Case Report

Primary Extramedullary Plasmacytoma of the Lung with Production of M-protein : a case report

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Abstract：We describe here a rare case of primary extramedullary plasmacytoma of the lung in an 86-year-old Japanese man. Immunohistochemical staining of biopsy specimens for IgG-kappa was positive, and serum immunoelectrophoresis showed monoclonal IgG-kappa. There was no evidence of the presence of multiple myeloma. Chemotherapy was given, but tumor size did not decrease significantly.

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Key words： Extramedullary plasmacytoma of the lung, Immunohistochemistry, Immunoelectrophoresis, M-protein, IgG-kappa

1. Introduction

Primary extramedullary plasmacytoma is a tumor resulting from the neoplastic proliferation of plasma cells in the absence of multiple myeloma. It represents less than 10 per cent of all plasma cell dyscrasia. Most primary extramedullary plasmacytomas arise in the upper respiratory tract and oral cavity[1]. Involvement of other sites, such as the gastro-intestinal tract, lung, skin, breast, testis, thyroid, lymph nodes, and spleen, is rare. We report a case of primary extramedullary plasmacytoma of the lung with production of M-protein.

2. Case Report

An 86-year-old Japanese man was referred to our hospital on March 4,1991 because of an abnormal shadow on chest X-ray detected by his family doctor whom he consulted with a complaint of cough which had started gradually two months previously. He had a history of smoking and of prostatic hypertrophy. The physical examination revealed no abnormalities except prostatic enlargement.

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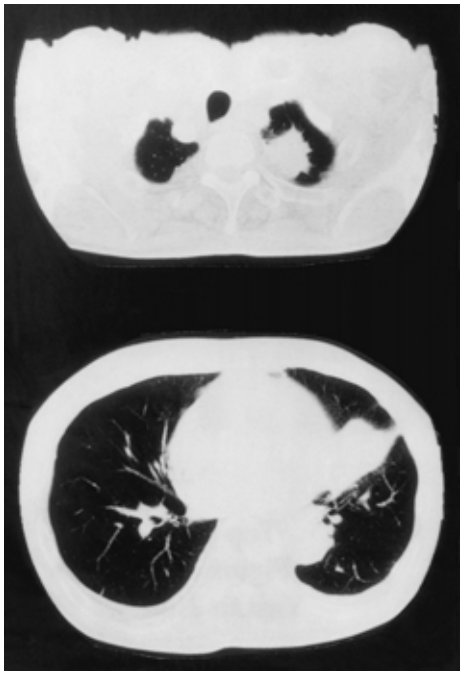
Laboratory studies disclosed the following values : hemoglobin, 13.4 g/dl ; hematocrit, 40.1% ; red blood cell count, 4,280,000 ; white blood cell count, 6100 (71%neutrophils, 17%lymphocytes, 8%monocytes, and 4%eosinophils) ; serum protein, 8.8 g/dl (albumin, 51.9% ; α_1-globulin, 3.9% ; α_2-globulin, 9.1% ; β-globulin, 7.9% ; γ-globulin, 3.5% ; M-protein, 23.7%) ; lactic dehydrogenase, 418 U/l ; beta-2-microglobulin, 1.4 mg/l ; serum cal-

Fig. 1. CT of the chest through the left upper lobe showed a tumor radiating multiple spicules (upper) and a tumor with peripheral atelectasis (lower).



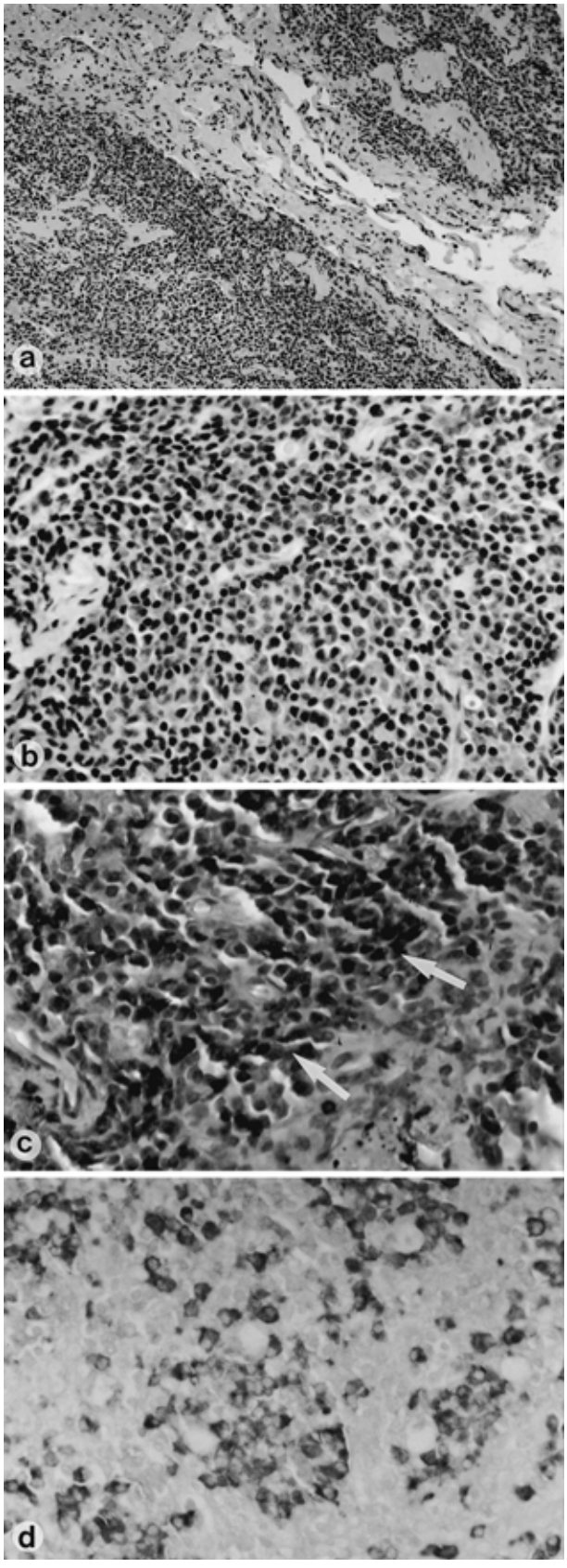


Fig. 2. Tumor was not distinctly encapsulated but separated from the surrounding normal alveolar tissue a)(H. E., ×120). Microscopic examination revealed relatively mature plasma cells and immature and atypical plasma cells with an increased nuclear-cytoplasm ratio b)(H. E., ×260). Immunohistochemical detection of IgG (white arrows) c) (counterstained with hematoxylin, ×400) and kappa light chains d)(counterstained with methylgreen, ×400) in the cytoplasm of the tumor cells.

cium, 4.7 mEq/l ; uric acid, 5.5 mg/dl ; blood urea nitrogen level, 19 mg/dl ; creatinine, 1.0 mg/dl ; IgG, 2,510 mg/dl ; IgA, 261 mg/dl ; and IgM, 72 mg/dl. Serum immunoelectrophoresis showed the monoclonal IgG-kappa. Urine was negative for Bence-Jones protein. Examination of bone marrow smears disclosed the following values : nucleated cells, 89,000/mm^3 ; ratio of granulocytes to nucleated red cells, 2 : 1 ; megakaryocytes, 47/mm^3 ; plasma cells, 4.1% ; and normal morphological appearance. The immunocytochemical staining of bone marrow smears for immunogloblins showed that the plasma cells were polyclonal in nature.

Chest X-ray revealed masses in the left upper lobe (S^{1+2}, S^4+S^5). Chest CT revealed a tumor 4 cm in diameter in the S^{1+2} and a tumor with atelectasis of peripheral lung in S4+S5 (Figure 1). Examination by fiberoptic bronchoscopy showed no abnormality in the lumen of the bronchi. Transbronchial biopsy specimens showed plasma cell infiltration (Figure 2a, b). Immunohistochemical staining was positive for IgG-kappa (Figure 2c, d) and negative for CD 20. Amyloid deposits were not found with Congo-red staining.

Examination of upper respiratory tract, bone survey and radionucleotide bone scan, CT of the head, CT of the abdomen, upper gastrointestinal tract endoscopy and roentgenologic examination of the colon with barium enema revealed no abnormality. There were no other extramedullary plasmacytomas and no systemic amyloidosis. Subsequently, the diagnosis was primary extramedullary plasmacytoma of the lung. According to Wiltshaw stage classification, the patient had Stage III disease[1].

Three courses of chemotherapy with melphalane, prednisolone, vincristine, and ranimustine were administered. Tumor size decreased only slightly, and the level of serum IgG and M-protein decreased to 2150 mg/dl and 7.6 g/dl (M-protein, 19%), respectively. The patient refused further treatment, such as surgery and radiation, and was discharged from our hospital. On an outpatient basis, the

patient then received six courses of chemotherapy every two months and 29 months after the initial diagnosis, the patient died of pneumonia. Permission for autopsy was not granted. There was no evidence of myelomatosis in laboratory findings.

3. Discussion

Primary extramedullary plasmacytoma of the lung is rare. To our knowledge, only 27 cases have been reported in the international literature, including 4 cases of endobronchial extramedullary plasmacytoma[2)~9)]. Usually, tumor cells are formed into sheets or strands, and there is little or no stroma of extramedullary plasmacytoma except in the cases where amyloid is present [1)6)]. Primary extramedullary plasmacytoma of the lung should be distinguished from pulmonary localized amyloidosis, pulmonary involvement of multiple myeloma, plasma cell granuloma, pseudolymphoma, and low-grade BALT lymphoma.

Histologically, plasma cell granuloma is composed of various proportions of lymphocytes, histiocytes, plasma cells, macrophages, foam cells, fibroblasts, spindled myofibroblasts, and collagen. Immunohistochemical study shows that the plasma cells are a polyclonal infiltrate[10)]. Pseudolymphoma of the lung presents as a localized nodule histologically characterized by infiltrates of heterogeneous cells composed of plasma cells, histiocytes, and lymphoid cells with reactive germinal centers. Immunohistochemical study shows that plasma cells and B-lymphocytes are polyclonal in nature. Exact diagnosis is based on the molecular techniques used to demonstrate an absence of gene rearrangement of immunoglobulin heavy chain in order to exclude low-grade BALT lymphoma[11)].

Low-grade BALT lymphoma of the lung often presents as solitary or multiple nodules. Histologic findings showed that tumor cells have inconspicuous irregularity and sometimes present plasma cell differentiation. Most of the cases are of B-cell lineage and immunohistochemical study is necessary to investigate B-cell clonality.

Localized nodular pulmonary amyloidosis usually presents as a solitary nodule and is histologically characterized as amorphous eosinophilic material with foreign-type giant cells, infiltrating lymphocytes and plasma cells. Immunohistochemical studies revealed that infiltrating plasma cells in amyloidosis were positive for polyclonal immunogloblins. Therefore, the diagnosis of extramedullary plasmacytoma must be based on proof that the origin of the tumor cells is monoclonal in nature. Several reports pointed out that in some cases of plasmacytoma, there was no evidence of the monoclonality of plasma cells[2)4)]. Immunohistochemical staining for monoclonal immunogloblin, for example, could disclose the monoclonality of plasma cells[6)]. In large tumors, M-protein in the serum can be detected[12)13)].

Surgery and/or irradiation are used for the treatment of localized plasmacytoma of the lung[2)9)]. After surgical resection or radiation therapy, serum monoclonal immunogloblin levels have been shown to return to normal[12)~14)]. There has been no report of the effect on systemic chemotherapy on primary extramedullary plasmacytoma of the lung. However, seven cases of extrathoracic extramedullary plasmacytoma were treated by chemotherapy alone with favorable results[1)15)]. In our case, the patient refused both surgery and irradiation, therefore, chemotherapy was administered. Insufficient tissue level of carcinostatic agents might have been one cause of failure of systemic chemotherapy in our patient because tumors were large.

Five patients have been reported to develop to multiple myeloma[14)]. Recently, Laso et al. reported a case with extramedullary plasmacytoma of the lung and demonstrated that plasma cells with normal morphological apperance in bone marrow were of the same clonality as tumor cells of the lung by DNA analysis using flow cytometry and fluorescence in situ hybridization[5)]. They suggested that, in some cases, extramedullary plasmacytoma and multiple myeloma are same entity of plasma cell disorder, and that the development of myelomatosis in extramedullary plasmacytoma could be predicted using precise technique.

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