CASE REPORT

BALToma masquerading as pulmonary tuberculosis

Rahul Magazine,¹ Hameed Aboobackar Shahul,¹ Vidya Monappa,² Bharti Chogtu³¹Department of Pulmonary Medicine, Kasturba Medical College, Manipal, Karnataka, India²Department of Pathology, Kasturba Medical College, Manipal, Karnataka, India³Department of Pharmacology, Kasturba Medical College, Manipal, Karnataka, India**Correspondence to**Dr Hameed Aboobackar Shahul,
doctorshahul@yahoo.com

Accepted 23 October 2014

SUMMARY

A 53-year-old man with a significant smoking history presented with chronic cough, exertional breathlessness, intermittent fever, weight loss and anorexia. A review of his past medical records revealed he was diagnosed to have sputum smear-positive pulmonary tuberculosis 5 years earlier, for which he had received multiple courses of incomplete antitubercular therapy. This time, though he was primarily suspected to have active pulmonary tuberculosis, lack of microbiological evidence and further investigations including histopathological evaluation of lung lesions confirmed a diagnosis of Marginal zone B cell lymphoma of mucosa-associated lymphoid tissue (MALToma/BALToma). The patient was managed with radical radiation therapy to which he responded well.

BACKGROUND

BALToma (B-cell lymphoma of bronchus-associated lymphoid tissue) is a low-grade non-Hodgkin's lymphoma that presents with unilateral or bilateral pulmonary involvement.¹ It constitutes only 0.5–1% of malignant tumours of the lung.² It has been observed that there is an association between chronic inflammatory conditions and BALToma.³ Coexistence of BALToma with tuberculosis has been reported.⁴ The clinical and radiological features of BALToma are non-specific and hence can easily be confused with other more common lung diseases.⁵ We present a case of BALToma who had a history of inadequately treated pulmonary tuberculosis and hence was misdiagnosed as a case of relapse of pulmonary tuberculosis.

CASE PRESENTATION

A 53-year-old man presented to the outpatient department of pulmonary medicine with a 5-year history of productive cough, 1-year history of exertional breathlessness and intermittent fever, significant weight loss and anorexia of 15 days duration. Review of his past medical records revealed that he had been diagnosed with sputum smear-positive pulmonary tuberculosis 5 years earlier and had been prescribed antitubercular therapy (ATT), which he had defaulted on multiple occasions. He was a chronic smoker and he consumed alcohol. General physical examination was normal with no significant palpable lymphadenopathy. He was afebrile with a respiratory rate of 24/min, pulse rate of 108/min and blood pressure of 110/80 mm Hg. Chest examination revealed end inspiratory crepitations over right infra-axillary, infrascapular and interscapular areas and bronchial breath sounds over the right infrascapular area. Examination of cardiovascular system, abdomen and other systems

did not reveal any abnormality. There was no palpable hepatosplenomegaly.

INVESTIGATIONS

A haemogram showed a low haemoglobin level (10.4 g/dL), leucocytosis (12 800/mm³) with neutrophilia and an elevated erythrocyte sedimentation rate (67 mm/h). The patient's random blood sugar, serum electrolyte levels, renal and liver function tests were normal. Routine urine analysis was unremarkable. Sputum Gram staining, Ziehl-Neelsen staining for mycobacteria and bacterial culture were normal. Similar results were obtained when sputum analysis was repeated. Frontal view of the chest roentgenogram (figure 1) showed left upper zone cavities with bilateral lower zone consolidation. CT of the thorax (figure 2) revealed bilateral cavities, areas of consolidation and ground glassing with centrilobular nodules, predominantly over the right side, in addition to multiple emphysematous bullae over the right apex and a few left hilar lymph nodes, the largest measuring 2×1.4 cm. CT findings were compatible with a mixture of healed tubercular lesions and active tuberculosis, but with a fair suspicion of malignancy.

Since active tuberculosis could not be proved by sputum smear microscopy, a fibre optic bronchoscopy was planned so as to facilitate examination of bronchoalveolar lavage (BAL) fluid by smear microscopy and mycobacterial culture and later on

Figure 1 Chest roentgenogram showing left upper zone cavities with bilateral lower zone consolidation.

CrossMark

To cite: Magazine R, Shahul HA, Monappa V, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-206997

Figure 2 Contrast-enhanced CT of the thorax showing bilateral cavities ((A) white arrows) and areas of consolidations ((B) white arrows), in addition to multiple emphysematous bullae over the right apex ((B) black arrow).

for drug sensitivity tests in case of culture positivity. A bronchoscopic examination would also detect any intrabronchial lesion and facilitate biopsy. However, fibreoptic bronchoscopy did not reveal any major abnormality. BAL fluid smear for acid-fast bacilli (AFB) and mycobacterial culture was negative while bacterial and fungal cultures were sterile.

Considering the extent of the radiological lesions, active tuberculosis in the absence of microbiological evidence from sputum and BAL smear microscopy and mycobacterial culture seemed unlikely. Hence, we felt that a trial of second line ATT at this point was not justified and a biopsy from the lesion seemed a more feasible test for definitive diagnosis. CT-guided Trucut biopsy (figure 3) of the right-sided consolidation showed diffuse sheets of monotonous small lymphoid cells with round nucleus, fine chromatin and scant cytoplasm. Immunohistochemical studies showed that the neoplastic lymphoid cells were positive for CD20 and negative for CD3, CD5, CD23 and cyclin D1. The presence of lymphoepithelial islands (figure 3; black arrow) was a clue to the diagnosis of mucosa-associated lymphoid tissue lymphoma. Bone marrow cytology and biopsy did not reveal any evidence of marrow infiltration.

Figure 3 Lung biopsy showing diffuse sheets of monotonous small lymphoid cells with round nucleus, fine chromatin and scant cytoplasm. Black arrow shows bronchial glands with intraepithelial lymphocytes (lymphoepithelial islands) H&E, $\times 200$.

DIFFERENTIAL DIAGNOSIS

We evaluated the case with a provisional diagnosis of active pulmonary tuberculosis as the presenting symptoms and radiological features were suggestive of the same. The failure to respond to ATT in the past was thought to be due to development of resistance to one or more drugs or non-compliance to treatment. It can also result from underlying immunocompromised states such as HIV/AIDS, uncontrolled diabetes mellitus or chronic kidney disease. Alternatively, some patients may continue to have symptoms despite sputum conversion (from AFB positive to negative) due to the development of complications such as bronchiectasis, recurrent secondary infections, aspergillosis, extensive fibrosis and scarring. Scar carcinoma is a rare differential diagnosis in this clinical setting. Moreover, BALTomas once suspected have to be differentiated from follicular lymphomas, chronic lymphocytic leukaemia, small lymphocytic lymphoma and mantle cell lymphoma by immunohistochemical studies. In BALTomas, neoplastic lymphoid cells are positive for CD20 and negative for CD3, CD5, CD23 and cyclinD1. Follicular lymphomas show a typical follicular pattern (that may be difficult to appreciate on needle biopsies). Low and intermediate grade follicular lymphomas often show many cells with cleaved nuclei. Chronic lymphocytic leukaemia/small lymphocytic lymphoma is CD23 positive and Mantle cell lymphoma is cyclinD1 and CD5 positive.^{6 7} Lymphoepithelial islands are diagnostic histopathological clues.⁸

TREATMENT

The patient was referred to the department of radiation oncology where he was staged to have stage extranodal disease and managed with radical radiation therapy to mediastinum in addition to antibiotics and other supportive care.

OUTCOME AND FOLLOW-UP

The patient successfully completed the course of radiotherapy without major intolerance. He improved symptomatically and his chest symptoms were well controlled at follow-up after 10 months from completion of therapy.

DISCUSSION

Though primary pulmonary lymphomas are rare, approximately 70% of them are BALTomas.⁹ BALTomas usually have an indolent clinical course. Most patients are asymptomatic and when present, symptoms are non-specific and include dyspnoea,

cough, fever, haemoptysis and weight loss.¹⁰ They can have varied presentations radiologically—consolidations, ground glassing, small and large nodules, effusions or cavitations.¹¹ The presentation of the patient is frequently attributed to tuberculosis, primarily due to the similarity in symptoms and abnormal radiological findings. In the absence of a proper diagnostic work up, many physicians tend to treat these patients empirically with antitubercular therapy, especially in primary healthcare facilities in developing countries.

In the present case, this approach led to the patient receiving multiple courses of antitubercular therapy by physicians outside our centre, without microbiological evidence. At our centre we could, however, rule out active tuberculosis with a BAL fluid analysis—the smear for AFB and mycobacterial culture was negative.

Some reports have proposed BALToma development to be associated with chronic inflammation and autoimmune diseases.³ Askling and Ekblom¹² reported an increasing risk of non-Hodgkin lymphoma in patients following pulmonary tuberculosis infection who have received inadequate chemotherapy.

Considering the history of smear positive pulmonary tuberculosis and improper chemotherapy in our case, this association seems likely. It has been proposed that T-cell and macrophage activation in tuberculosis induces B-cell proliferation that leads to the development of BALToma. Coexistence of active pulmonary tuberculosis and BALToma has also been reported in the literature.⁴ Hence, in a developing country such as India, where the incidence of pulmonary tuberculosis is high, it is important that we rule out such coexistence. There have also been cases reported in the literature, which link BALToma with amyloid deposits in patients with coexisting Sjogren's syndrome,¹³ fungal ball¹⁴ and hyalinising granuloma.¹⁵

A lung tissue sampling for histopathological examination and immunological studies will help to clinch the diagnosis and rule out alternative diagnoses. Transthoracic Trucut needle biopsy under CT guidance is favoured, as it might provide sufficient tissue samples in lung lesions for immunological studies.¹⁶

Learning points

- ▶ B-cell lymphoma of bronchus-associated lymphoid tissue (BALTomas) should be included in the differential diagnosis of patients with chronic pulmonary symptoms, especially in the setting of improperly treated pulmonary tuberculosis.
- ▶ A tissue diagnosis is indicated in cases presenting with consolidations that do not respond to antibiotics or antitubercular therapy.
- ▶ A lung biopsy is ideal for diagnosis and sufficient tissue samples should be obtained for immunological studies.

BALTomas should be considered in patients presenting with chronic pulmonary symptoms or as a non-resolving pneumonia, especially if the patient has associated history of chronic inflammatory disease. Our case highlights the importance of further diagnostic work up and tissue diagnosis in such cases, particularly if the microbiological evidence does not reveal the presence of any active infection.

Contributors RM was involved in the management of the case and manuscript revision. HAS was involved in the preparation of the draft manuscript. VM interpreted the pathological reports and revised the manuscript. BC was involved in revising the manuscript for important intellectual content.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Karadag F, Polatli M, Kacar F, *et al.* A Case of baltoma diagnosed by transthoracic true-cut needle biopsy. *Turk Respir J* 2004;5:178–82.
- 2 Rivera CM, Vilaplana MB, Adiego CS, *et al.* Primary pulmonary lymphoma presenting as a pulmonary mass with cavitation. *Arch Bronconeumol* 2004;40:94–6.
- 3 Isaacson PG. Mucosa-associated lymphoid tissue lymphoma. *Semin Hematol* 1999;36:139–47.
- 4 Inadome Y, Ikezawa T, Oyasu R, *et al.* Malignant lymphoma of bronchus-associated lymphoid tissue (BALT) coexistent with pulmonary tuberculosis. *Pathol Int* 2001;51:807–11.
- 5 Li AW, Xu JF, Zhou CC, *et al.* Clinical characteristics and diagnosis of pulmonary mucosa associated lymphoid tissue-derived (MALT) lymphoma: a retrospective analysis of 29 cases. *Zhonghua Zhong Liu Za Zhi* 2012;34:390–3.
- 6 Ahmed S, Siddiqui AK, Rai KR. Low-grade B-cell bronchial associated lymphoid tissue (BALT) lymphoma. *Cancer Invest* 2002;20:1058–68.
- 7 Wotherspoon AC, Dogan A, Du MQ. Mucosa-associated lymphoid tissue lymphoma. *Hematology* 2002;9:50–5.
- 8 Harris NL. Low grade B-cell lymphoma of mucosa-associated lymphoid tissue and monocytoid B-cell lymphoma: related entities that are distinct from other low grade B cell lymphomas. *Arch Pathol Lab Med* 1993;117:771–5.
- 9 Fitch M, Capron F, Berger F, *et al.* Primary pulmonary non-Hodgkin's lymphomas. *Histopathology* 1995;26:527–9.
- 10 Ahmed S, Kussick SJ, Siddiqui AK, *et al.* Bronchial-associated lymphoid tissue lymphoma: a clinical study of a rare disease. *Eur J Cancer* 2004;40:1320–6.
- 11 Bae YA, Lee KS, Han J, *et al.* Marginal zone B-cell lymphoma of bronchus-associated lymphoid tissue: imaging findings in 21 patients. *Chest* 2008;133:433–40.
- 12 Askling J, Ekblom A. Risk of non-Hodgkin's lymphoma following tuberculosis. *Br J Cancer* 2001;84:113–15.
- 13 Nakamura N, Yamada G, Itoh T, *et al.* Pulmonary MALT lymphoma with amyloid production in a patient with primary Sjogren's syndrome. *Intern Med* 2002;41:309–11.
- 14 Mhawech P, Krishnan B, Shahab I. Primary pulmonary mucosa associated lymphoid tissue lymphoma with associated fungal ball in a patient with human immunodeficiency virus infection. *Arch Pathol Lab Med* 2000;124:1506–9.
- 15 Ben Y, Raitz EAN, Lee KR, *et al.* Pulmonary small lymphocytic lymphoma (mucosa associated lymphoid tissue type) associated with pulmonary hyalinizing granuloma. *Chest* 2001;120:1027–30.
- 16 Wong PW, Stefanec T, Brown K, *et al.* Role of fine-needle aspirates of focal lung lesions in patients with hematologic malignancies. *Chest* 2002;121:527–32.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow