5-7]. Ulceration of the lesions is rare. Because of the

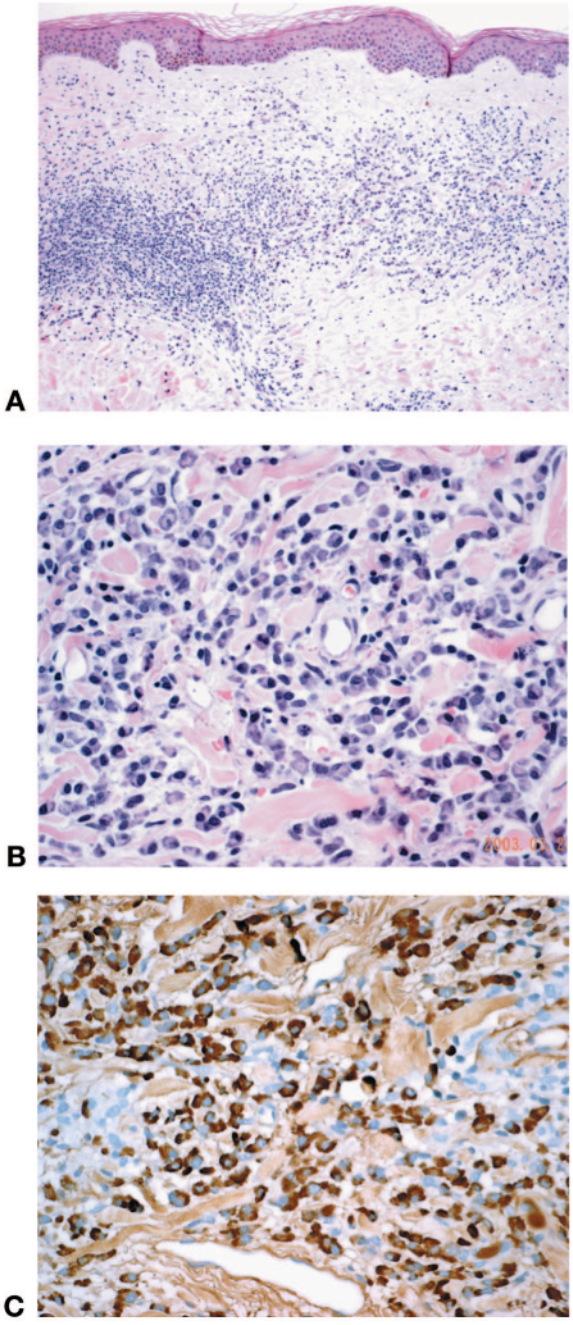

Figure 2. A, Diffuse plasma cell infiltrate (hematoxylin and eosin, original magnification ×2). B, Atypical plasma cells with hyperchromic and binucleate nuclei (hematoxylin and eosin, original magnification ×20). C, Plasma cells with light chain κ positivity (immunohistocytochemical, original magnification ×20).

paucity of the cases for which long-term follow-up information is available, the course of the disease and its prognosis are difficult to evaluate. Disease progression with systemic involvement has been reported in 7 of 14 patients with more than 3 years of follow-up [8]. Four of 14 achieved complete remission, and the others had local recurrences. As for prognostic factors, some authors [5-8] differentiate solitary and multiple forms of the disease, the latter apparently having a more aggressive course with higher mortality. Clinicopathological findings, such as IgA secretion by neoplastic cells, may be indicative of a more aggressive course [8].

Cancer is a well-known complication of solid organ transplantation. Furthermore, a multicenter study demonstrated that the incidence of cancer among patients receiving dialysis for end-stage renal disease is higher than that in the general population [9,10].

The incidence of lymphoma among transplant recipients is 20 times higher than in an age- and sex-matched control population [1,2]. Much confusion has arisen about the nomenclature of the majority of the lesions; consequently, the nonspecific term PTLD has been widely accepted [3,11]. This term covers a very wide spectrum of disorders ranging from benign hyperplasia at one end to frankly malignant lymphoma at the other. Of the 1931 cases of PTLD in the Cincinnati Transplant Tumor registry that were studied immunologically, 86% were of B-cell origin, 14% were of T-cell origin, and rare cases were null cell origin or were combined B- and T-cell lymphoma [1]. Myeloma/plasmacytoma accounted for only 4% of all the cases [12,13]. The reason for the low incidence of this malignancy in comparison with that of lymphoma is poorly understood [14].

Multiple risk factors for PTLD have been reported: aggressive immunosuppression with more than 2 or 3 drugs and the use of antilymphocyte globulin or muromonab-CD3 (OKT3). Heart and lung transplant recipients who need aggressive treatment of acute rejection have a higher risk [15-17]. More than 90% of patients with PTLD have positive results for EBV. Plasmacytoma may follow reactivation of EBV infection after transplantation [18,19].

Plasmacytoma in transplant recipients may affect bones, the oral cavity, the skull, the abdomen and, in a few cases, the skin [20,21]. There are few data on the prognosis and survival of patients with posttransplantation plasmacytoma. Plasmacytoma occurring within the first year after transplantation generally presents as localized disease and is associated with a significantly lower mortality rate. It usually responds favorably to a decrease in immunosuppressive therapy and to chemotherapy. In contrast, the mortality among patients developing late plasmacytoma is as high as 80%. This late form is frequently disseminated disease and sometimes does not respond to a reduction of immunosuppressive therapy [22-25].

These differences may reflect a continuous transition from benign B-cell hyperplasia in response to EBV infection to oligoclonal or monoclonal proliferation. Given the small number of reported cases, the role of immunosuppression in the etiology of posttransplantation myeloma has not been clearly established. Immunosuppressive therapy may be reduced or discontinued in renal allograft recipients, and such patients have a better prognosis than nonrenal allograft recipients [22-25].

Possible therapeutic strategies for plasmacytoma include local radiotherapy, chemotherapy alone or with autologous peripheral blood stem cell transplantation or hematopoietic stem cell transplantation [26-35].

Malignant plasma cells are extremely sensitive to radiation [26]. A solitary extramedullary plasmacytoma can be successfully irradiated. Radiation also can be used to treat symptomatic lesions, to stabilize bones at risk of fracture, and to treat spinal cord compression. Patients often benefit from the expertise of an orthopedic surgeon skilled in cancer management, because prophylactic fixation of impending pathological fractures is occasionally warranted.

Several chemotherapeutic agents are used to treat multiple myeloma. The regimen most often used is melphalan and prednisone (M and P) orally administered for 4 to 7 days. The cycle is repeated every 4 to 6 weeks, depending on recovery of blood cell counts. Patients tolerate this therapy extremely well but, rarely, report nausea or fatigue. The overall response rate is approximately 50%.

Although many other combinations of chemotherapy (eg, vincristine, bischloroethylnitrosourea [BCNU], melphalan, cyclophosphamide, and prednisone [VBMCP]; vincristine, adriamycin, and dexamethasone [VAD]; and VBMCP/vincristine, BCNU, adriamycin, and prednisone [VBAP]) exist, in 2 metaanalyses investigators compared M and P with combination chemotherapy and found no significant advantage in response percentage, response duration, or survival rates with combination chemotherapy [27,28]. Bisphosphonates are used to promote bone healing and to provide secondary prophylaxis against skeletal events (eg, bone fracture and spinal cord compression) [29].

Only a few cases of bone marrow transplantation (BMT) for hematologic neoplasia after solid organ transplantation have been reported in the literature. Possible reasons are that the patients were too ill to tolerate high-dose chemotherapy and the presence of graft-versus-host disease (GVHD), major organ toxicity, and infections. Furthermore, the risk of organ rejection after BMT cannot be ignored [30-34].

Autologous peripheral blood stem cell transplantation was performed in a kidney transplant recipient affected by multiple myeloma. After 2 years of follow-up the patient was alive and well, and no recurrences of the myeloma had been detected. Peripheral stem cell grafts contain approximately 10 times more T- and-B cells than do marrow grafts. Because these cells may survive for a long time in transplant recipients, patients who receive such grafts may be less immunocompromised than recipients of marrow. Immune reconstitution seems to be faster with a peripheral source of stem cells than with BMT. CD3 counts are reconstituted to normal levels 2 to 4 months after transplantation, whereas CD4 may remain at low levels for at least the first year [30].

A case of disseminated EBV-related plasmacytoma [35], which occurred in a renal allograft recipient 13 years after transplantation, has been described. The patient's son had donated the kidney. Nonmyeloablative hematopoietic stem cell transplantation with peripheral blood from the kidney donor was performed. With the onset of GVHD, the myeloma resolved. A subsequent isolated relapse occurred in the central nervous system, ultimately leading to the patient's death.

In conclusion, our patient may be of interest because his is the first case of PCP reported in a dialysis patient. The patient presented with a solitary lesion on the right leg. According to the patient, the lesion had appeared 2 years after hemodialysis was restarted, approximately 1 year before he sought medical advice. The lesion had grown slowly. Despite the long delay between the onset of the first lesion and the diagnosis, none of the investigations revealed any systemic disease. The tumor responded well to radiation therapy. After 2 years no recurrences had been found.

In light of our clinical experience and the data literature, we suggest that dialysis patients undergo regular skin examinations. Any suspicious lesion should be immediately referred to a dermatology department for prompt diagnosis and therapy.

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