Diffuse Panbronchiolitis Associated with Malignant Thymoma

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CLINICAL SUMMARY

A 50-year-old woman diagnosed to have thymoma type B2 on thoracotomy, was referred with complaints of cough, mucoid sputum and exertional dyspnoea of six months duration. There was no fever, symptoms suggestive of connective tissue disorders, history of drug therapy or exposure to dust. Oxygen saturation (SpO_2) by pulse oximetry showed significant post-exercise desaturation from 94 percent to 85 percent. Other vital parameters were normal. Except for crackles on chest auscultation, rest of the systemic examination was unremarkable.

INVESTIGATIONS

Laboratory results showed normal haemogram and serum chemistry. Serum immunoglobulin A (IgA) was 607 mg/dL (normal 68-378 mg/dL). Serum acetylcholine receptor antibody (ACRAB) was 5.44nMol/L (normal up to 0.4nMol/L). Chest radiograph (Figure 1) showed mediastinal widening with presence of sternal sutures. Contrast enhanced computed tomography (CECT) of the thorax (Figure 2) showed an encapsulated mass in the perivascular space of mediastinum measuring 5.7cm × 3.8cm. High resolution computed tomography (HRCT) of the thorax (Figure 3) showed centrilobular and branching nodules with tubular bronchiectasis predominantly in the lower lobes. Hypo-attenuation and air trapping was not seen. ^{18}F-fluoro-deoxy glucose positron emission tomography (FDG-PET) showed mild diffuse tracer uptake in the anterior mediastinum.

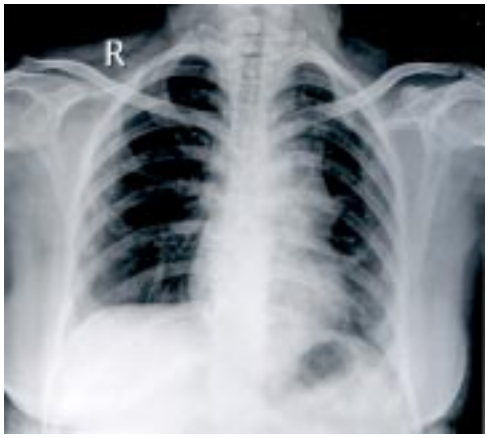

Figure 1. Chest radiograph showing mediastinal widening with presence of sternal sutures form previous thoracotomy.

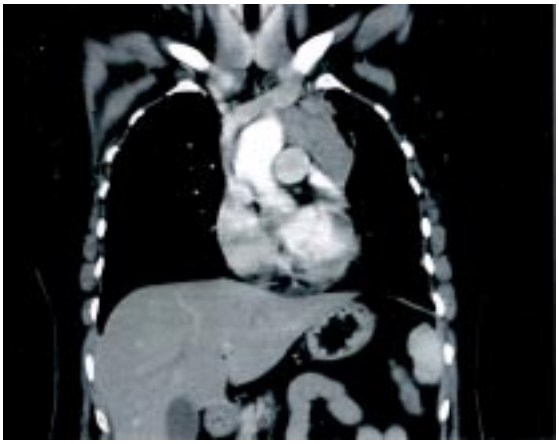

Figure 2. Contract enhanced computed tomography of thorax (coronal section) showing an encapsulated anterior mediatinal mass measuring 5.7cm x 3.8cm.

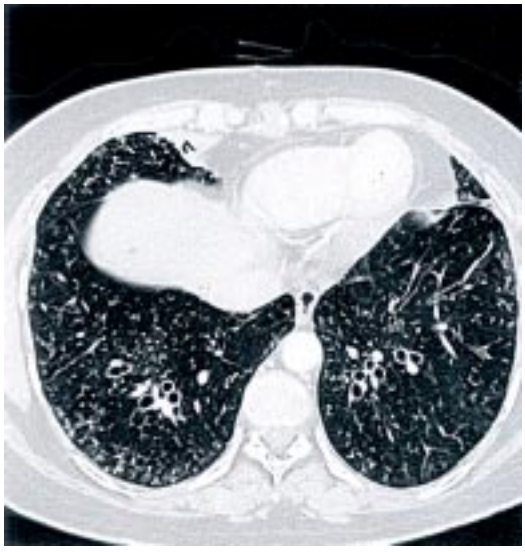

Figure 3. High resolution computed tomography of the thorax showing centrilobular and branching nodules and tubular bronchiestasis predominantly in the lower lobes.

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Spirometry showed forced vital capacity (FVC) 1.10L (predicted 2.94L) and forced expiratory volume in one second (FEV_1) 1.06L (predicted 2.5L). Arterial blood gas analysis showed pH 7.44, partial arterial oxygen tension (PaO_2) 61mmHg, partial carbon dioxide tension ($PaCO_2$) 34.1mmHg and serum bicarbonate (HCO_3^-) 23.5mmol/L.

The patient was started on oral azithromycin 500 mg daily for DPB. She experienced significant improvement soon after. The HRCT done after six months of therapy showed reduction in the density of nodules (Figure 4) and spirometry showed improvement: FVC 1.69L (58% predicted) and FEV_1 1.32L (56% predicted).

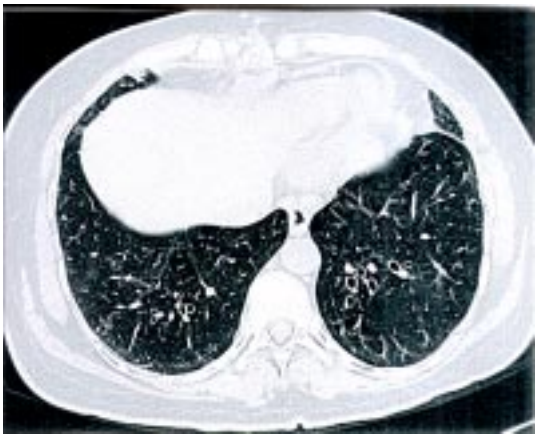

Figure 4. High resolution computed tomography of the thorax after six months of therapy with azithromycin showing reduction in the density of nodules.

DIAGNOSIS

Diffuse panbronchiolitis (DPB) associated with malignant thymoma, type B2.

DISCUSSION

Diffuse panbronchiolitis is an idiopathic chronic obstructive airways disease first reported in 1969.[1] Although DPB has been frequently reported amongst Japanese subjects, only sporadic cases have been reported in Caucasians, Koreans, Indians, black subjects, and Hispanics.[2] The clinical diagnostic criteria[2] include: *(i)* cough, sputum production and exertional dyspnoea; *(ii)* wheeze or crackles; *(iii)* radiological evidence of diffuse nodular shadow with lower zone predominance and hyperinflation; *(iv)* pulmonary functions: FEV_1/EVC<70% or FEV_1<70% predicted, FVC<80% predicted, residual volume (RV)>150% predicted and PaO_2<80mmHg, and *(v)* additional non-diagnostic features include chronic paranasal sinusitis, increased serum IgA and IgG levels, increased CD4+/CD8+T-lymphocyte ratio, proof of human leukocyte antigen (HLA) Bw54 antigen, positive rheumatoid factor and increased serum cold haemagglutinins. Although histological confirmation is lacking in our case, the typical clinical picture, physiologic and serological findings and plain radiograph chest and thoracic HRCT features meet the diagnostic criteria for DPB.[2] The HRCT grading was type 2 as described by Akira *et al.*[3]

The DPB complicated with thymoma is uncommon; only four cases have been reported till date.[4-6] Immunological factors probably play an important role in the pathogenesis of DPB associated with thymoma. Unlike the cases reported initially[4,5] who died of respiratory failure, the two cases with encapsulated thymoma described later[5] showed good response to macrolide therapy after thymectomy. The DPB is highly responsive to treatment with macrolides usually in low doses but is fatal if untreated.[7] The mechanism of action of macrolides in DPB is likely to be anti-inflammotory rather than antimicrobial.

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