An unusual presentation of gastric mucosa associated lymphoid tissue (MALT) lymphoma

Barratt SL[1], Medford ARL[2], Edey A[3], Adamali H[1]

ABSTRACT

Organising pneumonia is an inflammatory process of the lung that is pathologically defined by the presence of granulation tissue in the alveolar ducts and alveoli. We report a case of a 64 year old man who presented with relapsing-remitting organising pneumonia, who was subsequently identified as having co-existent gastric mucosa associated lymphoid tissue (MALT) lymphoma. Treatment of the gastric MALT lymphoma coincided with remission of the organising pneumonia. Whilst direct causality cannot be definitively determined in this case, we hypothesise that the lymphomatous process was driving the inflammatory lung disease. We advocate screening for occult malignancy in cases of organising pneumonia, particularly those displaying a relapsing-remitting natural history.

Key words: Organising pneumonia, gastric MALT lymphoma, lymphoma.

Iraqi New Medical Journal July 2019;4(10)

CASE STUDY

A 64 year old gentleman was referred to the interstitial lung disease clinic in 2013 with a 6 week history of cough, breathlessness and malaise. Exercise capacity was reduced, with a Medical Research Council (MRC) dyspnoea scale 2. There were no other systemic symptoms of night sweats, fatigue or weight loss. He had been treated with several empirical courses of antibiotics with no improvement. He was a lifelong non-smoker with no significant occupational exposures. Past medical history included an episode of cryptogenic organising pneumonia in 2010 that fully resolved with 8 weeks of oral prednisolone and a malignant melanoma that was excised from his left forearm in 2012. He was not taking any prescribed or over-the-counter medications. There were no symptoms suggestive of a connective tissue disease (CTD).

On examination, blood pressure was 145/81 mmHg, pulse rate 68 bpm, oxygen saturations 97% air, height 171.2 cm; weight 96.9 kg, BMI 33.06 kg/m^2. There were no peripheral features of CTD. He was not clubbed. Respiratory and cardiovascular examinations were normal.

The initial Chest x ray prompting referral (**Figure 1a and b**) demonstrated new bilateral patchy consolidation. Subsequent CT Chest (**Figure 1c**) revealed bilateral patchy ground glass opacification and bronchocentric consolidation with some minor perilobular thickening in the mid zone and bases that was new compared to archival imaging.

Auto-immune screen including rheumatoid factor, Hep 2 cell immunofluorescence and ANCA were negative. HIV screen was also negative. Urinary dipstick was negative for blood or protein. His spirometry was consistent with a restrictive pattern with FVC 2.70 (70% predicted); FEV1 2.10 (70% predicted); FEV1/FVC ratio 78%; TLC 4.28 (65% predicted); RV 1.47 (61% predicted) TLCO 7.24 (83% predicted); KCO 1.82 (137% predicted).

Given his previous history and imaging findings, the appearances were thought to be consistent with new areas of organising pneu-

[1] Consultant Respiratory Physician, Bristol Interstitial Lung Disease Service, Southmead Hospital, North Bristol NHS Trust, Bristol, UK
[2] North Bristol Lung Centre, Southmead Hospital, North Bristol NHS Trust, Bristol, UK.
[3] Department of Radiology, Southmead Hospital, North Bristol NHS Trust, Bristol, UK.

Corresponding Author: Dr. **Shaney Barratt**, Consultant Respiratory Physician and ILD Specialist. Bristol Interstitial Lung Disease Service, North Bristol NHS Trust, Westbury on Trym, UK. E mail: Shaney.Barratt@nbt.nhs.uk.

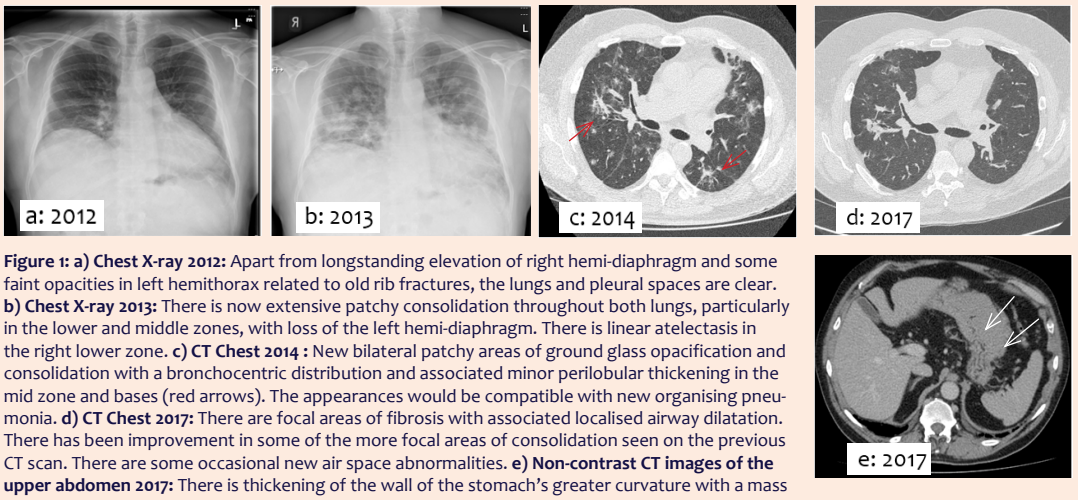

Figure 1: a) Chest X-ray 2012: Apart from longstanding elevation of right hemi-diaphragm and some faint opacities in left hemithorax related to old rib fractures, the lungs and pleural spaces are clear. **b) Chest X-ray 2013:** There is now extensive patchy consolidation throughout both lungs, particularly in the lower and middle zones, with loss of the left hemi-diaphragm. There is linear atelectasis in the right lower zone. **c) CT Chest 2014 :** New bilateral patchy areas of ground glass opacification and consolidation with a bronchocentric distribution and associated minor perilobular thickening in the mid zone and bases (red arrows). The appearances would be compatible with new organising pneumonia. **d) CT Chest 2017:** There are focal areas of fibrosis with associated localised airway dilatation. There has been improvement in some of the more focal areas of consolidation seen on the previous CT scan. There are some occasional new air space abnormalities. **e) Non-contrast CT images of the upper abdomen 2017:** There is thickening of the wall of the stomach's greater curvature with a mass like abnormality measuring 9 cm in length and 4 cm in depth (white arrows). There was also caking of the omentum and abnormal lesser gastric lymph nodes measuring up to 11 mm visible on other images.

monia. He was initially treated with 500 mg intravenous Methylprednisolone for three days followed by a tapering doses of oral prednsiolone.

Whilst an initial CT Chest demonstrated improvement in changes post methylprednisolone, upon tapering of the prednisolone, new multi-focal air space nodularity occurred, requiring reescalation of his prednisolone regime. He continued to have a relapsing remitting course of disease over the subsequent 18 months, despite repeated courses of prednisolone then additional macrolide therapy (clarithromycin). Consequently, he was treated with intravenous cyclophosphamide therapy. Follow up CT (**Figure 1d and e**), performed to assess response to cyclophosphamide therapy, demonstrated evidence of some established fibrosis with reticulation and traction dilatation, improvement in the focal areas of consolidation but occasional new airspace opacities. Incidentally a mass was identified on the greater curvature of the stomach, associated with thickening of the omentum.

He proceeded to endoscopy and biopsy, with histology demonstrating an extra-nodal marginal zone lymphoma (or gastric mucosa-associated lymphoid tissue (MALT) lymphoma stage 3E). He was commenced on *Helicobacter Pylori* eradication therapy followed by RCVP (rituximab, cyclophosphamide, vincristine sulfate, and prednisone) chemotherapy. Subsequent CT Chest 12 months later, demonstrated only residual focal areas of fibrosis (not shown).

Three years on, there has been no further recrudescence of his organising pneumonia or recurrence of his MALT lymphoma. He currently persists on Prednisolone 5 mg, and is receiving support from endocrinology teams to taper this further.

DISCUSSION

Organising pneumonia (OP) is an inflammatory process resulting from lung injury that pathologically is defined by the presence of granulation tissue in the alveolar ducts and alveoli (Masson bodies).[1] It can be classified according to the presence of a known cause such as infection, drug reactions, radiation injury or in association with connective tissue disease. It can also occur as a primary interstitial lung disease, where it is deemed idiopathic or cryptogenic (COP).[2]

Typical radiological features are of peripheral consolidation with a bronchovascular distribution but a single area of consolidation or more diffuse infiltrates have also been described.[3]

The association of organising pneumonia with malignancy is well described. Firstly, as a complication of treatment, including chemotherapy, radiotherapy,[4] bone marrow transplantation[5] and in up to 40-60% patients following haemopoietic stem cell transplant.[6] Secondly, with lung cancer, both as a direct influence of the tumour on the surrounding parenchyma or a consequence of bronchial obstruction[7, 8] and thirdly as a diagnostic dilemma if occurring as

a solitary area of consolidation, requiring histological examination to exclude recurrence or metastatic disease. In a study of 151 patients with biopsy proven OP and a history of malignancy, OP most commonly presented radiologically as a diffuse process with an ill-defined margin on CT Chest (41%),[9] a pattern reported in various studies of oncological patients and attributed to a desmoplastic response,[10] but importantly there was no definitive way to differentiate COP from a secondary organising pneumonia, based purely on radiological findings. A second study of 43 patients with an antecedent or concomitant diagnosis of cancer and histologically confirmed OP,[8] identified that 63% patients (n=27) had solid organ tumours, whilst the remainder had haematological malignancies (37%, n=16). Of those with solid organ tumours, approximately 75% of these were distant to the lung, but the data was complicated by the fact that all patients had undergone treatment for their malignancy, 72% patients having received more than one mode of therapy.

MALT lymphomas are a distinct subgroup of non-Hodgkin's lymphoma, commonly involving the gastrointestinal tract (>60% cases) and often occurring in patients with autoimmune disease or chronic inflammatory conditions.[11, 12] Gastric MALT lymphomas have a low tendency to spread outside the primary origin site, reported to be confined in up to 90% cases.[13] Antibiotic therapy is an established standard of care; *H. pylori* eradication leads to the regression of gastric lymphoma in 35–75% of cases.[14, 15]

This case highlights the known association between organising pneumonia and malignancy. Whilst direct causality cannot be definitively determined in this case, we hypothesise that the lymphomatous process was driving the inflammatory lung disease.

We advocate imaging for occult malignancy, particularly of the abdomen and pelvis, as part of the work up of all cases of suspected organising pneumonia, with particular vigilance in patients with relapsing remitting disease.

REFERENCES

1. Colby TV. Pathologic aspects of bronchiolitis obliterans organizing pneumonia. *Chest*. 1992;102(1 Suppl):38S-43S.
2. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med*. 2011;183(6):788-824.
3. Cordier JF. Cryptogenic organising pneumonia. Eur Respir J. 2006;28(2):422-46.
4. Crestani B, Valeyre D, Roden S, Wallaert B, Dalphin JC, Cordier JF. Bronchiolitis obliterans organizing pneumonia syndrome primed by radiation therapy to the breast. The Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires (GERM"O"P). *Am J Respir Crit Care Med*. 1998;158(6):1929-35.
5. Cordier JF. Organising pneumonia. *Thorax*. 2000;55(4):318-28.
6. Yoshihara S, Yanik G, Cooke KR, Mineishi S. Bronchiolitis obliterans syndrome (BOS), bronchiolitis obliterans organizing pneumonia (BOOP), and other late-onset noninfectious pulmonary complications following allogeneic hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant*. 2007;13(7):749-59.
7. Romero S, Barroso E, Rodriguez-Paniagua M, Aranda FI. Organizing pneumonia adjacent to lung cancer: frequency and clinicopathologic features. *Lung Cancer*. 2002;35(2):195-201.
8. Mokhtari M, Bach PB, Tietjen PA, Stover DE. Bronchiolitis obliterans organizing pneumonia in cancer: a case series. *Respir Med*. 2002;96(4):280-6.
9. Long NM, Plodkowski AJ, Schor-Bardach R, Geyer AI, Zheng J, Moskowitz CS, et al. Computed Tomographic Appearance of Organizing Pneumonia in an Oncologic Patient Population. *J Comput Assist Tomogr*. 2017;41(3):437-41.
10. Yang PS, Lee KS, Han J, Kim EA, Kim TS, Choo IW. Focal organizing pneumonia: CT and pathologic findings. *J Korean Med Sci*. 2001;16(5):573-8.
11. Thieblemont C, Bertoni F, Copie-Bergman C, Ferreri AJ, Ponzoni M. Chronic inflammation and extra-nodal marginal-zone lymphomas of MALT-type. *Semin Cancer Biol*. 2014;24:33-42.
12. Thieblemont C, Zucca E. Clinical aspects and therapy of gastrointestinal MALT lymphoma. *Best Pract Res Clin Haematol*. 2017;30(1-2):109-17.
13. Montalbán C, Castrillo JM, Abraira V, Serrano M, Bellas C, Piris MA, et al. Gastric B-cell mucosa-associated lymphoid tissue (MALT) lymphoma. Clinicopathological study and evaluation of the prognostic factors in 143 patients. *Ann Oncol*. 1995;6(4):355-62.
14. Roggero E, Zucca E, Pinotti G, Pascarella A, Capella C, Savio A, et al. Eradication of Helicobacter pylori infection in primary low-grade gastric lymphoma of mucosa-associated lymphoid tissue. *Ann Intern Med*. 1995;122(10):767-9.
15. Savio A, Franzin G, Wotherspoon AC, Zamboni G, Negrini R, Buffoli F, et al. Diagnosis and posttreatment follow-up of Helicobacter pylori-positive gastric lymphoma of mucosa-associated lymphoid tissue: histology, polymerase chain reaction, or both? *Blood*. 1996;87(4):1255-60.

Abbreviation list: Body mass index (**BMI**), Cat scan (**CT**), Centimetre (**cm**), Connective Tissue Disease (**CTD**), Cryptogenic Organising pneumonia (**COP**), Forced Expiratory Volume (**FEV1**), Forced vital capacity (**FVC**), Human Immune Deficiency virus (**HIV**), Kilogram / Square metre (**kg/m²**), Medical Research Council (**MRC**), Millimetre mercury (**mmHg**), Mucosa-associated lymphoid tissue (**MALT**), Organising pneumonia (**OP**), Pulse per minute (**bpm**), Residual Volume (**RV**), Total Lung Capacity (**TLC**), Transfer Factor of the Lung for Carbon Monoxide (**TLCO**)

Conflict of interest: Authors have nothing to declare.

Funding: Authors received no funds to complete this case presentation a part from self funding.