

CLINICAL MEETING 22ND SEPTEMBER 2016

A Simple CAP

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Initial presentation

Mr Cheung is a 65 years old ex-smoker. He enjoyed good past health. He was presented with 2 months' history of cough with whitish sputum and weight loss. He had attended GP for more than 10 times and had received multiple course of antibiotics.

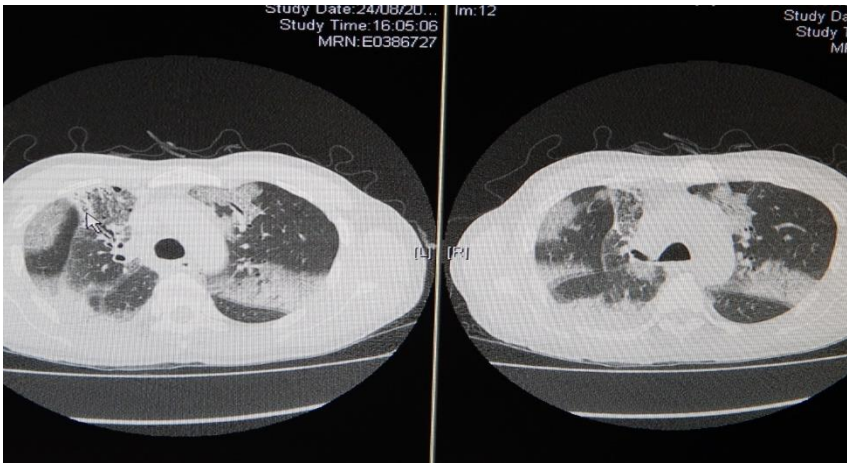
He had fever for 2 days before admitted to Yan Chai Hospital. He had travelled and stayed in China for 1 month before the illness.

On admission, blood test found elevated WBC $17.6 \times 10^9/L$, eosinophil count $7.9 \times 10^9/L$, ESR 65 mm/hr and CRP 105g/L. His liver and renal function test were normal. CXR found RUL consolidation. He was immediately transferred to isolation ward for suspected pulmonary tuberculosis. Sputum culture found streptococcus pneumoniae. Sputum for AFB smear were negative in 3 consecutive specimens. He was managed as community acquired pneumonia with augmentin and klacid.

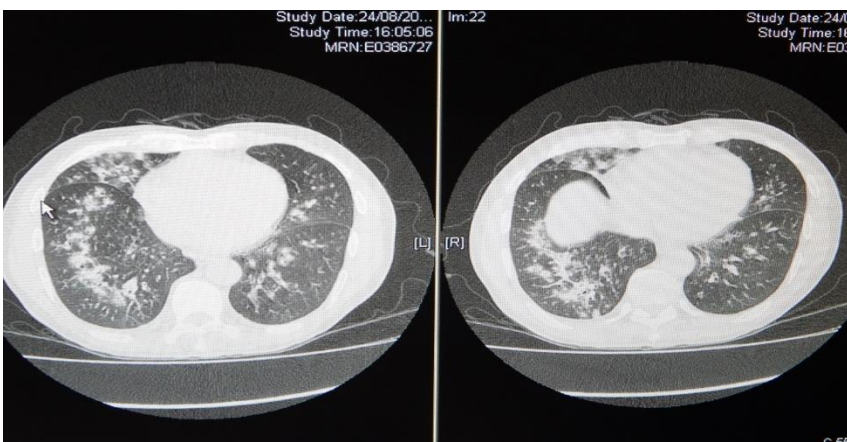


CXR D1

CXR D5



HRCT D6

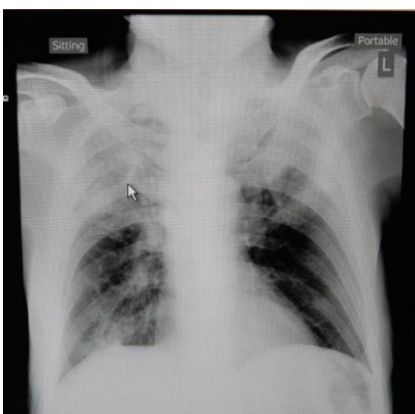


HRCT D6

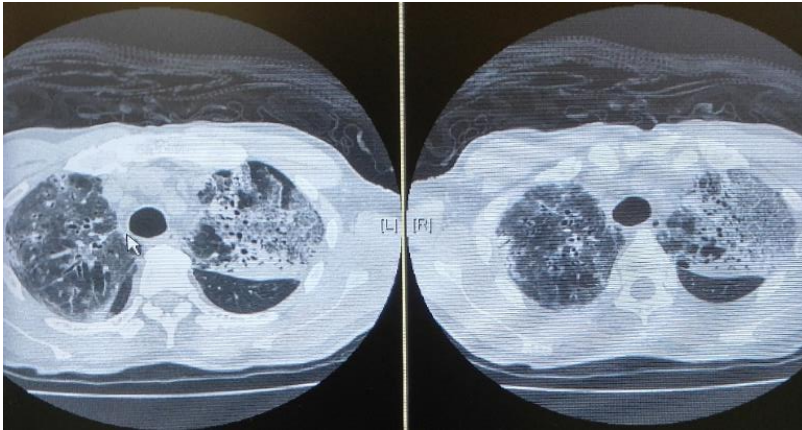
Progress

CXR on day5 of admission showed that RUZ consolidation partially cleared up. HRCT on day6 found bilateral upper zone consolidations and bilateral lower zone centrilobular nodules. Serial blood taking found further elevation of

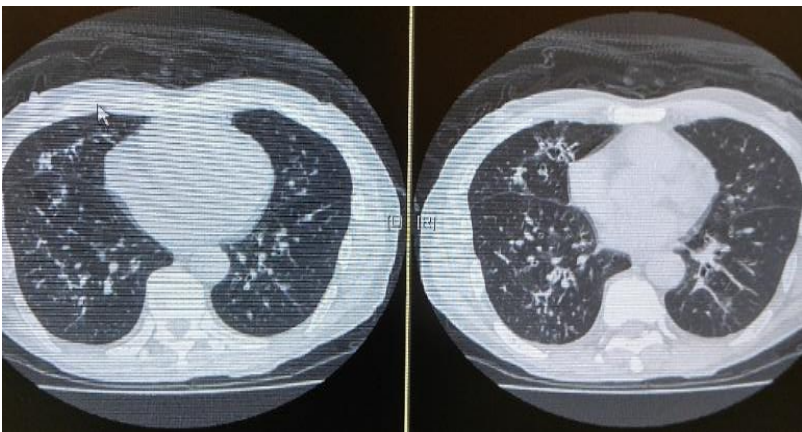
ESR up to 92 mm/hr and elevation of eosinophils count up to $11.3 \times 10^9/L$. Patient had persistent fever despite a total 10 days of augmentin and 9 days of klacid. Tazocin was given on day11 of admission.



CXR D15



HRCT D18

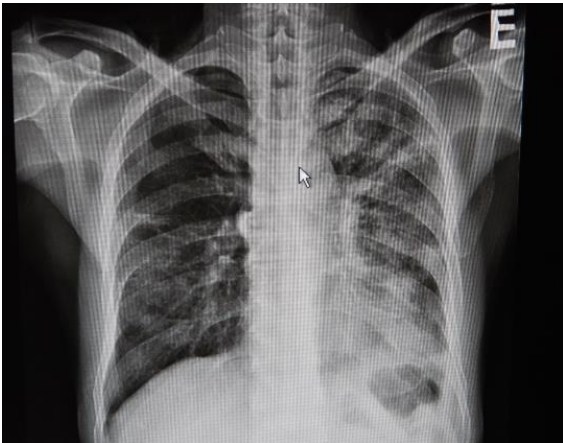


HRCT D18

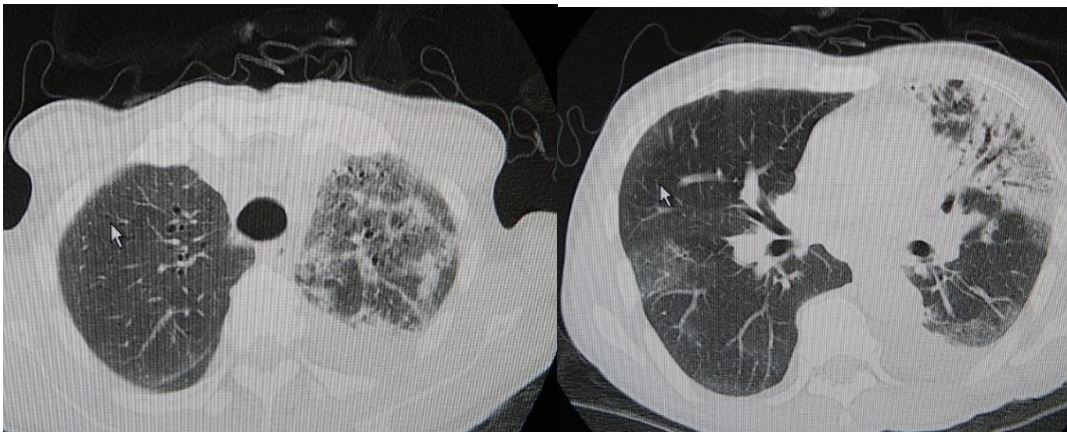
CXR on day 15 showed bilateral upper zones consolidation. HRCT on day 18 showed decreasing opacities in RUZ but mildly increasing opacities in LUZ when compared with HRCT in day 6. Sputum fungal culture was negative. Aspergillus antibody, galactomannan assay, ANA, ANCA and anti-HIV were all negative. Stool ova and cyst grew clonorchis ova, He was given praziquatel on day 19. Bronchoscopy was performed because of fleeting lung shadows on CXR and high eosinophils count. There was no endobronchial lesion. Bronchoalveolar lavage for AFB smear, cytology and ova and cyst were all negative. Differential cell count of bronchoalveolar

lavage in RUL found macrophage 25% (normal range <85%) neutrophils 22% (normal range <3%), lymphocytes 42% (normal range 10-15%), eosinophils 4% (normal range <1%), squamous cells 6% and airway epithelial cells 1% (normal range <5%; >5% suggest suboptimal samples).

Patient was eventually became afebrile after completion of one week course of tazocin. He was discharged on day 20 of admission and arranged follow up in respiratory clinic. When patient was followed up in respiratory clinic 4 weeks later, he still had persistent cough. Blood test found elevated ESR up to 108mm/hr.



CXR 1 months later



HRCT 1 months later

CXR found R lung clear but patchy consolidations in L lung which was further confirmed by HRCT. Bronchoscopy was performed which again found no endobronchial lesion. Bronchoalveolar lavage for AFB smear, ova and cyst and cytology were all negative. Transbronchial biopsy of left lingular lobe was performed. Histology found thickening of interalveolar septa with infiltration by eosinophils, lymphocytes and some foamy cells. There was reactive organizing features with focal fibroblastic proliferation and some

eosinophils in alveolar spaces. Ziehl Neelsen stain for acid fast bacilli and PAS-D for fungal stain were both negative. PCR for MTB complex target IS6110 and mtp40 were both negative. The whole picture was compatible with eosinophilic pneumonia with causes like infective, drug-induced and allergy should be ruled out.

Subsequent follow up found that eosinophils count, CRP and ESR were all normalized. Repeat stool ova and cyst was negative. CXR was clear.



CXR 2 months later

Discussion

Eosinophilic lung disease is a heterogeneous group of pulmonary disorders characterized by increasing numbers of eosinophils in the airway

of lung parenchyma. It was first introduced the terms ‘PIE syndrome’ (pulmonary infiltrates with blood eosinophilia) by Reeder and Goodrich in 1950s to classify these syndromes in which lung infiltrates on CXR associated with peripheral eosinophilia. Later it was revised by Allen in 1994 with diagnosis of eosinophilic lung disease can be suspected, based on either the finding of pulmonary disease with blood eosinophilic, pulmonary disease with bronchoalveolar lavage eosinophilia, or pulmonary disease with tissue eosinophilia on lung biopsy.

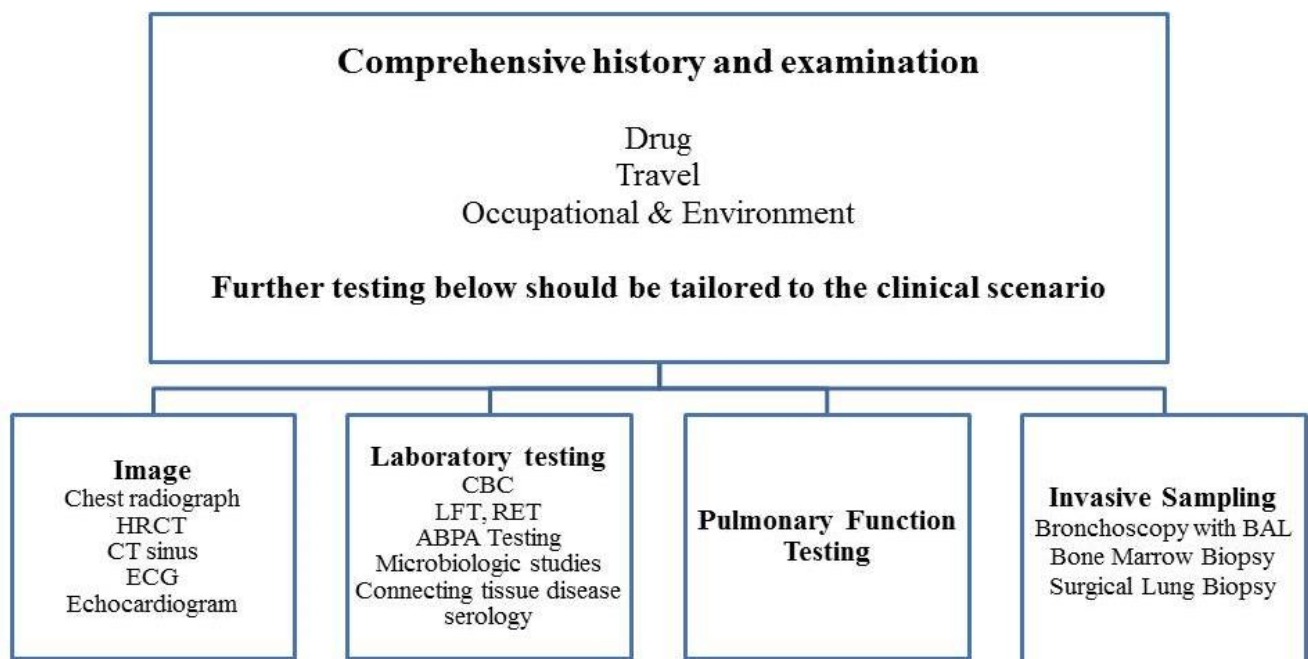


Figure 1. Approach to suspected eosinophilic lung disease

In our patient, the most likely cause of eosinophilic pneumonia was drug-related as patient had received multiple courses of antibiotics before the index admission. Parasites

were unlikely as clonorchiasis found in our patient is not typically associated with eosinophilic pneumonia. The most typical parasites causing eosinophilic pneumonia

include roundworms (*Ascaris lumbricoides*, *Ascaris suuis*, *Toxocara canis*), hookworm (*Necator americanus*, *Ancylostoma duodenale* and *caninum*) and microfilaria (*Wuchereria bancrofti*, *Dirofilaria immitis*).

Drugs and toxins resulting in eosinophilic lung disease were first mentioned in Liebow's original paper on the eosinophilic pneumonia in 1969. Antibiotics and non-steroidal anti-inflammatory drugs are the most common causes of eosinophilic pneumonia. Other identified drugs include anti-convulsants, anti-depressants and cardiovascular medications (ACE-inhibitors, beta-blockers, amiodarone). Cigarette smoke is also a cause of toxin-induced eosinophilic pneumonia. A recent example of an undefined toxin-induced eosinophilic pneumonia is the report of a fire-fighter working at the wreckage of the World Trade

Center who developed an acute eosinophilic pneumonia picture and was found to have asbestos fibers, fly ash and degraded fibrous glass on bronchoalveolar lavage.

There were several clinical patterns of eosinophilic pneumonia from Drug and Toxins. These include simple eosinophilic pneumonia, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, churg-strauss syndrome and isolated eosinophilic pleural effusion. Criteria of diagnosis include 1 no other cause of lung disease, 2 symptoms consistent with suspected drug or toxin, 3-time course compatible with drug or toxin-induced lung disease, 4 tissue or BAL findings compatible with drug or toxin induced lung disease and 5 improve after offending agent is discontinued.

Clinical patterns of Eosinophilic Pneumonia from Drug and Toxins

- **Simple eosinophilic pneumonia (Loffler's syndrome)**
 - most common form
 - asymptomatic or mild cough or dyspnoea
- **Acute eosinophilic pneumonia**
 - minocycline particularly frequently associated
 - new exposure to tobacco smoke also linked
 - acute febrile illness, diffuse alveolar infiltrates , severe hypoxemia and eosinophils on BAL
 - cessation of suspect drug +/- corticosteroid
- **Chronic eosinophilic pneumonia**
 - subacute presentation with cough or dyspnea for weeks or months
 - in contrast to idiopathic chronic eosinophilic pneumonia usually with systemic symptoms such as rash or fever
- **Churg-Strauss syndrome**
 - leukotriene inhibitors
 - cannot be distinguished from idiopathic Churg-Strauss syndrome
 - antecedent asthma and allergic rhinitis followed by high blood eosinophilic count and vasculitis
 - long term corticosteroid and cytotoxic medications
- **Isolated eosinophilic pleural effusion**

Criteria of diagnosis of eosinophilic pneumonia from Drug and Toxins

- **1 no other cause of lung disease**
- parasites, fungal infection
- **2 symptoms consistent with the suspected drug or toxin**
- **3 time course compatible with drug or toxin-induced lung disease**
- **4 tissue or BAL findings compatible with drug or toxin induced lung disease**
 - confirm the presence of eosinophilic lung infiltration
 - rule out other causes of pulmonary infiltrates such as infection
 - BAL fluid characteristics differ among acute, chronic, and drug-induced eosinophilic lung disease
 - BAL in drug-induced lung disease: elevated eosinophils and lymphocytes
 - BAL in acute eosinophilic pneumonia: elevated eosinophils, neutrophils and lymphocytes
 - BAL in chronic eosinophilic pneumonia: elevated HLA-DR⁺ cells and CD8 lymphocytes
- **5 improve after offending agent is discontinued**
 - when offending agent withdrawn spontaneous resolution within 4-5 weeks
 - severe situation with acute respiratory failure corticosteroid indicated

Conclusion

Our patient is suffered from eosinophilic pneumonia as supported by fleeting CXR shadows, high eosinophils count and transbronchial biopsy result. The cause is most likely related to drug as supported by clinical history.

6 Drug-Toxin-,Radiation Therapy-Induced Eosinophilic Pneumonia, Semin Respir Crit Care Med 2006;27:192-198

7 Eosinophilic Pneumonia Due to Toxocariasis: An Adult Case Report, Turkiye Parazitol Derg 2012;36:258-9

Reference

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- 4 Loffler's syndrome Associatged with Clonorchis Sinensis Infestation, The Korean Journal of Internal Medicine:18:255-259, 2003
- 5 Drug-induced eosinophilic lung disease, Clini Chest Med 25 (2004) 77-88