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Case report

An unusual tumour of the lung

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Key words

Mastocytoma • Lung • Mast cells • Tumour

Summary

We report a case of a 51-year-old woman with a solitary mast cell tumour of the lung, a rare neoplasm with only three previously-reported cases reported in the literature. Unlike previous cases, the tumour in the present case was bulky, measuring 14 cm in diameter and budding into the segmental bronchus. Histologically, it showed proliferation of typical metachromatic mast cells intermingled with undifferentiated cells with a ratio of 3:1. The neoplastic mast cells stained strongly with tryptase, CD117, CD68 and CD45, CD14 and CD33; whereas the undifferentiated cells lacked all these markers and expressed EMA and cytokeratin. Histological examination of bone marrow and laboratory data were unremarkable. To our knowledge, this is the fourth case of solitary extracutaneous mastocytoma of the lung. The differentiating features of this neoplasm and a review of literature are presented.

Introduction

Mastocytosis is a local or systemic disease characterised by infiltration and expansion of mast cells in various tissues [1]. The WHO classification for mastocytosis includes two major categories, namely cutaneous mastocytosis (CM) and systemic mastocytosis (SM). In CM, mast cell infiltration remains confined to the skin, whereas SM is characterised by involvement of at least one extracutaneous organ with no evidence of skin lesions. Extracutaneous mastocytoma (ECM) is a variant of SM defined by a localised tumour consisting of accumulation of mature-appearing mast cells with indistinct cytology and a non-destructive growth pattern [2]. ECM of the lung is extremely rare; to our knowledge, only three cases have been reported in the literature to date [3]. We report the fourth case of solitary mastocytoma of the lung and compare our findings with the available literature.

Case presentation

A 51-year-old woman presented with a history of dyspnoea, chest pain and cough evolving for one week. Her physical examination was unremarkable. There were no cutaneous lesions, hepatosplenomegaly or lymphadenopathy. The patient had no history of urticaria or allergy.

Laboratory examinations yielded a peripheral white blood cell count of 5600 cells/mm^3 with 56.8% neutrophils, 33.6% lymphocytes, 8% monocytes, 0.9% eosinophilic cells and 0.7% basophilic cells. Red blood cell counts and thrombocytes were normal.

Chest X-ray and computed tomography scan of the chest showed a round well-circumscribed mass without calcification measuring 15 ´ 11 cm in the right lower lung field with numerous small mediastinal lymphadenopathies. Abdominopelvic ultrasonography revealed no other lesions, and none in the liver and the spleen.

A biopsy of the tumour was obtained. At histological examination, the tumour was composed of a diffuse infiltration of uniform, densely packed, mature mast cells with eccentric round to ovoid small nuclei, and abundant faintly eosinophilic granular cytoplasm. These cells were intermingled with undifferentiated cells with clear non-granular cytoplasm and large oval to reniform vesicular nuclei (Fig. 1). The undifferentiated cells represented approximately one-third of the total neoplastic cell population. Mitotic figures were not present. Special stains (toluidine blue) revealed the presence of blue to

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Fig. 1. Mast cell tumour containing numerous mast cells with abundant eosinophilic cytoplasm and undifferentiated cells with no granules (haematoxylin eosin: x400).

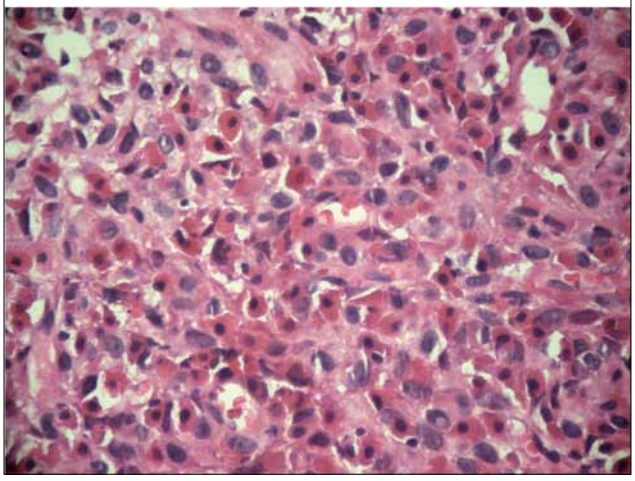
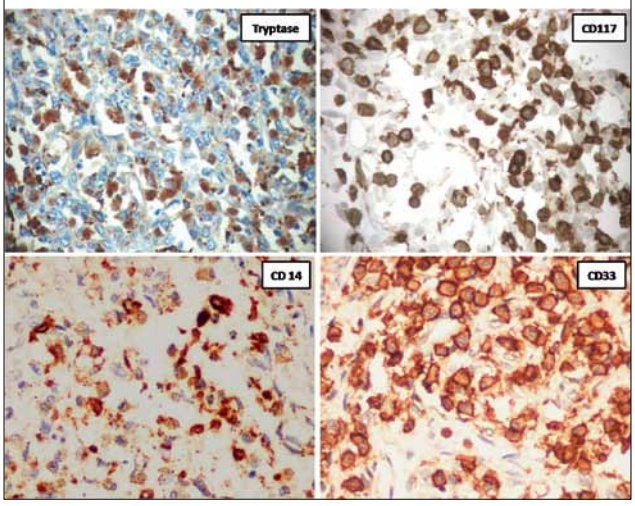


Fig. 3. Immunohistochemical reactivity of mast cells with tryptase, CD117, CD14 and CD33.



violet metachromatic granules within the cytoplasm of mast cells (Fig. 2). Immunohistochemical study demonstrated strong immunoreactivity with tryptase, CD117, CD68, CD14, CD45 (LCA) and CD33. The undifferentiated cells had no granules and lacked all these markers, but were strongly positive for EMA and showed weak positivity for cytokeratin (CK). The immunostaining for cytokeratin was restricted to cells that lied beneath the bronchial epithelium (Fig. 3). Neoplastic cells lacked CD2, CD25 and myeloperoxidase (MPO). Nuclear immunolabelling for Ki-67 was present in less than 1% of all neoplastic cells. Considering all these findings, a diagnosis of mastocytoma of the lung was suggested. The right lower and medium lobes of the lung were resected. Grossly, resected lobes measured 22 x 18 x 11 cm. On dissection, a well-circumscribed white yellowish solid, non-tender nodule with haemorrhagic changes measuring 14 x 13 x 11 cm was found in this area, and was associated with an endobronchial mass (Fig. 4). Histo-

Fig. 4. Positive immunostaining of undifferentiated cells for EMA and cytokeratin.

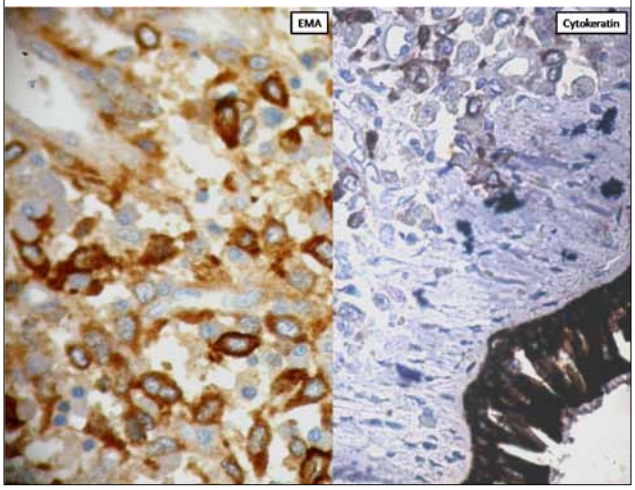
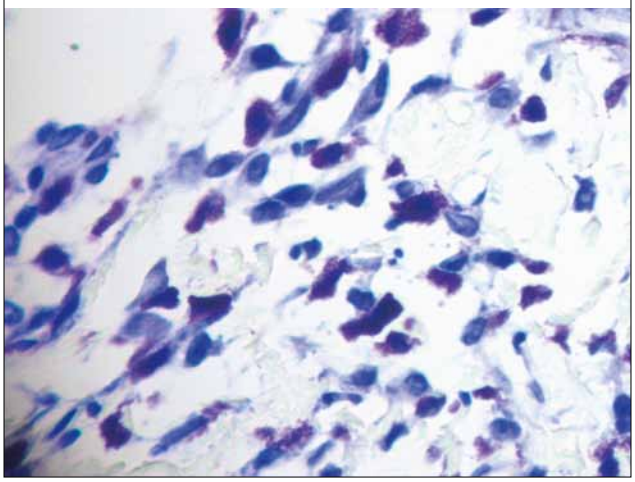


Fig. 2. Mast cells are highlighted with toluidine blue stain (x400).



logically, the tumour communicated focally with the segmental bronchus, and contained a thin fibrovascular stroma with foci of haemorrhage. Numerous lymphocytes were identified in some areas (Fig. 5). Entrapped terminal bronchioles and alveoli were seen also in the periphery of the tumour. There was no vascular invasion. The nodule was defined sharply from the surrounding parenchyma by a thin fibrous capsule and extended to within 0.1 cm of the overlying pleura (Fig. 6). Lymphadenopathies were not neoplastic. Examination of bone marrow showed no infiltration by mast cells and no haematopoietic or lymphoid disorder.

On the basis of histological and immunohistochemical results, and considering the World Health Organization (WHO) classification of mastocytosis, a diagnosis of extracutaneous mast cell tumour of the lung was made. The patient remains free from symptoms or relapse at 20 months after surgery.

Fig. 5. The cut surface shows a well demarcated whitish-yellow mass with foci of haemorrhage. Note the polypoid endobronchial mass (æ).

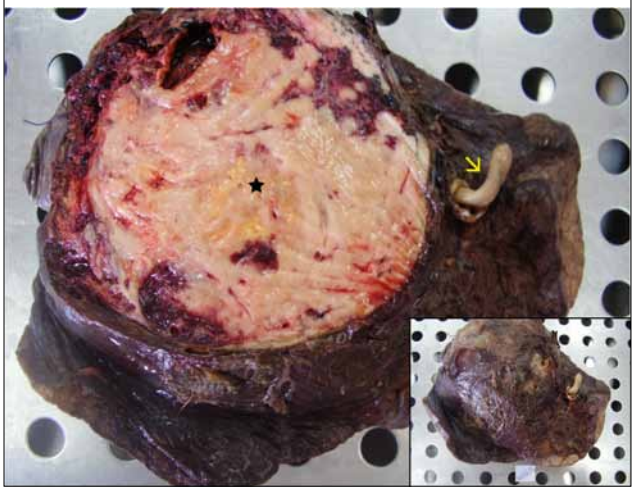
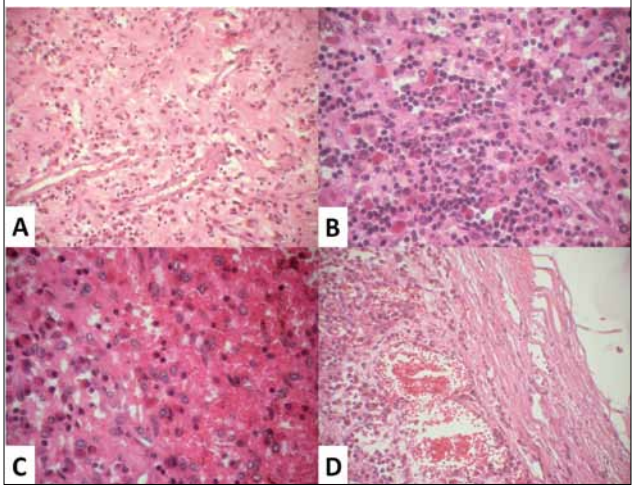


Fig. 6. (A) Haemangiopericytomatous vascular pattern. (B) Prominent lymphocytes infiltrate among tumour cells. (C) Focal areas of haemorrhage are present within the tumour. (D) The tumour is well delineated by a variably thick but distinct capsule (haematoxylin eosin: x400).



Discussion

Solitary extracutaneous mast cell neoplasms, either presenting as malignancy (mast cell sarcoma) or as benign tumours (extracutaneous mastocytoma: ECM) are very rare [4]. According to Mihm, a solitary mast cell tumour can affect the bone, spleen and lung [3]. Solitary mastocytoma of the lung is extremely rare; this is somewhat unexpected because in the normal human lung many mast cells can be demonstrated in perivascular and peribronchial connective tissue, in pleura, and to a lesser extent, in alveolar walls [1]. In 1965, Shervin et al. first reported a case of solitary "mast cell granuloma" of the lung. At the time, pathologists had difficulty in distinguishing the histological pattern of mast cell tumours from plasmacytoma because staining procedures and immunohistochemical markers were not well-established [4]. In 1966, Charrette et al. also reported a similar case that they termed "mast cell tumour" of the lung [1] and in 1988 Kudo et al. reported a similar third case [3]. To our knowledge, there have been no additional reports in the literature and our case thus represents the fourth (Tab. I).

Clinical and macroscopic features of mastocytoma are non-specific [6]. In the three previous reports, all patients were asymptomatic and the size of the lesion did not exceed 2.5 cm; in our case, the patient had respiratory symptoms and the tumour measured 14 cm in diameter. Grossly, mastocytomas are well circumscribed. Unlike the previous reports, the tumour in our case was locally aggressive, budding into the segmental bronchus. Kudo et al. observed entrapment of terminal bronchioles and alveoli without endobronchial budding [3]. Large areas of haemorrhage, as seen in our case, were not previously reported, although a few focal hemosiderin deposits

Tab. I. Published cases of solitary mast cell tumours of the lung.

Author (year)	Clinical findings Age	Gender	Symptoms	Location	Size (cm)	Histological findings	Communication with bronchi	Therapy	Follow-up (months)
Sherwin et al. (1965)	57	F	Asym*	Right upper lobe	2.5	Proliferation of mast cells and histiocytes	–	Right upper lobectomy	–
Charrette et al. (1966)	68	F	Asym*	Right upper lobe	2	Proliferation of mast cells and epithelioid cells	–	Right upper lobectomy	–
Kudo et al. (1988)	53	M	Asym*	Leftupper lobe	1.6	Proliferation of mast cells and clear cells	–	Partial resection of right upper lobe	2
Current case (2012)	51	F	Chest pain Cough dyspnea	Right lower and medium lobes	14	Proliferation of mast cells and undifferentiated cells	+	Resection of upper and medium right lobes	4

* Asymptomatic.

were present in the case reported by Sherwin et al. [4]. However, necrosis was not seen either in our case or in the previous reports.

Despite the indolent course of the disease, vascular invasion was reported by Kudo et al. [3].

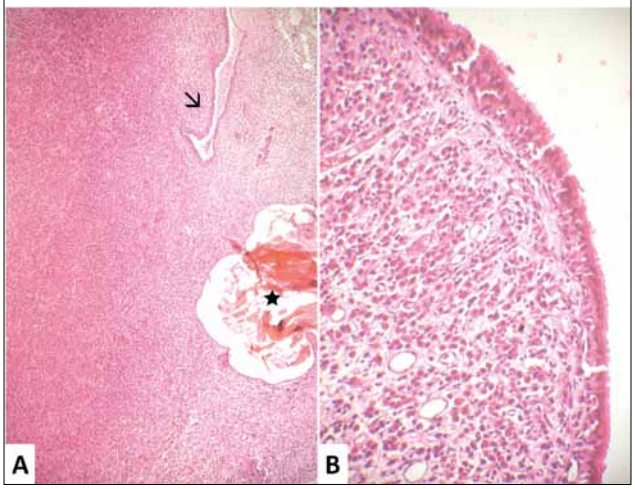
Mast cells are easily recognisable with special stains (toluidine blue, Giemsa and chloroacetate esterase). On immunohistochemistry, these cells express tryptase, CD117, CD33, CD43 and CD68. Of all these markers, tryptase is the most lineage specific, but may show high background staining in some cases. CD2 and/or CD25 may be aberrantly expressed in mast cells. A panel of tryptase, CD25 and CD117 is recommended to aid in confirming the mast cell lineage of the proliferation and to potentially identify an aberrant immunophenotype (CD25) [2].

In pulmonary mastocytomas, mast cells are intermixed with another type of cells; in the case of Sherwin et al., the lesion was composed of large histiocytes with a single prominent nucleolus and numerous interspersed mast cells [4], while in the case of Charrette et al. the tumour was composed of numerous mast cells and epithelioid cells [1]. In the case of Kudo et al., the mast cells were intermingled with clear cells [3]. The nature of these cells is controversial and there have been various hypotheses concerning their histogenesis (epithelial cells, plasmocytes, histiocytes, immature mast cells). In our case, these cells were strongly positive for EMA and showed focal immunostaining for cytokeratin that was limited to the tumour cells lying beneath the bronchial epithelium; these results may favour an epithelial origin. Positive immunostaining of the undifferentiated cells for EMA was reported by Kudo et al. [3], who considered that result confounding; however, positivity for cytokeratin has never been described. The positivity for cytokeratin demonstrated in our case is effective since it was confirmed by the positivity of the internal control (represented by the adjacent bronchial epithelium). Nevertheless, it should be noted that neither EMA nor cytokeratin are completely specific for epithelial origin since both markers can be aberrantly expressed in sarcomas and lymphomas [7-10]. On the other hand, the weakness as well as the highly focal character of staining for cytokeratin leads us to wonder if this staining is also aberrant.

If one admits that the undifferentiated cells are epithelial cells, then this tumour must be distinguished from sclerosing haemangioma. Sclerosing haemangioma of the lung is a benign neoplasm of epithelial origin with infiltrating mast cells; it differs from mastocytoma by the papillary and sclerotic architectural patterns and the presence of large blood-filled spaces [11]. Nonetheless, further studies are necessary to clarify the nature of the undifferentiated cells as well as the histogenesis of this tumour.

ECM should be distinguished from mast cell sarcoma, which is an extremely rare localised tumour that occurs in the absence of skin lesions or other systemic symptoms, and characterized by atypical mast cells with a destructive growth pattern [12]. In our case, mast cells showed no nuclear atypia and no mitotic activity, with low expression of Ki-67 (1%), but the tumour budded into the segmental bronchus and focally infiltrated its wall. Considering these findings, we concluded that this was a solitary mast cell tumour of the lung.

Fig. 7. (A) Entrapped terminal bronchioles (æ) and alveoli are seen in the periphery of the tumour (HE x200). (B) The polypoid endobronchial component showing the mast cell tumour growing in the submucosa of the bronchus can be seen. Note the preserved, intact respiratory epithelium (haematoxylin eosin: x400).



Differential diagnosis also includes systemic mastocytosis with involvement of the lung, which is also a very uncommon situation, with only a few cases reported in the literature [1]. Therefore, a diagnosis of ECM should be established only after careful investigation and definitive exclusion of all other SM criteria. In some instances, the haematopathologist may ask for another organ biopsy to detect a second infiltrate before making a final diagnosis of ECM. In our case, the bone marrow and the abdominopelvic ultrasonography were unremarkable [6].

The clinical course of ECM of the lung is that of a benign tumour with complete remission after resection [6]. Progression to aggressive disease has not been reported. In conclusion, solitary mastocytoma of the lung may present clinically as a malignant neoplasm. Once diagnosed, further investigations are recommended to rule out systemic mastocytosis with worse prognosis.

Acknowledgements

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References

1 Charrette EE, Mariano Av, Laforet EG. *Solitary mast cell "tumor" of the lung*. Arch Int Med 1966;118:358-62.

2 Horny HP, Metcalfe DD, Bennett JM, et al. *Mastocytosis*. In: S*werdlow S, Campo E, Lee Harris N, eds. WHO Classification of Tumours of Haematopoieticand Lymphoid Tissue*. 4th. Lyon: IARC Press 2008, pp. 54-63.

[3] Kudo H, Morinaga S, Shimosato Y, et al. *Solitary mast cell tumor of the lung*. Cancer1988;6:2089-94.

[4] Sherwin RP, Kern WH, Jones JC. *Solitary mast cell granuloma (histiocytoma) of the lung. A histologic, tissue culture and time-lapse cinematographic study*. Cancer 1965;18:634-41.

[5] Horny HP, Soltar K, Valent P. *Mastocytosis*. In Jaffe ES, Harris NL, Vadirman JW, et al., eds. *Hematopathology*. Philadelphia, PA: Saunders 2011, pp. 757-76.

[6] Valent P, Horny HP, Escribano L, et al. *Diagnostic criteria and classification of mastocytosis: a consensus proposal*. Leuk Res 2001;25:603-25.

[7] Layfield LJ, Emerson L, Crim JR, et al. *Squamous differentiation and cytokeratin expression in an osteosarcoma: a case report and review of the literature*. Clin Med Pathol 2008;1:55-9.

[8] Pinkus GS, Kurtin PJ. *Epithelial membrane antigen: A diagnostic discrimitant in surgical pathology*. Hum Pathol 1985;16:929-40.

[9] Chau K, Allen J. *Aberrant cytokeratin immunoreactivity in sarcomas*. Applied Immunohistochemistry and Molecular Morphology 1999;7:88.

[10] Nguyen TT, Kreisel FH, Frater JL, et al. *Anaplastic large-cell lymphoma with aberrant expression of multiple cytokeratins masquerading as metastatic carcinoma of unknown primary*. J Clin Oncol 2013;31:e443-5.

[11] Keylock JB, Galvin JR, Franks TJ. *Pulmonary sclerosing hemangioma*. Arch Pathol Lab Med 2009;133:820-5.

[12] Horny HP, Sotlar K, Valent P. *Mastocytosis: state of the art*. Pathobiology 2007;74:121-32.