Foreign body granulomatosis in intravenous drug addicts in Hong Kong

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Foreign body granuloma in the lung is not an uncommon finding in autopsies performed on intravenous drug addicts in Hong Kong, but the diagnosis is seldom made in life. We report three cases of foreign body granulomatosis in Chinese intravenous drug addicts. All three had miliary shadows on chest radiograph and the diagnosis was confirmed by transbronchial biopsy.

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Introduction

In an endemic area, miliary tuberculosis (TB) tops the list of differential diagnoses in a chest X-ray with miliary shadows, which are defined as shadows less than 2 mm, uniformly spread throughout the lung fields.[1] Other common causes include carcinomatosis, fungal diseases (e.g. histoplasmosis), pneumoconiosis, and sarcoidosis. If the patient happens to be a drug addict who injects crushed oral tablets intravenously, talcosis must be considered. The Hong Kong Department of Health's Chest Service Annual Report of 1993 did not give any statistics on the prevalence of pulmonary tuberculosis among drug addicts. However, the anti-narcotic campaign slogan of 1960, "Opium, Red Pills and White Powder are NOT a Cure for Tuberculosis,"[2] probably reflected the higher prevalance of tuberculosis among narcotic abusers than the general population at that time. There is pressure on the clinican to treat those patients who present with such shadows with anti-TB therapy until a diagnosis of TB has been eliminated. A transbronchial biopsy often helps to reveal the true diagnosis.

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Case reports

Case 1

A 26-year-old intravenous drug abuser presented with a one-week history of chest pain and fever. He was referred to a chest hospital because of miliary shadows on his chest X-ray. In addition to heroin he had been injecting crushed triazolam tablets until one week before admission. The total number of tablets injected before admission was not known. There was no history of occupational exposure to dust. On examination, his left leg was oedematous due to deep vein thrombosis from self-injection of heroin. Apart from scarred veins, no other abnormality was detected. The optic fundi were normal. His arterial blood gases revealed a pCO_2 of 5.97 kPa (normal range, 4.4-5.9 kPa), pO_2 of 11.5 kPa (normal range, 10.0-14.0 kPa) and his blood pH was 7.3. His sputum smear and culture failed to detect acid-fast bacilli. A chest X-ray showed miliary shadows (Fig 1a). The patient's bone marrow biopsy revealed no abnormality. His blood culture grew *Staphylococcus aureus*. His lung function test showed an FEV_1 of 3.21 L and FVC of 3.96 L. The echocardiogram was normal.

Staphylococcus aureus septicaemia was diagnosed by the referring unit and treatment begun. A provisional diagnosis of miliary TB was also made and the patient was commenced on anti-TB therapy. Bronchoscopy revealed no abnormal findings and a transbronchial biopsy revealed foreign body granulomatosis in which there were multiple small granulomas of the foreign-body type in the lung parenchyma against birefringent material. There was no caseation necrosis or tuberculoid granuloma (Figs 1b

Fig 1a. Chest X-ray of patient 1 showing miliary shadows

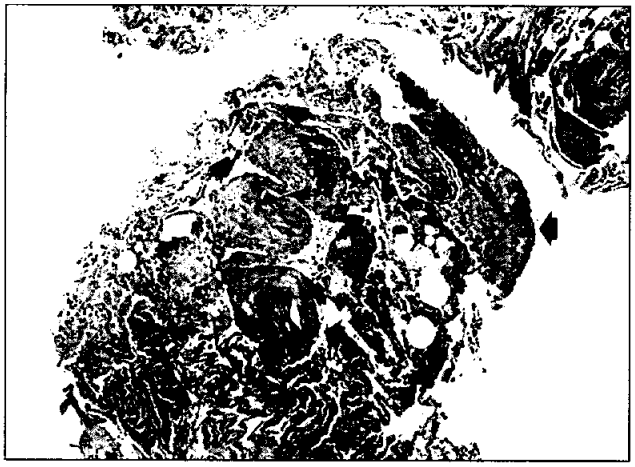

Fig 1b. Multiple round foreign body granulomas (arrow) consisting of foreign material (arrowhead) surrounded by multinucleate giant cells and fibrous tissue are seen in the lung biopsy (x 100 mag)

and 1c). As both biopsy and bronchial aspirate culture revealed no evidence of TB, the anti-TB drugs were stopped. The patient was discharged to be followed up at the chest clinic, but he did not return.

Case 2

A 23-year-old man was admitted because of heroin overdose. He had been an intravenous addict for eight years and had had a few similar previous admissions. Whether or not he had injected any crushed oral tablets intravenously was not known. He had no fever, night sweats, or weight loss. Physical examination revealed no abnormality other than scarred veins. The optic fundi were normal. His arterial blood gases showed a pH of 7.4, pCO_2 of 6.79 kPa, and pO_2 of 11.9kPa. His chest X-ray showed miliary shadows (Fig 2). There was no sputum available for examination. An early morning urine sample failed to reveal acid-fast bacilli on smear or culture. No endobronchial lesion could be seen on bronchoscopy, and the bronchial aspirate and brush smear showed no acid-fast bacilli on smear or culture. The transbronchial biopsy showed foreign body granulomatosis with birefringent particles, without evidence of TB. He did not attend for follow up after discharge.

Fig 1c. Higher magnification view under polarised light showing multiple fragments of birefringent foreign bodies (arrow) within a granuloma (x 400 mag)

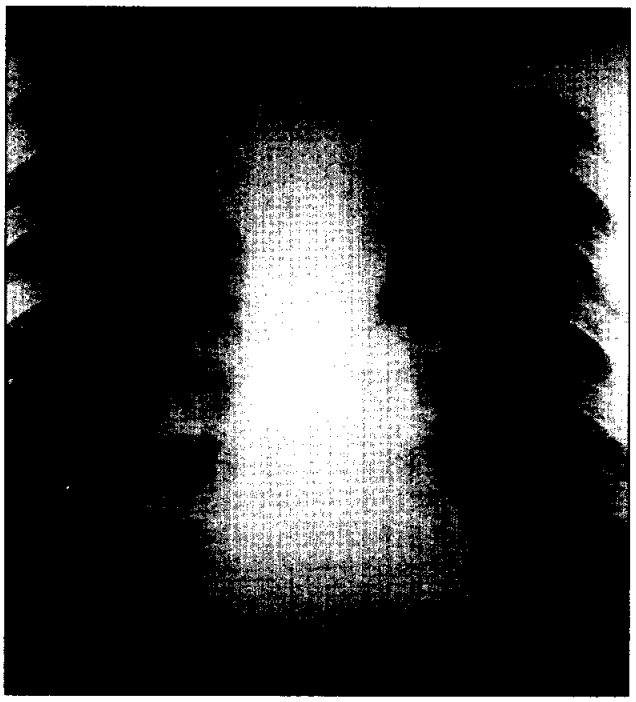

Fig 2. Chest X-ray of patient 2 showing miliary shadows

Case 3

A 26-year-old man was admitted because of chest pain of two weeks' duration, cough with blood-stained sputum of one month's duration, and a weight loss of 22.5 kg (50 lb) in two months. He was also an intravenous heroin addict and had injected crushed tablets of triazolam and flunitrazepam. The total number of tablets injected was approximately 70. A physical examination revealed injection scars over the groin region. The optic fundi were normal. His arterial blood gases showed a pCO_2 of 4.96 kPA, pO_2 of 10.7 kPa, and a blood pH of 7.4. His sputum showed no acid-fast bacilli on smear or culture. His chest X-ray showed miliary shadows, with a dense opacity in the left apex compatible with active pulmonary TB (Fig 3a). A computed tomography (CT) scan of his thorax confirmed the presence of miliary nodules (Fig 3b). Bronchoscopy showed no endoscopic abnormality. Bronchial aspirate and brush smear showed no tubercle bacillus. A transbronchial biopsy showed foreign body granulomatous inflammation. No caseation or Langerhans giant cells were present. As the left apical lesion on his chest X-ray was compatible with active TB, he was given anti-TB medication.

He attended follow up at the Chest Clinic once after discharge but later defaulted because he was arrested for drug trafficking. While in prison, he received six months' anti-TB therapy and showed radiological improvement (Fig 3c). His sputum was never positive for acid-fast bacilli.

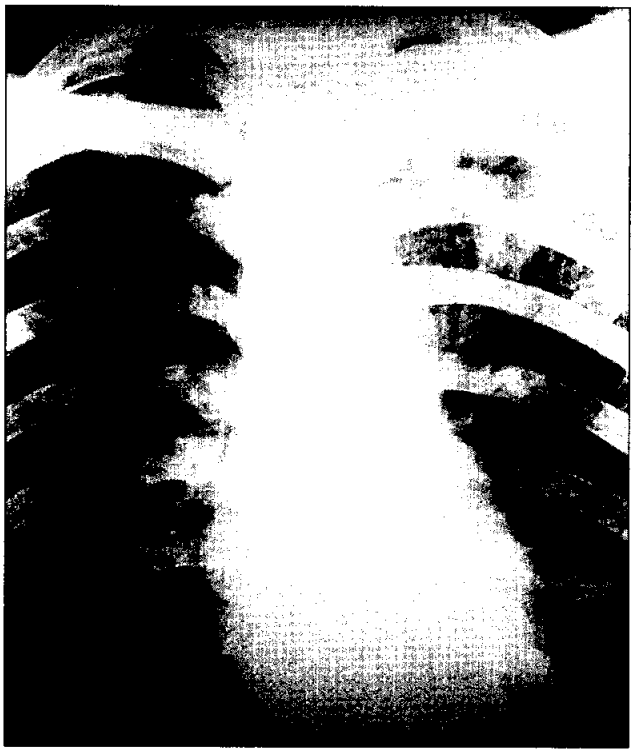

Fig 3a. Chest X-ray of patient 3 showing miliary shadows and left apical opacity

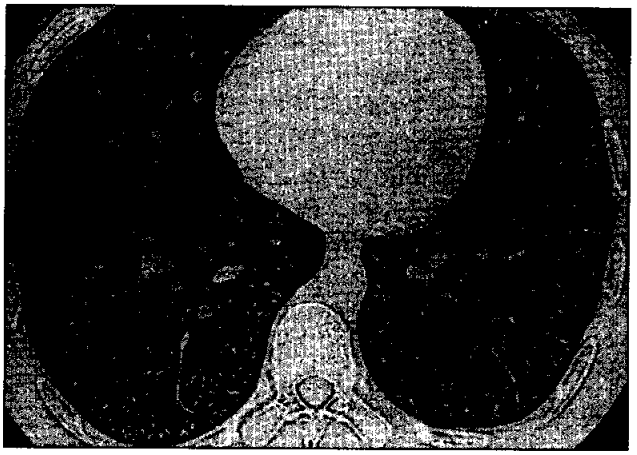

Fig 3b. High resolution computed tomography of patient 3 with 1 mm collimation, showing miliary nodules with a mainly interstitial distribution

Fig 3c. Chest X-ray of patient 3 after six months of anti-tuberculosis chemotherapy showing partial clearing of the left apical opacity

Discussion

The earliest report of lung granuloma in morphine addicts was made by Spain in 1950.[3] Since then, there have been a number of reports of foreign body granulomatosis in the lungs of intravenous addicts,

most of whom injected crushed tablets that were intended only for oral use.[4] The substance responsible is talc, which is used as a filler to prevent the tablets sticking to punches and dies. Talc is also present in some street heroin used for intravenous injection.

The histology consists of intravascular microemboli that cause angiothrombosis. With time, transvascular migration of particles occurs,[5] resulting in both diffuse intravascular and perivascular non-caseating granulomas.[6] Diffuse fibrosis develops, the severity being related to the total amount of tablets injected. Progressive massive fibrosis may subsequently occur.[7] There are foreign body giant cells containing birefringent talc particles, the size of these being larger than what could be inhaled. Pulmonary hypertension and cor pulmonale subsequently occur. Tomashefski and Hirsch found no difference in muscular arteries between intravenous abusers with scanty emboli and control subjects. This finding does not support the hypothesis that pulmonary hypertension and cor pulmonale are caused by vasoconstriction or other nonthrombotic reactions.[8]

In the three cases we report, the first and the third patient gave a definite history of injecting crushed tablets. Although the number of tablets injected was small, the pulmonary granulomas that we observed were probably caused by talc. In the second case, the pulmonary granulomatosis was probably due to talc or other impurities present in the heroin powder injected.

Hopkins reports 100 cases of autopsies performed on drug offenders.[9] Pulmonary granuloma was found in 15, angiothrombosis in 12, and histological evidence of pulmonary hypertension in eight. However, the percentage that presented with chest X-ray abnormality was not known. In our three cases, all had miliary shadows in their chest X-rays. Case number 3 also had patchy consolidation in the left upper lobe due to TB. Pare et al report on 17 addicts with prolonged and excessive parenteral use of oral medication.[10] Ten addicts had dyspnoea and four had cough. Fifteen had a fundal examination, with talc emboli being detected in nine. Chest X-ray abnormality was detected in seven addicts, four of whom had widespread nodular shadows with no change in lung volume, and two had shrinkage in lung volume. Of the 17 cases, only two had tissue confirmation of foreign body granulomas. Of our three cases, none presented with dyspnoea and none had talc emboli detected on fundal examination. However, all had transbronchial biopsy findings of foreign body granulomas.

After a 10-year follow up, Pare et al reported on the long term outcome of six cases of foreign body granulomatosis in the lungs.[11] The initially diffuse, pinpoint micronodularity subsequently conglomerated in the upper lobes, closely resembling the progressive massive fibrosis of pneumoconiosis. The lower lobes had become emphysematous with bullae formation and the development of pneumothorax. Three individuals had died from respiratory failure. The fate of our three cases is not known: Cases 1 and 2 defaulted follow up and case 3 is still under observation. None had respiratory symptoms that required treatment, for which corticosteroids have been reported to be effective.[12]

An additonal feature of cases in our locality is that pulmonary TB is endemic in Hong Kong. When a chest physician is confronted with an intravenous addict with miliary shadows, the pressure to start anti-TB treatment is enormous. As it is impossible to differentiate the two on chest X-ray, in places where facilities for tissue biopsy are not available (e.g. prison hospitals), the patient will probably be given a full course of anti-TB treatment and the true diagnosis will never be known. In fact, our third patient had both TB and foreign body granulomas.

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