Cutaneous Plasmacytosis with Multiple Nodular Eruptions and Polyclonal Hypergammaglobulinemia

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We report two patients with multiple peculiar skin eruptions and polyclonal hypergammaglobulinemia. Both patients visited our hospital for the evaluation of asymptomatic multiple nodular eruptions on almost their entire body except for the lower extremities. Histologic examinations disclosed prominent infiltration of plasma cells and lymphoid follicular hyperplasia in the dermis but these plasma cells showed neither a mitotic figure nor atypicalities. Laboratory examinations showed polyclonal hypergammaglobulinemias and increased erythrocyte sedimentation rates. In spite of various investigations, the cause of the hypergammaglobulinemia remained obscure. (Ann Dermatol 6:(2) 183-187, 1994)

Key Words: Cutaneous plasmacytosis, Polyclonal hypergammaglobulinemia

Plasma cells arise from antigenically stimulated B lymphocytes refered to as centroblast or immunoblasts. They are the effector cells of humoral immunity and do not enter the blood stream but discharge the immunoglobulins they produce into the blood[1]. Therefore, most proliferative plasma cell disorders relate to the secretion of cell product(immunoglobulin molecules or subunits, lymphokines).

We observed two patients who had multiple skin nodules infiltrated with the plasma cells and polyclonal hypergammaglobulinemia without any underlying disease. A few cases of multiple primary cutaneous plasmacytoma have been reported[2,3] but our cases can be differentiated from them in the respect of no atypism of infiltrated plasma cells and polyclonality-polyclonal hypergammaglobulinemia.

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REPORT OF CASES

Case 1

A 50-year-old man visited the Department of Dermatology, Seoul National University Hospital in August, 1990, with a complaint of multiple purplish brown macules and nodules on his face, neck and trunk. Skin eruptions on his face were first noticed about twelve years ago and these lesions have spread over his neck, anterior chest and back. There was no relevant family history. He had suffered from frequent upper respiratory infections and a carious tooth.

On physical examination, superficial lymph nodes were not palpable. His breath sound was slightly decreased on the whole lung field. His heart sound was normal. There was splenomegaly with two finger-breadth, however liver was not palpable and bone was not tender. Multiple purplish-brown macules and nodules measuring 0.5-1.5cm in diameter were found scattered over his face, neck, chest, abdomen and trunk(Fig. 1(a, b)).

The hemoglobin level was 10.8mg/dl, and the WBC count was 5,720/mm^3 with 66% neutrophils, 28% lymphocytes, 6% monocytes, no

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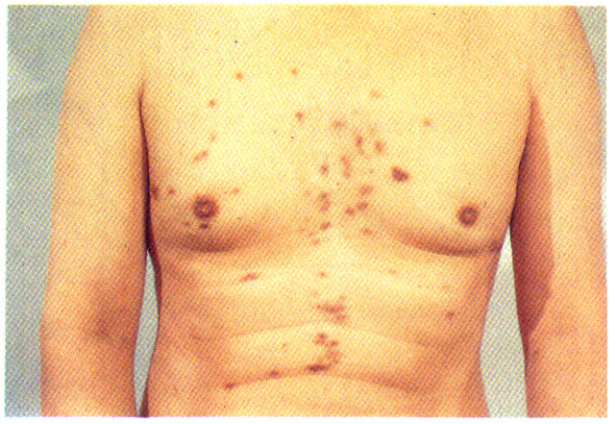

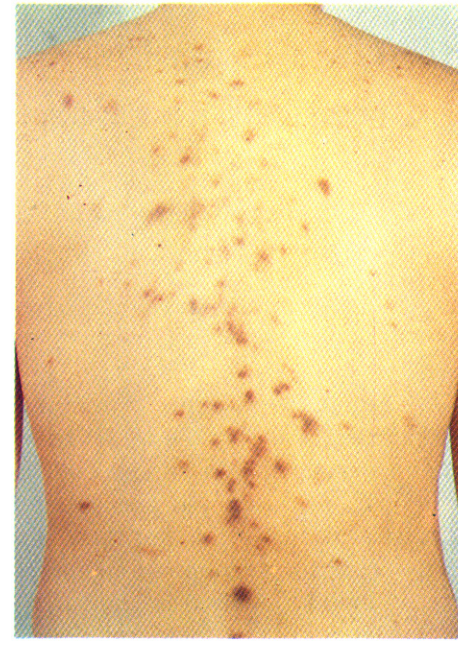

Fig. 1. Case 1, Multiple purplish-brown macules and nodules measuring 0.5-1.5 cm in diameter over the chest, abdomen(a) and trunk(b).

plasma cells and no atypical cells in the peripheral blood smear. The platelet count was 285,000/mm^3. The erythrocyte sedimentation rate(ESR) disclosed a significant increase of 133 mm/hour. Liver enzymes were normal. No Bence Jones protein was detected in the urine. The VDRL and TPHA were negative. Serum total protein level was 11.5 g/dl with a albumin of 2.5 g/dl. Serum immunoglogulin levels increased 4351 mg/dl(normal range, 408-1788 mg/dl) in Ig G, 782 mg /dl(normal range, 64-544 mg/dl) in Ig A and 587 mg/dl(normal range, 49-355 mg/dl) in Ig M. Serum protein electrophoresis and immunoelectrophoresis showed a polyclonal hypergammaglobulinemia. No hot spot was found on the bone scan. Liver ultrasonography showed a slightly increased echogenecity of liver with splenomegaly. The chest roentgenogram showed a reticulonodular infiltration and prominent both hilus. The high resolution computed tomography of chest revealed diffuse interstitial infiltration of the whole lungs and diffuse mediastinal lymph node enlargement. But further evaluation of the radiologic abnormalities of his lung have not been undertaken. A biopsy specimen of skin from the lesion on the neck revealed a diffuse infiltrate of well-differentiated plasma cells in the dermis. These plasma cells displayed neither atypism nor mitoses. There were several lymphoid follicle-like structures intermingled with lymphocytes in the dermis(Fig. 3, 4). Bone marrow aspirate with biopsy disclosed normocellular marrow with a slightly increase of plasma cells. But there were no findings that suggested myeloma.

The patient was treated with a regimen of melphalan 8 mg/day and prednisolone 60 mg/day orally for one week and then rest for three weeks. He took in total seven cycles of the above regimen for about seven months without any evidence of improvement. Since then no specific treatment has been undertaken and there is also no marked changes in clinical and laboratory findings without treatment.

Case 2

The patient was a 49-year-old man. He visited our clinic in September 1991 with multiple asymptomatic lesions of the skin that involved his face, neck and trunk. A few of these had shown partial spontaneous resolution but more lesions had continued to appear.

On physical examination, scattered over his body were multiple dermal nodules and macules of sizes varying from 0.5 to 1.5 cm in diameter. These were bluish or purplish brown(Fig. 2(a, b)). Findings from examination of the respiratory and cardiovascular system were unremarkable. The liver, spleen and superficial lymph nodes were not palpable. Otherwise they were normal.

No abnormality was found in the complete blood cell count or in the smear of peripheral

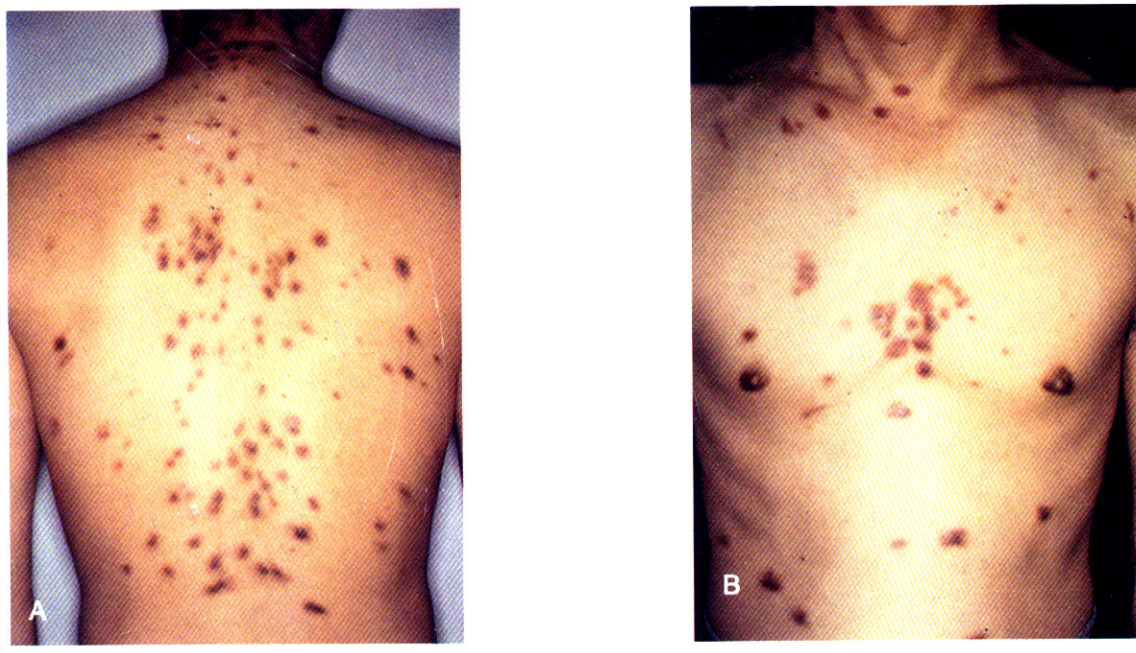

Fig. 2. Case 2, Multiple macules and nodules on the trunk(a), chest and abdomen(b)

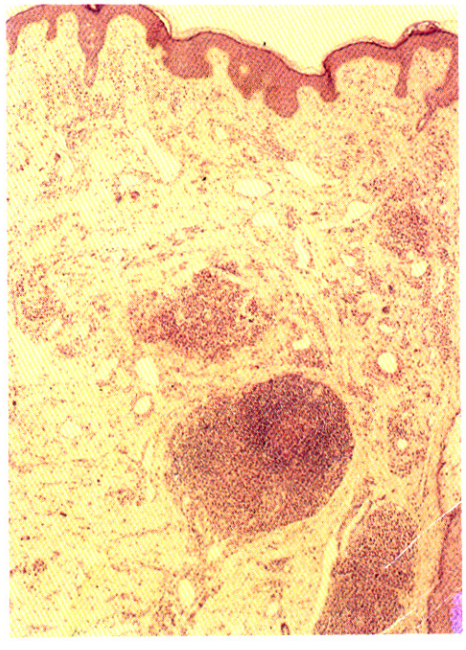

Fig. 3. Case 1, Diffuse infiltration of plasma cells in the upper and middle dermis, a lymphoid follicle-like structure intermingled with lymphocytes in the dermis(hematoxylin-eosin, × 40).

blood. ESR was 105 mm/hour. Results of urinalysis were normal. No Bence Jones protein was detected

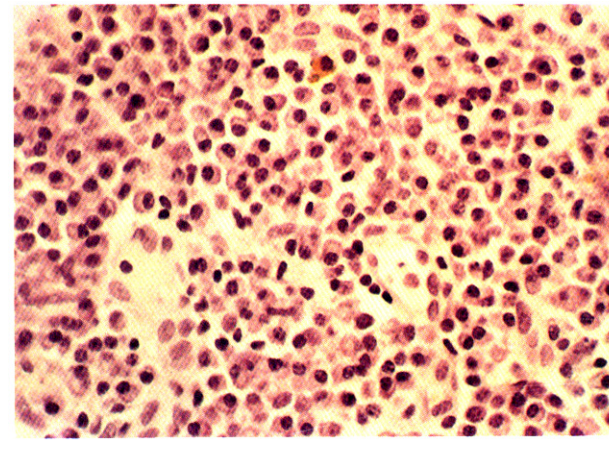

Fig. 4. Case 1, Plasma cells show neither atypism nor mitoses(hematoxylin-eosin, × 400).

in the urine. Serum total protein level was 8.8 g/dl with an albumin of 3.1 g/dl. The BUN and serum creatinine, and liver enzyme levels were all normal. A serologic test for syphilis were negative. Chest roentgenogram and ^{99m}Tc-MDP bone scan for the whole body were normal. Serum protein electrophoresis and immunoelectrophoresis showed the results of polyclonal hypergammaglobulinemia. Bone marrow aspirate and biopsy specimen were normocellular with several collections of plasma cells(10-20 plasma cells/collection). The

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resected inguinal lymph node revealed reactive hyperplasia with heavy plasma cell infiltration. A biopsy specimen of one of the skin nodules showed diffuse and moderate perivascular mononuclear cell infiltration in the dermis. Most of these infiltrating cells were plasma cells intermingled with a small number of lymphocytes. Several lymphoid follicle-like structures were observed in the dermis. No atypism was noted in these cells.

The patient was given oral prednisolone(30-40 mg/day) therapy for twelve weeks without any evidence of effectiveness.

DISCUSSION

The presented cases are characterized by multiple skin eruptions accompanied by polyclonal hypergammaglobulinemia and several abnormal results of laboratory studies. Histologically, diffuse and aggregated infiltration of plasma cells intermingled with a small number of lymphocytes was noted in the skin erupions. These plasma cells were mature without atypism. There are various skin disorders of the infiltration of many plasma cells including early syphilis, rhinoscleroma, granuloma inguinale, mycosis fungoides, solar keratosis, chronic deep folliculitis and balanitis chronica plasmacellularis.[1] However, the clinical, laboratory and histological findings of our cases did not fit a diagnosis for any of above diseases.

In 1966, Mach and Wilgrim[4] examined 115 case of cutaneous lymphoplasia(lymphocytoma), histologically, and classified them into 5 different types. According to their description the plasma cell type(about 5 % of whole), one of the 5 varieties, is characterized by small clusters of plasma cells. Cutaneous lymphoplasia is considered as a localized proliferation of the preexisting lymphoreticular tissue due to external stimulation. Frequently, there was a strong admixture of lymphoid cells in germinal center-like arrangements. In our cases the specimens of the lesions contained plasma cells rather than lymphoid cells. Clinically cutaneous manifestations of our cases showed more widely scattered nodules and macules on almost the whole of the upper half of the body than that of cutaneous lymphoplasia. Our cases also had a more chronic course without complete spontaneous resolution.

Cutaneous plasmacytoma should also be included in the differential diagnosis. Cutaneous plasmacytoma can be classified into two groups; primary cutaneous plasmacytoma[2,3,5-7] and secondary(or metastatic) cutaneous plasmacytoma.[7-11] The former, a distinct entity from multiple myeloma, is rare. Only a few cases have been reported in the literature. Especially, the primary cutaneous plasmacytoma of multiple skin lesions without detectable multiple myeloma in the bone is very rare.[2,3] In order to diagnose the presence of true primary cutaneous plasmacytoma, one must prove the malignant nature of plasma cell in the skin and exclude multiple myeloma, soft tissue plasmacytoma, and bony plasmacytoma with metastasis to the skin. However, some of the reported primary cutaneous plasmacytoma were incompletely documented or lacked long term follow up studies for subsequent development of systemic multiple myeloma. Cutaneous extramedullary plasmacytoma may appear as the first presenting sign of multiple myeloma, or they occur several years after the diagnosis of multiple myeloma has been established.

Shah et al[9] reported a case of multiple myeloma first observed as multiple cutaneous plasmacytomas. They emphasized the necessity of follow up evaluation of such patients for the delayed development of systemic multiple myeloma. In both primary and secondary cutaneous plasmacytoma most of the plasma cells apear atypical and vary in size and shape as well as atypical mitotic figure, and usually monoclonal gammaglobulinemia is documented. In these respects, our cases differ from cutaneous plasmacytoma.

Kitamura et al[12] reported a case entitled "A case of plasmacytosis with multiple peculiar eruptions". Their case is very similar to our cases with nodular skin eruptions and polyclonal gammopathy but is different from ours only in the presence of generalized lymphadenopathy. Aso and Shimao[13] and Ishii et al[14] reported cases with multiple reddish brown papules located mainly on the trunk and upper extremities and plasma cell infiltration in the dermis. These cases didn't show lymphadenopathy or polyclonal hypergammaglobulinemia. In 1986 Watanabe et al[15] described two patients with peculiar multiple skin eruptions, asymptomatic generalized lymphadenopathy, and polyclonal hypergammaglobulinemia. In one of these cases lymphoid interstitial pneumonia (LIP) was demonstrated by lung biopsy. They called their cases

"systemic plasmacytosis" that is accompanied by plasma cell proliferation in more than two kinds of organs, such as skin, lymph nodes, and lung. They considered that it was a B-cell proliferative disorder produced as a result of an immunologic overresponse to an antigen or antigens of unknown origin. In our case 1 there were radiologic evidences of lung infiltration. Though we have not confirmed the nature of radiologic abnormalities of the lung the possibility of interstitial pneumonitis by infiltration of plasma cells could be considered.

We have examined our patients at regular intervals for only one year and no marked change in the skin lesions has been observed. We consider our cases not to be one of a true tumor but one of a rather benign reactive proliferation of plasma cells in the skin, although its etiology is unclear. We need to follow up our patients for a long time to be certain whether these develop or not to multiple myeloma

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