CASE REPORT

Lung consolidation responding to chemotherapy

Prasanth Balasubramaniam,¹ Ram V Nampoothiri,² Nalini Gupta,² Pankaj Malhotra^{1,3}¹Department of Internal Medicine, PGIMER, Chandigarh, India²PGIMER, Chandigarh, India³Department of Hematology, PGIMER, Chandigarh, India

Correspondence to

Dr Pankaj Malhotra, hematpgi@gmail.com

Accepted 6 January 2017

SUMMARY

Consolidations in the pulmonary parenchyma are mostly infective, although they can rarely be due to autoimmune and neoplastic processes. Consolidations, especially in the setting of underlying immunosuppressive haematological malignancy, are usually presumed infective by the treating physician. Pulmonary involvement in chronic lymphocytic leukaemia presenting as consolidations and type 1 respiratory failure, responding to systemic chemotherapy, is a rare and uncommon presentation.

BACKGROUND

Chronic lymphocytic leukaemia (CLL), the most common leukaemia in the west, constitutes ~30% of all adult leukaemias.¹ Pulmonary involvement is seen in up to 40% of cases in CLL in autopsy studies. However, most of these infiltrations are patchy, asymptomatic and do not appear on chest radiographs.^{2 3} We describe a case of CLL who presented with type 1 respiratory failure. On investigation, he had lung consolidation secondary to leukaemic infiltrates which was proven by fine needle aspiration cytology. The condition of the patient improved after initiation of chemotherapy. We discuss the differential diagnosis of lung nodules in patients with CLL with a review of previous literature.

CASE PRESENTATION

A man aged 71 years was diagnosed with CLL in 2009 when he was incidentally found to have raised total white cell count (WCC—152 000 cells/ μ L). Further investigations revealed that he had anaemia (haemoglobin of 86 g/L) and thrombocytopenia (platelet count—74 000/ μ L). He was staged as Binet-C and Rai IV and was started on chlorambucil (45 mg/m² over 5 days) and prednisolone (60 mg/m²/day for 5 days) regimen given every 28 days. The chemotherapy was stopped after 10 cycles as his anaemia and thrombocytopenia recovered (haemoglobin of 121 g/L, platelet count of 167 000/ μ L) with raised total white cell count (WCC—62 000 cells/ μ L). He was thereafter kept under observation with regular follow-up. He presented in September 2016 with cough of 2 months duration, which increased over 1 week, with scanty expectoration. This was associated with severe dyspnoea (grade IV in Modified Medical Research Council (MMRC) dyspnoea scale). There was no history of fever, wheeze, orthopnoea or paroxysmal nocturnal dyspnoea. On examination, the patient was conscious and oriented but was dyspnoeic at rest. He had tachycardia (pulse rate—120 bpm), blood pressure of 110/76 mm Hg and a

respiratory rate of 36 breaths/min with a peripheral oxygen saturation of 90% on room air. General physical examination revealed pallor and subcentric generalised lymphadenopathy. Respiratory system examination revealed bronchial breath sounds associated with coarse crackles in both the basal lung fields. The rest of the cardiovascular, abdominal and central nervous system examination was within normal limits. The patient's blood counts revealed anaemia with haemoglobin—72 g/L (normocytic and normochromic), raised white cell count which was lymphocyte predominant (TLC—175 $\times 10^9$ /L, differential counts—polymorphs 6%, lymphocytes 91%, eosinophils 1% and monocytes 2%) and a platelet count of 191 $\times 10^3$ /L. Peripheral smear showed mature lymphocyte predominance with occasional smudge cells. Cytogenetics from peripheral blood revealed deletion of 13q14 loci (low risk mutation). Biochemical investigations revealed hypoalbuminaemia (serum albumin—1.9 g/dL). Liver and renal function tests and serum electrolytes were normal. Arterial blood gas analysis at room air showed a type 1 respiratory failure pattern with a pH—7.35, pO₂—48 mm Hg, pCO₂—38 mm Hg, HCO₃—23 mmol/L and oxygen saturation of 88%. The patient was initially treated with oxygen 10 L/min via a venture mask and received 3 doses of antibiotics (Piperacillin + Tazobactam). Blood cultures taken before treatment initiation were sterile and sputum workup was negative for gram stain, acid-fast bacilli (AFB) and fungal elements, with sterile bacterial and fungal cultures. PCR for tuberculosis from the sputum was also negative. C reactive protein (CRP) and serum procalcitonin were also negative. Chest X-ray revealed bilateral reticular infiltrates in both lower lobes of the lungs (figure 1A). High-resolution CT chest with contrast revealed multiple mediastinal and hilar lymphadenopathy with a patchy area of consolidation in the bilateral lower lobes (figure 1B and C). Two-dimensional echo for cardiac function was normal. Fiberoptic bronchoscopy (FOB) with bronchoalveolar lavage (BAL) was suggestive of sheets of mature lymphocytes. Gram stain of BAL fluid was negative bacterial and fungal cultures were sterile and RT-PCR (GeneXpert) for tuberculous bacilli was also negative. Antibiotics were stopped in view of the lack of fever, negative cultures, negative infectious markers (CRP, serum procalcitonin) and a strong suspicion of leukaemic pulmonary infiltrates. Ultrasonogram (USG)-guided fine needle aspiration was performed from the right lower lobe consolidation revealed sheets of monomorphic population of small-sized lymphoid cells and smudge cells (figure 2). No granulomas or fungal profiles were seen and stain

CrossMark

To cite:

Balasubramaniam P, Nampoothiri RV, Gupta N, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-218304

Figure 1 A panel of radiology photographs; (A) chest skiagram PA view showing reticulonodular opacities in mid and basal zones of bilateral lung fields; (B and C) CT chest showing bilateral consolidation in the basal areas. (D) Partial resolution of the radiological lesions after the institution of chemotherapy.

Figure 2 A panel of micro-photographs; (A) fine needle aspirate from a pulmonary lesion showing sheets of a monomorphic population of small-sized lymphoid cells (MGG ×20); (B) lymphoid cells and smudge cells admixed with a pigment containing macrophages (MGG ×40); (C) aggregates of small-sized lymphoid cells and alveolar macrophages (H&E ×20); (D) lymphoid cells and alveolar macrophages containing anthracotic pigment (H&E ×40).

for AFB was negative. Hence, a diagnosis of leukaemic pulmonary infiltration with type 1 respiratory failure was made and the patient was restarted on chlorambucil and prednisolone regimen. The patient did not require intubation and invasive ventilation and his respiratory failure gradually improved with the aforementioned treatment regime and he was weaned off oxygen support within 7 days. Repeat chest X-ray showed partial clearance of infiltrates (figure 1D). The patient was discharged and is on regular follow-up.

DISCUSSION

Infections are the most common cause of bilateral or unilateral radiological (X-ray or CT) infiltrates and consolidations in CLL. Typical organisms (including mycobacterium tuberculosis) and atypical organisms have been reported in CLL.¹ Other causes of infiltrates on X-ray include pulmonary haemorrhage, infarcts,

pulmonary injury secondary to chemotherapeutic agents (especially chlorambucil, bleomycin, fludarabine and rituximab), radiation therapy and secondary malignancies. Pulmonary parenchymal infiltrates causing consolidation in chest X-ray and CT are rarely due to basic disease itself, that is, leukaemic pulmonary infiltration or leukostasis.⁴ The pulmonary infiltrates due to direct leukaemic infiltration are seen more common in CLL (up to 17%), whereas pulmonary leukostasis is a more common finding in acute leukaemias and chronic myeloid leukaemia.^{4 5}

The radiographic appearance of pulmonary leukaemic infiltrates manifests as diffuse reticular infiltrates as the leukaemic cells have a very high propensity to invade the peribronchial and peribronchiolar areas of the lung. Pulmonary nodules and consolidation are less commonly seen and are due to infiltration of the leukaemic cells in the adjacent air spaces.⁶ Fretz *et al*⁷ reported a case of CLL with pulmonary infiltrates that had a 'tree-in-bud' appearance in CT chest and was proven as leukaemic infiltrates on transbronchial biopsy.

Autopsy studies have shown that pulmonary infiltration by leukaemia is a relatively common autopsy finding in acute and chronic leukaemias. However, during life, nearly all patients were asymptomatic with no clinical or radiological evidence of the same. Maile *et al*² in their autopsy-based radiographic-pathological correlation study in 113 adult patients of leukaemia showed that haemorrhage is the most common autopsy finding (74%) followed by infectious infiltrates (67%), pulmonary oedema (57%) and leukaemic infiltration (26%). Abnormalities in chest radiographs were seen only in 5% of leukaemic infiltrates.

The pathogenesis of leukaemic infiltration was initially thought to be due to a 'passenger-effect' that is due to leucocytosis and as a result of other inflammatory processes in the lung. However, in their series of 38 patients with CLL/SLL cases with 49 lung biopsies, Hill *et al*⁸ demonstrated that leukaemic pulmonary infiltrates are unrelated to acute or chronic pulmonary inflammation, like infection, and represent a distinct pathological process.

The diagnostic evaluation of pulmonary parenchymal infiltrates in CLL includes performing a contrast-enhanced CT scan of the chest followed by FOB and BAL. BAL is a valuable diagnostic tool in infectious aetiologies (gram/fungal staining, culture and PCR techniques) and also in malignant infiltration (cytological examination and immunohistochemistry). Flow cytometry from BAL samples can confirm the monoclonality of the mature B lymphocytes.^{9 10} Transbronchial or transthoracic biopsy with immunohistochemistry may be confirmatory when the analysis of the BAL specimen is inconclusive.^{7 9}

Pulmonary leukaemic infiltrates in CLL respond well to standard chemotherapeutic regimens. Ahmed *et al*¹¹ studied 110 patients with CLL with pulmonary complications retrospectively and observed that nitrogen (BUN) levels 20 mg/dL and admission absolute neutrophil counts $<0.5 \times 10^9/L$ but not leukaemic infiltrates were correlated significantly with mortality. Long-term remissions with prompt institution of chemotherapy in CLL with leukaemic pulmonary infiltrates have been reported.¹²

Thus, this case illustrates that pulmonary consolidation and resulting respiratory failure in a case of CLL need not always be due to infection, and can also be due to an uncommon presentation of the basic disease. Hence, the possibility of leukaemic pulmonary infiltration should be kept by the treating physician as these patients benefit from chemotherapy with sustained remissions.

Patient's perspective

My father keeps having recurrent lung and urinary infection before and after he was diagnosed with blood cancer. So when he had shortness of breath and cough again, we thought he had pneumonia and brought him to the hospital. Surprisingly, this time he had no fever. Only when the doctors diagnosed that his lung problem was due to his basic cancer and restarted him on chemotherapy, did he improve. I was told that such florid lung involvement in this cancer is not very common. Anyway, as of now, he is better and we are relieved.

Learning points

- ▶ Lung consolidations are not always infective and can be a manifestation of the basic underlying disease.
- ▶ Chronic lymphocytic leukaemia (CLL) can cause infiltration into the lung parenchyma, although these are rarely symptomatic or visible in chest radiographs.
- ▶ Bronchoalveolar lavage and flow cytometry from the sample, along with fine needle aspiration from the consolidation, are confirmatory tests to confirm leukaemic infiltration into the lung
- ▶ Leukaemic infiltration into the lung is an indication of treatment in CLL, and responds well to standard chemotherapy, as in the index case.

Contributors PB is responsible for preparing the manuscript. RVN is responsible for editing the manuscript, managing patient and literature review. NG is responsible

for histopathological diagnosis, images and flow cytometry. PM is responsible for concept of the article, managing patient and literature review.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Lad D, Malhotra P, Varma N, *et al*. CLL: common leukemia; uncommon presentations. *Indian J Hematol Blood Transfus* 2016;32:268–75.
- 2 Maile CW, Moore AV, Ulreich S, *et al*. Chest radiographic-pathologic correlation in adult leukemia patients. *Invest Radiol* 1983;18:495–9.
- 3 Barcos M, Lane W, Gomez GA, *et al*. An autopsy study of 1206 acute and chronic leukemias (1958 to 1982). *Cancer* 1987;60:827–37. <827::AID-CNCR2820600419>3.0.CO;2-A
- 4 Berkman N, Polliack A, Breuer R, *et al*. Pulmonary involvement as the major manifestation of chronic lymphocytic leukemia. *Leuk Lymphoma* 1992;8:495–9.
- 5 Lester TJ, Johnson JW, Cuttner J. Pulmonary leukostasis as the single worst prognostic factor in patients with acute myelocytic leukemia and hyperleukocytosis. *Am J Med* 1985;79:43–8.
- 6 Blank N, Castellino RA, Blank N, *et al*. The intrathoracic manifestations of the malignant lymphomas and the leukemias. *Semin Roentgenol* 1980;15:227–45.
- 7 Fretz G, Krause M, Thurnheer R. Chronic lymphocytic leukaemia, dyspnoea and tree-in-bud sign on chest CT scan. *BMJ Case Rep* 2009;2009.
- 8 Hill BT, Weil AC, Kalaycio M, *et al*. Pulmonary involvement by chronic lymphocytic leukemia/small lymphocytic lymphoma is a specific pathologic finding independent of inflammatory infiltration. *Leuk Lymphoma* 2012;53:589–95.
- 9 Hummel M, Rudert S, Hof H, *et al*. Diagnostic yield of bronchoscopy with bronchoalveolar lavage in febrile patients with hematologic malignancies and pulmonary infiltrates. *Ann Hematol* 2008;87:291–7.
- 10 Kumar N, Varma N, Varma S, *et al*. Study of diagnostic and prognostic parameters (including flow cytometry) in chronic lymphoproliferative disorders: the Indian perspective. *Anal Quant Cytol Histol* 2009;31:296–303.
- 11 Ahmed S, Siddiqui AK, Rossoff L, *et al*. Pulmonary complications in chronic lymphocytic leukemia. *Cancer* 2003;98:1912–7.
- 12 Hildebrand FL, Rosenow EC, Habermann TM, *et al*. Pulmonary complications of leukemia. *Chest* 1990;98:1233–9.

Copyright 2017 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