Case Report

Rhodococcus equi infection in a patient with spinocellular carcinoma of unknown origin

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A *Rhodococcus equi* pulmonary infection in a 63-year-old man receiving chemotherapy and radiotherapy for spinocellular carcinoma is described. The patient, a knife-grinder, was promptly treated with levofloxacin plus amikacin followed by rifampicin for 2 months, and he is still in good clinical condition after an 8-month follow-up.

Introduction

Rhodococcus equi is a Gram-positive, non-motile, environmental, aerobic, coccobacillary organism that primarily causes zoonotic infections (Scott *et al.*, 1995). Human infections are predominantly airborne, but can also occur by oral ingestion or wound contamination (Garthwaite *et al.*, 2007; Kwak *et al.*, 2003). *R. equi* infects primarily immunocompromised patients and pathogenicity is related to its survival inside macrophages (Meeuse *et al.*, 2007). AIDS, organ transplant, chemotherapy and steroid therapy are often predisposing factors (Lasky *et al.*, 1991). The lung is the most commonly involved site and clinical resemblance to mycobacterial, fungal or nocardial pulmonary infections contributes to the delay in an accurate diagnosis (Weinstock & Brown, 2002). The infections reported in non-immunocompromised subjects involve, in the great majority, subjects having contact with farm animals (Prescott, 1991). We describe here a case of pulmonary *R. equi* infection in a cancer patient.

Case report

A 63-year-old man diagnosed with a spinocellular carcinoma (G1) of unknown origin localized in laterocervical and mediastinal lymph nodes started concomitant chemotherapy (cisplatin 100 mg m⁻² every 21 days) and radiotherapy. Two months later, 3 weeks after the second cycle of chemotherapy, the patient was admitted for fever not responsive to paracetamol ($T_{\max}$ 38.5 °C), cough, oral mucositis with dehydration, and iatrogenic neutropenia. Clinical examination revealed pulmonary rhonchi associated with global murmur reduction. Blood examina-

tions showed leukopenia (white cells 1700 µl⁻¹; neutrophils 68 %) and increase of inflammatory index (C-reactive protein >90 mg l⁻¹). A chest X-ray and a subsequent CT scan revealed a large infiltrate at the lower left pulmonary lobe with dishomogeneous features due to the presence of a cavitory area with air levels compatible with a phlogistic abscess. Other smaller phlogistic infiltrates were present in the entire right lung and in the upper segment of the lower left lobe (Fig. 1). Blood gas analysis showed normo-capnic hypoxia (pO₂=55 mmHg; pCO₂=46 mmHg; pH=7.47; SO₂=91 %). An empirical treatment with ceftazidime plus amikacin was initiated without a significant clinical improvement, and therefore antibiotic treatment was modified to levofloxacin (500 mg b.i.d.) plus amikacin (15 mg kg⁻¹). Considering the immunocompromised status and the chest X-ray features, a fibro-bronchoscopy was performed, allowing a bronchoalveolar lavage (BAL) sample collection. Microscopy and culture were consistent with *R. equi*. The antibiotic treatment was continued i.v. for 3 weeks with a progressive clinical and radiological improvement. After discharge, therapy (rifampicin 600 mg q.d. plus levofloxacin 500 mg b.i.d.) was administered per os for 4 weeks; after antibiotic interruption no recurrences were observed in an 8-month follow-up.

Microbiological features

The BAL was sent to two different laboratories of our University Hospital, where cultures for bacteria and fungi were performed. In the mycological laboratory, microscopic examination with KOH showed a high number of polymorphonuclear leukocytes, therefore Gram and Ziehl–Neelsen stains were performed. The Gram stain revealed the presence of coccobacillary Gram-positive bacteria,

Abbreviation: BAL, bronchoalveolar lavage.

Fig. 1. Patient's chest CT scan showing in the lower left lobe the presence of an extensive phlogistic infiltrate limited by the anterior scissura. Within the infiltrate, a large cavitary area, containing secretions and air-fluid levels, is appreciable.

some in polymorphonuclear leukocytes. Weak acid-fast-positive coccobacillary forms were seen with the Ziehl–Neelsen stain (Fig. 2), so a possible aerobic actinomycete infection was suspected. For fungal cultures, in order to prevent bacterial growth, the BAL was treated with a Pen-Strep solution and inoculated on both Sabouraud agar plates and slants. The cultures were incubated under aerobic conditions at 30 °C and 37 °C for 7–10 days. Only mouth commensal micro-organisms grew on standard bacteriological media, whereas on Sabouraud agar plates, pale-pink and non-slimy colonies developed in 1 week at both temperatures. Microscopic examination of the colonies developed on Sabouraud agar plates at both

Fig. 2. Ziehl–Neelsen stain of the BAL sample. Black arrows show weak acid-fast coccobacillary forms, a few of them intracellular.

temperatures confirmed the presence of coccobacillary Gram-positive forms as well as a weak acid-fastness with the Ziehl–Neelsen stain. The bacterium was catalase-positive and urease- and oxidase-negative, confirming our suspicion of an *R. equi* isolate, the only species in the genus considered to be pathogenic for humans.

Discussion

We describe the case of an *R. equi* infection diagnosed during concomitant chemo-radiotherapy; it cannot be stated with certainty whether the infection was already present before this treatment. Since the patient was a knife-grinder occasionally working in an equine butchery as a more detailed anamnesis revealed, one might assume that it may have been silent or slowly progressing and asymptomatic until starting chemotherapy.

Early recognition of *R. equi* infection is important because clinical isolates are usually susceptible to the appropriate antibiotic therapy. However, aetiological diagnosis can be difficult because of its similarity to non-pathogenic commensals and the slow growth rate, making it necessary to suspect the possible presence of this micro-organism to reach a proven diagnosis (Brown *et al.*, 1999). Although *R. equi* is the most common pathogen isolated within the genus, its pleomorphic appearance by Gram staining is often responsible for misidentification as diphtheroids. When clinical specimens are stained with the Ziehl–Neelsen stain, *R. equi* can exhibit a weak acid-fastness that is easily lost when smears are prepared from cultures. Microscopic morphology varies from coccoid to bacillary forms, and the latter are best visualized in *R. equi* cultured in liquid media. The late development of the colonies' characteristic pink colour may be another confounding feature. Any body site can be involved during infection, but the lung is the most common site. Bacteraemia can occur

in about 80 % of immunocompromised hosts and in 30 % of immunocompetent subjects (Weinstock & Brown, 2002).

In this case, the anamnestic risk factor had been initially unrecognized, and discovered only when the microbiological diagnosis was made. Obtaining a complete detailed anamnesis is mandatory, as highlighted previously by Kedlaya *et al.* (2001), especially when exposure to livestock is a requisite for considering an *R. equi* infection in the differential diagnosis of lung lesions in immunocompromised individuals (Koya *et al.*, 2007). The *R. equi* had been isolated only from BAL cultures on Sabouraud agar plates and not on bacteriological media. This can be explained by the overgrowth of micro-organisms representing the normal bacterial flora of the upper respiratory tract; the treatment of the specimen with an antibiotic solution for the fungal cultures; and the slow growth rate of *R. equi*. Modification of the empiric antibiotic treatment to a more specific regimen (levofloxacin plus amikacin) resulted in a progressive improvement of the patient's clinical condition, as also confirmed by radiological reduction of the phlogistic infiltrate in the lower left lobe. Isolates of *R. equi* are usually susceptible to aminoglycosides, rifampicin, erythromycin, fluoroquinolones, glycopeptides and imipenem, so the patient benefited from the antibiotic therapy even though it had been established on the basis of clinical experience and published case reports (Weinstock & Brown, 2002; Meeuse *et al.*, 2007).

When rare aetiology may cause life-threatening diseases in immunocompromised patients, it is very important to obtain a correct laboratory-supported diagnosis, as this case underlines. Additionally, our patient history confirms the great importance of a detailed anamnesis in such a population to better direct the diagnosis, microbiological

examination, and ultimately the correct clinical management.

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