Pulmonary nodules due to Corynebacterium ulcerans

R.B. Dessau*, M. Brandt-Christensen**, O.J. Jensen*, P. Tønnesen**

ABSTRACT: A 53 year old male with symptoms of coughing for 6 months presented with bilateral multiple pulmonary nodules suggestive of metastatic disease. By surgical resection 4 out of 6 nodules were removed. Histopathological examination showed granulomatous necrotizing inflammation with growth of Corynebacterium ulcerans, which did not produce diphtheria toxin. The patient was treated with penicillin for 1 week. Follow-up for 2 yrs showed no sign of recurrence.


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Corynebacteria are a group of gram-positive, usually nonmotile and pleomorphic rods. Corynebacteria other than Corynebacterium diphtheriae are part of the normal mucocutaneous flora of many animals and humans, and are widely distributed in soil, fresh water and salt water. They often contaminate cultures, and many species are not well-defined and are not routinely differentiated in the laboratory. It is now increasingly recognized that nondiphtheria Corynebacteria may cause human disease, especially in the immunocompromised host [1, 2].

Corynebacterium ulcerans is a commensal microorganism in cattle and horses. Human disease usually occurs after exposure to livestock and raw milk [3–5]. In humans, C. ulcerans may cause pharyngitis and diphtheria-like disease [6–8]. Some strains of C. ulcerans produce diphtheria toxin. A fatal case of pneumonia caused by C. ulcerans was reported in a 78 year old man suffering from lung cancer with metastases [9]. Another fatal case was reported in a previously healthy 73 year old women [10]. A total of two cases of C. ulcerans infection have been reported in Denmark between 1956 and 1989 [11].

This is the first report of C. ulcerans associated with multiple nodular pulmonary infiltrates, presenting histologically as necrotizing granulomatous inflammation.

Case report

The patient was a 53 year old man with left-side chronic otitis of 10 yrs duration, but otherwise healthy. A cholesteatoma was removed in 1975, and resection of the mastoid was performed in 1981. The patient had smoked 10 cigarettes daily for 30 yrs (except for a period of 10 yrs) until 2 months before referral. He drank 0–2 beers daily, received no medication, and had no previous pulmonary symptoms. He had been mildly exposed to asbestos 2–3 times yearly during the last 13 yrs, when removing insulation.

Except for mild increasing cough with white sputum for 6 months, the patient was well, without symptoms. Two months before referral, he had been treated with penicillin for 2 weeks due to clinical diagnosis of pneumonia.

On referral, chest radiography showed two nodules, and computerized tomographic (CT) scan revealed five rounded nodules located peripherally in the right lung (upper lobe and lower lobe) and one nodule in the left lower lobe, all approximately 1 cm in diameter, suggesting metastatic disease (figs. 1 and 2). Slight pleural

Fig. 1. – Posteroanterior chest radiograph before surgery. Only two nodules are visible on the right side.
thickening was found in the basal area of the right lung. Laboratory analyses were all within normal limits (peripheral blood count, blood biochemistry, germinal cell tumour markers, human immunodeficiency virus (HIV) test, antinuclear cytoplasmatic antibodies (ANCA)). Lung function was normal with a forced vital capacity (FVC) of 4.4 l and a forced expiratory volume in one second (FEV1) of 3.4 l. Ultrasound examination of the abdomen was normal.

Fibrebronchoscopy showed slight inflammatory changes of the bronchial mucosa, with negative cultures for bacteria. A right-sided transthoracic thin needle aspirate of a nodule was performed under fluoroscopic guidance. Microscopy of the aspirate showed normal cells (macrophages, lymphocytes, alveolar cells). Cultures were negative for bacteria, including Mycobacteria.

Two months after referral, a right-sided explorative thoractomy was performed. Some pleural fluid was present. The visceral pleura was thickened on the upper, middle and lower lobes, with fibrous changes on the lower lobe. Four infiltrates on the right side were removed surgically. In the first 24 h following the operation 5 million IU of penicillin-G i.v. were given i.v. After 2 weeks, 1 million IU of penicillin-G i.v. was administered for one week due to possible wound infection.

Histological examinations showed granulomas of moderate size, with central necrosis, with neutrophils and cellular debris surrounded by epithelioid and giant cells, lymphocytes and fibrous tissue. Moderate infiltration with eosinophils was also present. No signs of vasculitis were found (fig. 3). No ferruginous bodies (asbestos bodies) and no foreign bodies were present. Acid-fast bacteria were not found, but several grouped bacteria-like organisms were seen which stained positively with periodic-acid-Schiff (PAS) and Grocott-Gomori stain. The visceral pleura was fibrous and without signs of malignancy.

Nonpigmented large colonies without haemolysis were cultured from the nodules. Gram-staining showed Gram-positive short coryneform rods. The stain grew well on tellurite agar with a greyish coloured reaction, fermented starch, and was positive for catalase, urease, glucose and maltose. The stain was thus identified as a C. ulcerans, in agreement with the identification table [2]. Identification of the strain was confirmed by the Danish Reference Laboratory (Statens Seruminstitut), where it was found to be diphtheria toxin negative, as determined by the Elek test. The isolate was found to be sensitive to penicillin, ampicillin, erythromycin, cefuroxime and gentamicin. Culture for Mycobacteria was negative.

At follow-up 1 yr after surgery, the patient was in good health, with no pulmonary complaints except for mild expectoration. CT-scan of the chest showed no new infiltrates; in the right upper and lower lobe, two small consolidations much smaller than the original nodules were seen, whilst the nodule on the left side had disappeared. Two years after surgery, chest radiography was still unchanged and the patient was in good health.

Ear, nose and throat (ENT) specialist examination of the left ear showed a small amount of fluid in the middle
ear cavity, with positive culture of Pseudomonas and no growth of *C. ulcerans*.

**Discussion**

*C. ulcerans* appears to be another cause of necrotizing granulomas in the lung. As *C. ulcerans* was found both at microscopy and in cultures from the nodules, it is highly probable that this bacterium induced the granulomas.

Some nondiphtheria species of Corynebacterium can produce endocarditis, pneumonitis, pharyngitis, cutaneous infections, and granulomatous lymphadenitis [1]. Necrotizing granulomas of the lung caused by a Corynebacterium species have not been described previously.

Tuberculosis was excluded by negative microscopy and culture. Several other differential diagnoses, such as Wegener's granulomatosis [12], lymphomatoid granulomatosis, benign lymphocytic angiitis and granulomatosis, and necrotizing sarcoid granulomatosis were less possible, as there were no signs of vasculitis and negative ANCA. Although there were some histological similarities to bronchocentric granulomatosis, this diagnosis seems less probable because the necrotic lesions had no relationship to the bronchi, and there were no signs of peribronchial inflammation [13, 14]. Signs of malignancy were not found either histologically or on chest radiography during 1 yr of follow-up. No impairment in immunofunction was observed. The patient appeared healthy, except for one-sided chronic otitis.

Although the treatment course with penicillin was short, it may have cured the patient in combination with surgical removal of the majority of the nodules. As the chest radiograph showed no sign of progression, and the patient was in excellent health, we chose not to treat him further with penicillin. The two very small consolidations seen on CT-scan after 1 yr probably represent fibrous changes after the surgical resection, confirmed by unchanged chest radiography for up to 2 yrs after surgery.

In summary, *C. ulcerans* infection has to be added to the list of necrotizing granulomas and pulmonary nodules.

**References**