

Primary Extramedullary Plasmacytoma of the Lung

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A case with primary plasmacytoma of the lung is described. The patient, a 55-year-old Japanese female, who simultaneously had a pulmonary plasmacytoma and bladder carcinoma. The bladder tumor was treated with transurethral resection. Pathologically, the bladder tumor was a non-invasive, papillary transitional cell carcinoma, grade II. The lung tumor was located in the right upper lobe and upper lobectomy was performed. The tumor measured $2.8 \times 2.7 \times 2.0$ cm and had a white-yellowish cut surface. Histologic, electron microscopic and immunohistochemical examinations of the lung tumor revealed monoclonal proliferation of plasma cells (IgA, lambda light chain). There was no evidence of multiple myeloma. (Internal Medicine 31: 1396–1400, 1992)

Key words: solitary myeloma, multiple myeloma, lymphoma, monoclonality, immunohistochemistry

Introduction

Extramedullary plasmacytoma, a rare tumor occurring in any part or organ of the body outside the bone marrow, is usually found in the soft tissue of the head and neck, notably in the upper air passages; over 80% arise in the upper airway, nasal cavity, and paranasal sinuses (1–6). Extramedullary plasmacytoma of the lung is extremely rare. Since several early case reports of plasmacytoma of the lung erroneously included cases of plasma cell granuloma, the precise number of reported cases of pulmonary plasmacytoma has not been clearly estimated. To our knowledge, only 9 convincing cases have been reported in the English language literature to date (7–13). Here, we describe a case of pulmonary plasmacytoma confirmed by microscopic, immunohistochemical, and electron microscopic study.

Case Report

The patient, a 55-year-old Japanese female, had complained of dysuria for two months. She was admitted to the Department of Urology of Kanazawa University Hospital on July 15, 1991. Physical examination revealed no lymphadenopathy, hepatomegaly or other abnormalities. Routine chest radiograph revealed a coin lesion

in the right upper lobe of the lung. Urine cytology revealed erythrocytes and atypical cells suggestive of bladder carcinoma. Routine laboratory investigations were within normal limits. The bladder tumor was treated by transurethral resection on August 23, 1991. Pathologically, the bladder tumor was a non-invasive, papillary transitional cell carcinoma, grade II. On September 10, she was transferred to the Department of Surgery for further evaluation of an abnormal pulmonary shadow. Admission electrolytes, peripheral blood counts, and urinalysis were within normal limits. Total serum protein was 6.3 g/dl, with 3.6 g/dl of albumin and 1.1 g/dl of gamma globulin. Bronchoscopy and sputum cytology were normal. Sputum culture was normal. Tumor aspiration cytology was negative for malignancy. However, radiographic and computed tomographic findings could not rule out malignancy. Exploratory thoracotomy was performed on September 13. Pathological examination during surgery by frozen section revealed a plasmacytoma and upper lobectomy was performed. Examination of the urine for Bence-Jones protein was negative. Serum IgG concentration was 1,626 mg/dl (normal, 1,300–1,774), IgM 121 mg/dl (98–235), IgA 150 mg/dl (178–355), IgD 1.3 mg/dl (0.2–19.5), and IgE 8 IU/ml (below 450 IU/ml). Serum protein electrophoresis was normal and no monoclonal spike was demonstrated. A skeletal

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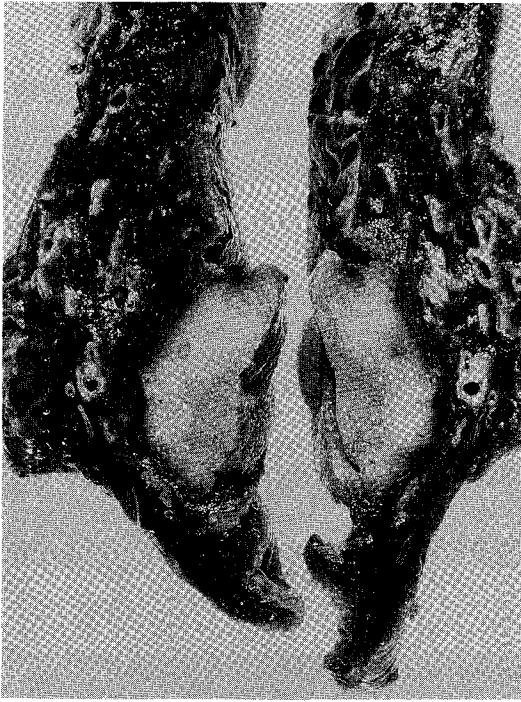


Fig. 1. Cut surface of the lung tumor, presenting as a relatively ill-defined, gray-white subpleural mass.

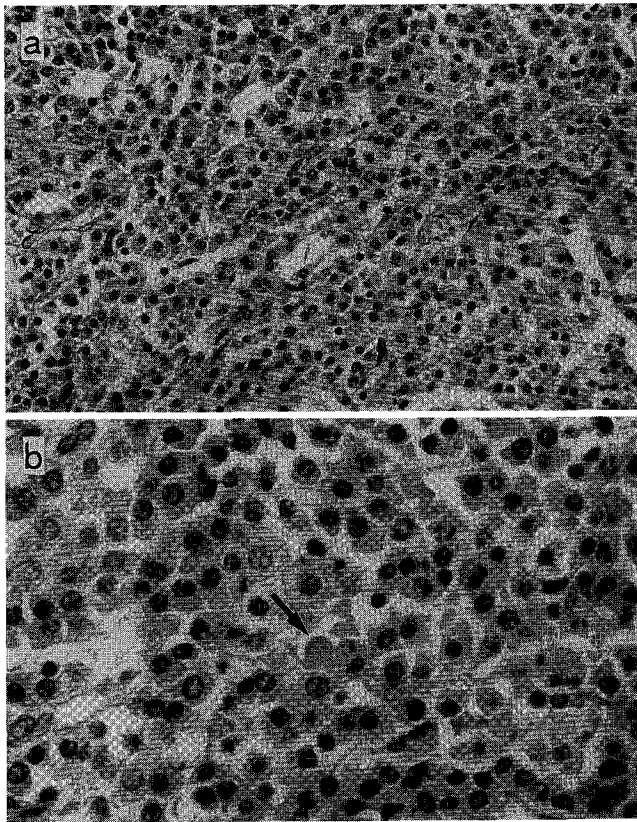


Fig. 2. Histologic picture of the tumor showing monotonous proliferation of plasma cells (a). The nuclei are eccentric and most are quite mature. Binucleated plasma cells and Russell bodies (arrow) are occasionally seen (b) (HE stain, a: $\times 400$, b: $\times 1,000$).

survey and bone marrow biopsy specimen performed during her hospitalization revealed no abnormality suggestive of multiple myeloma or generalized myelomatosis.

Pathologic findings

The resected right upper lobe contained a relatively ill-defined, firm, gray-white mass measuring $2.8 \times 2.7 \times 2.0$ cm (Fig. 1). There was no relation to the bronchus or pleura. Microscopically, the tumor was composed of

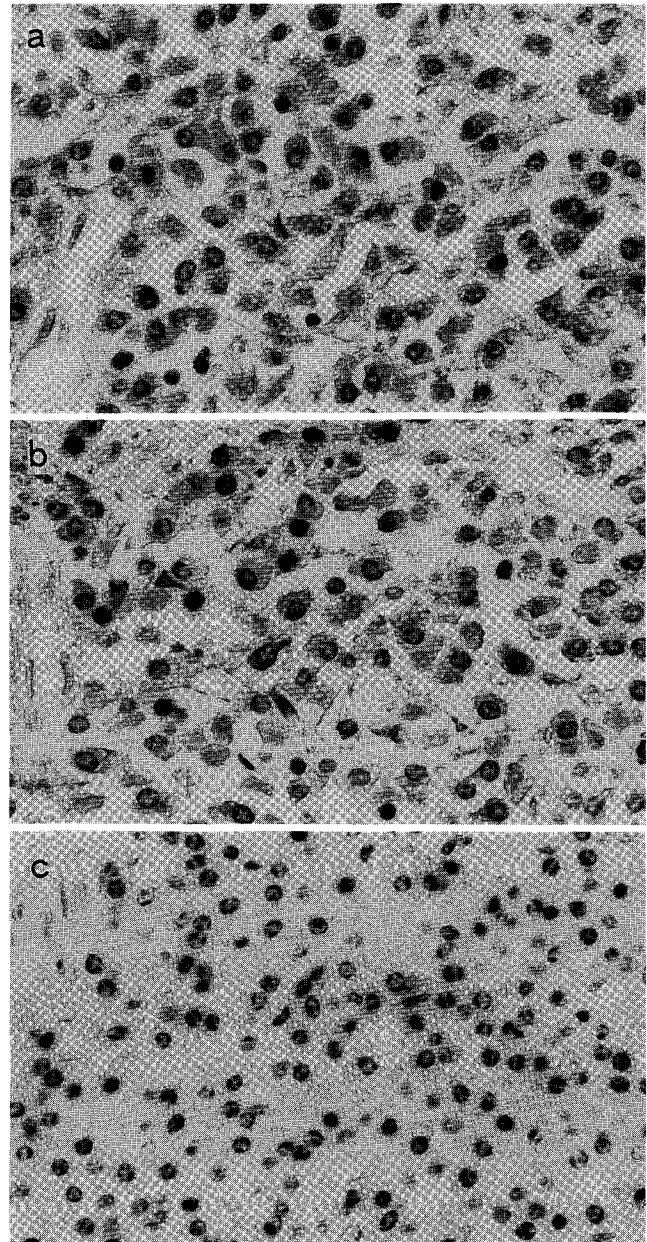


Fig. 3. Immunohistochemical staining of the tumor for immunoglobulin IgA (a) and lambda (b). Nearly all tumor cells are positive for both immunoglobulin IgA and lambda. A section of negative control in which phosphate-buffered saline instead of primary antibody was applied, shows no positive staining (c). ABC immunoperoxidase stain counterstained with hematoxylin (a, b, and c, $\times 1,000$).

plasma cells with a very small number of scattered lymphocytes and macrophages (Fig. 2). The plasma cells were well differentiated with minor variation in nuclear size and cytoplasm content. They had characteristic eccentric nuclei, with clumped chromatin in a cart-wheel-like appearance. Binucleated plasma cells were rarely found. Intracytoplasmic or extracellular Russell bodies were occasionally found (Fig. 2).

The immunoperoxidase technique on formalin-fixed paraffin-embedded tissue, as reported previously (14), demonstrated that the tumor consisted of a monoclonal plasma cell population producing IgA, lambda light chains (Fig. 3). Neither parabronchial nor tracheal lymph nodes, which were resected during the operation, involved tumor cells.

Electron microscopy revealed a tumor composed of well-differentiated plasma cells, exhibiting a heterochromatin pattern of the nuclei, and abundant stacked, rough endoplasmic reticulum, except in the paranuclear region occupied by the Golgi zone (Fig. 4).

Follow-up

The postoperative course was uneventful, and the patient was discharged from the hospital on October 28, 1991. After 12 months of follow-up, there has been no recurrence of the tumor and no clinical, radiologic, biochemical, or hematologic evidence of further extra-

medullary plasmacytoma or myelomatosis.

Discussion

Extramedullary plasmacytoma is a relatively uncommon but distinctive neoplasm. This tumor is most frequently reported in the upper respiratory tract. Other primary sites include the conjunctiva, pleura, mediastinum, ovary, thyroid, kidney, intestine, stomach, lymph nodes, spermatic cord and skin (1-6). A primary origin in the lung is very rare although a few convincing cases have been reported. From the histologic point of view, plasma cell tumors of the lung are classified into two categories; plasmacytoma which is a true primary tumor consisting solely of plasma cells which proliferate monoclonally, and plasma cell granuloma which is an inflammatory reactive process consisting mainly of plasma cells, but the plasma cells are polyclonal, and lymphocytes, leukocytes, and fibroblasts are also present in varying numbers in the tumor and constitute integrated parts of the tumor (15). The latter is easily confused with true pulmonary plasmacytoma both clinically and histologically, and an error in diagnosis has occasionally been made. Although careful examination together with the clinical appearance will lead to the correct diagnosis in most cases, demonstration of the monoclonal nature of the proliferated plasma cells is essential for the exact

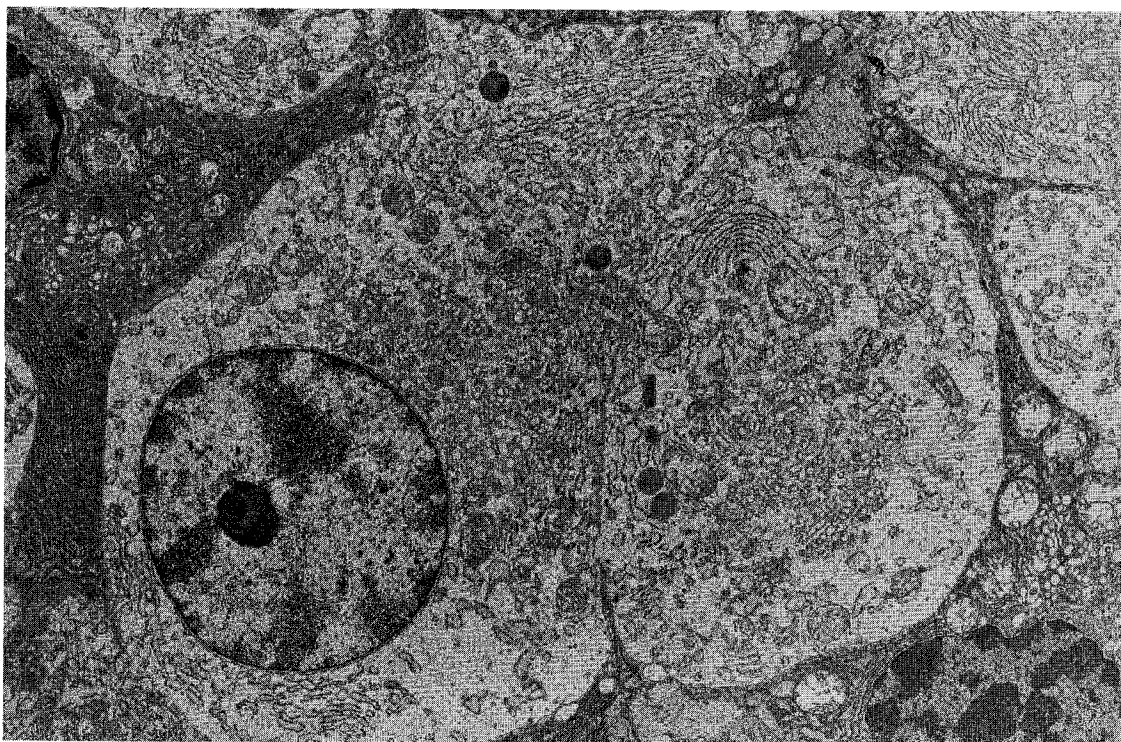


Fig. 4. Electron photomicrograph of the tumor cells, showing peripheral clumping of nuclear chromatin, closely packed rough endoplasmic reticulum, prominent Golgi apparatus, and dense bodies, which are characteristic of plasma cells ($\times 7,500$).

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diagnosis of plasmacytoma. However, in the majority of previously reported cases of pulmonary plasmacytoma, the monoclonal nature of the proliferated plasma cells has not been proved, except for cases associated with urinary secretion of Bence-Jones protein, serum mono-

clonal gammopathy, or subsequently developed metastases or multiple myeloma. Thus, the literature is confused by a number of reports in which the tumors are called pulmonary plasmacytoma, but which in fact appear to be plasma cell granulomas.

Table 1. Clinicopathologic Summary of Reported Cases with Convincing Plasmacytoma of the lung

Case No.	Authors	Age /Sex	Symptoms and signs of tumor	Tumor size /Location	Treatment	Histologic features	Monoclonality	Remarks	Follow-up
1	Robson and Knudsen (1959)	48/F	Cough, sputum, night sweats, chest pain	3 cm/LLL	Thoracotomy and generous resection, and gastrectomy	Plasmacytoma	Later serum M-protein by electrophoresis	Gastric plasmacytoma 9 months after thoracotomy; MM 14 months after gastrectomy	Died 15 months after gastrectomy and autopsied
2	Kernen and Meyer (1966)	67/M	None	6 × 3 × 3 cm/ LUL	Left upper lobectomy and radiation	Malignant plasmacytoma with lymph node metastasis	Serum M-protein by electrophoresis	Autopsy; lymph node and vertebral metastases	Died 3.5 months after surgery
3	Wile et al (1976)	40/M	Fever, cough nasal congestion	12 cm/LLL	Left pneumonectomy	Plasmacytoma	Urine Bence-Jones protein		NS
4	Baroni et al (1977)	14/M	Fever, asthenia weight loss	8 cm/RUL	Right upper lobectomy and chemotherapy	Plasmacytoma	Serum M-protein by electrophoresis	No other lesions	22 months well
5	Amin (1985)	63/M	Cough, shortness of breath, hemoptysis, chest pain	NS/RUL	Biopsy and radiation	Plasmacytoma	Later urine Bence-Jones protein	MM 6 months later Radiation and chemotherapy	Died 7 months after 1st admission
6	Amin (1985)	72/F	Chest pain, shortness of breath	NS/LLL	Lobectomy, incomplete, and radiotherapy	Plasmacytoma	Later serum M-protein	MM 14 months later Radiation and chemotherapy	Died 25 months after 1st admission
7	Amin (1985)	66/F	Lower neck mass and cough	NS/RUL?	Biopsy and radiation	Plasmacytoma	Later serum M-protein	MM 16 months later	Died 4 years after 1st admission
8	Roikjaer and Thomsen (1986)	65/M	None	1) 4 cm/LUL (1976) 2) 6.5 × 6.6 × 3 cm/LLL (1981)	1) Left upper lobectomy 2) Segment resection	Plasmacytomas with different phenotype. 1) IgM, kappa 2) IgG, kappa	Immunohistochemically, monoclonal plasma cell growth	No other lesions	4 years, well after the last operation
9	Morinaga et al (1987)	54/F	Right shoulder pain	3.5 × 3 × 3 cm/ LLL	Left lower lobectomy	Plasmacytoma; IgG, kappa	Immunohistochemically, monoclonal plasma cell growth	Nodular deposits of immunoglobulin No other lesions	6 months, well
10	Present case	55/F	None	2.8 × 2.7 × 2 cm/ RUL	Right upper lobectomy	Plasmacytoma IgA, lambda	Monoclonal plasma cell growth by immunohistochemically	No other lesions	12 months, well

F: female, M: male, LUL: left upper lobe, LLL: left lower lobe, RUL: right upper lobe, RLL: right lower lobe, NS: not specified, M-protein: monoclonal protein, MM: multiple myeloma.

We describe a case with pulmonary plasmacytoma, in which the tumor consisted solely of plasma cells, and the monoclonal nature of the plasma cells was immunohistochemically identified. It is possible to differentiate the monoclonal nature of the plasma cells in plasmacytoma from the polyclonal nature of the cells in plasma cell granuloma using an immunoperoxidase technique (12, 13, 16). To our knowledge, only 10 convincing cases of pulmonary plasmacytoma have been reported in the English literature, including the present case (7–13) (Table 1). Five were male and 5 female, having a mean age of 54.4 years (range, 14 to 72). Eight of the 10 cases were over the age of 50, and half of the cases were older than 60 years of age. Half of the reported cases subsequently developed generalized myelomatosis or multiple myeloma within 16 months, all of whom had serum M-protein or urine Bence-Jones protein and died within 4 years, indicating that half of the cases of pulmonary plasmacytoma represent the initial manifestation of multiple myeloma, and that the presence of serum M-protein or urine Bence-Jones protein at the initial diagnosis may be a hallmark of later progression to multiple myeloma or generalized myelomatosis. The presenting symptoms were cough and pain, which were found in 4 cases, followed by fever or shortness of breath in two. However, there were no symptoms in three cases. Although the lesion was solitary in nine of the ten cases, one interesting case reported by Roikjaer and Thomsen (12) had two tumors of different immunologic type in different lobes of the lung, occurring within an interval of 5 years. Five lesions were located in the left lower lobe of the lung, 4 in the right upper lobe, and two in the left upper lobe. The case presented herein had no serum M-protein or urine Bence-Jones protein and no evidence for generalized myelomatosis or multiple myeloma at the time of hospitalization. Furthermore, during the 12-month follow-up, there has been no recurrence of the tumor and no clinical, radiologic, biochemical, or hematological evidence of further generalized myelomatosis or multiple myeloma, indicating that the tumor of the present case was solitary and localized only in the lung, and is considered to be a localized primary extramedullary plasmacytoma of the lung.

Histologically, plasmacytoma consists solely of plasma cells with delicate vascular stroma and differs from plasma cell granuloma which is composed of an admixture of other types of inflammatory cells, including histiocytes, and varying amounts of fibroblasts. Lymphoid follicles are not found in plasmacytoma in contrast to plasma cell granuloma. Proliferated plasma cells in plasmacytoma often exhibit nuclear pleomorphism, but cellular atypia is usually mild and mitotic figures are rarely found,

giving an appearance of well-developed plasma cells (7–13). Therefore, in the differentiation from plasma cell granuloma, demonstration of the monoclonal nature of the plasma cells is essential for the pathologic diagnosis of plasmacytoma.

The first choice of treatment is resection of the tumor, and chemotherapy may be added depending on the presence or absence of multiple myeloma. Since it is generally accepted that plasmacytomas are radiosensitive, radiation therapy may be effective. However, prognosis is poor in cases who develop generalized myelomatosis; all reported cases have died within 4 years (8, 11).

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