Case Report

A rare pulmonary infection caused by *Arthrographis kalrae*

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Arthrographis kalrae is a rare isolate in clinical specimens. Only ten cases of infection with this species have been described so far. To our knowledge, we report the first case of a pulmonary infection caused by *A. kalrae* in a patient with a past history of stage IIA Hodgkin's lymphoma and demonstrate that this organism can act as an opportunistic human pathogen.

Introduction

Arthrographis kalrae is a rare isolate in clinical specimens. Only ten cases of infection with this species have been described so far (Biser *et al.*, 2004; Chin-Hong *et al.*, 2001; de Diego Candela *et al.*, 2010; Degavre *et al.*, 1997; Perlman & Binns, 1997; Pichon *et al.*, 2008; Sugiura & Hironaga, 2010; Thomas *et al.*, 2011; Volleková *et al.*, 2008; Xi *et al.*, 2004.). To our knowledge, we report the first case of a pulmonary infection caused by *A. kalrae* and demonstrate this organism can act as an opportunistic human pathogen.

Case report

A 61-year-old Caucasian non-smoking male was admitted to the emergency department with a 1-day history of haemoptysis. Only small amounts of blood were expectorated. The patient had a several-month history of a cough with purulent sputum. There was no fever, dyspnoea or pain. There was a past history of stage IIA Hodgkin's lymphoma, 17 years ago, which had affected the neck and mediastinal lymph nodes. The patient received radiotherapy to the chest, spleen and para-aortic lymph nodes.

The patient received thyroxin supplements for subsequent hypothyroidism. Two years after having been treated for M. Hodgkin he underwent a wedge resection and pleurectomy because of recurrent right-sided pneumothorax. Prior to this presentation there had been two episodes of haemoptysis, 3 years apart, of which the aetiology remained unclear.

Physical examination was unremarkable and blood pressure, heart rate and temperature were normal. Laboratory testing showed normal inflammatory parameters including a C-reactive protein (CRP) level of 6 mg l^{-1}, leukocyte count of 9.5×10^9 l^{-1} and haemoglobin level of 14.5 g dl^{-1}. A chest radiograph revealed a mass in the apex of the right upper lobe. A computerized tomography (CT)-scan showed a round solid mass in the apex of the right upper lobe with pleural thickening, suggestive of an aspergilloma (Fig. 1). The patient underwent a right upper lobectomy combined with a transposition of the major pectoral muscle to fill up the remaining cavity, since the middle and lower lobe could not fill the entire right hemithorax, being fixed to the thoracic wall after radiation therapy and the wedge resection of bullae and pleurectomy that was performed 15 years ago. The operation was complicated by pulmonary embolism, which was treated with acenocoumarol. Histopathology demonstrated no signs of *Aspergillus* infection. The resected mass was, however, not submitted for culture. In two sputum cultures, taken about 1 week later, an *Arthrographis* species was isolated. The fungus was regarded as a contaminant and the patient was not treated with antifungals.

One year later, the patient had further haemoptysis and a productive cough. A CT-scan demonstrated, again, a mass in the cavity of the apex with the radiographic appearance of an aspergilloma and signs of a bronchopleural fistula. At thoracotomy, a cavity with necrotic tissue and pus was found. A chest wall fenestration and necrotectomy were performed and the pus was sent for culture. Unfortunately, no material was sent for histopathology. The patient was treated with itraconazole for suspected aspergilloma. After 5 days of incubation on Sabouraud agar at 25° and 37 °C, there was growth of small, dense cream–yellow mould colonies that were slightly fissuring into the agar (Fig. 2). Microscopic examination revealed hyaline, septate hyphae with one-celled, smooth-walled arthroconidia and blastoconidia directly on the sides of undifferentiated hyphae. The isolates were identified as *A. kalrae* by means of 18S rRNA PCR using general primers followed by sequencing.

Abbreviation: CT, computerized tomography.

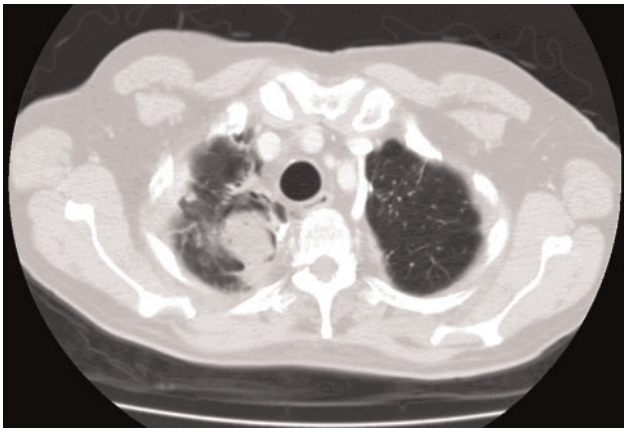

Fig. 1. A chest CT scan demonstrating a cavitating lesion in the right upper lobe and pleural thickening.

We were not able to test the susceptibility to antifungals of our isolates. No bacterial pathogens were isolated in this specimen. The patient was treated with itraconazole (200 mg twice daily for 2 weeks) and further recovery was uneventful. Six months later a partial thoracoplasty (resection of the dorsal parts of rib 1–4) and an anterior serratus muscle transposition were performed in order to fill the cavity and close the bronchopleural fistula. During the 2.5 years of follow-up observations there were no signs of a recurrence of the infection. Initially, a small bronchopleural fistula persisted which produced decreasing amounts of pus. Eventually, this fistula closed without further intervention. Follow-up cultures of the pus that was produced by the fistula remained negative.

Discussion

The genus *Arthrographis* consists of five species: *A. kalrae*, *A. cuboidea*, *A. lignicola*, *A. pinicola* and *A. alba*. Identification of the species is difficult by microscopy alone. *A. kalrae* is a dimorphic fungus and an uncommon human pathogen. Only 10 cases of infection with this species have been described so far (Biser *et al.*, 2004; Chin-Hong *et al.*, 2001; de Diego Candela *et al.*, 2010; Degavre *et al.*, 1997; Perlman & Binns, 1997; Pichon *et al.*, 2008; Sugiura & Hironaga, 2010; Thomas *et al.*, 2011; Volleková *et al.*, 2008; Xi *et al.*, 2004). These infections included keratitis (Biser *et al.*, 2004; Perlman & Binns, 1997; Thomas *et al.*, 2011), mycetoma of the hand (Degavre *et al.*, 1997), sinusitis (Chin-Hong *et al.*, 2001; Xi *et al.*, 2004), meningitis (Chin-Hong *et al.*, 2001), ophthalmitis (Xi *et al.*, 2004), onychomycosis (Sugiura & Hironaga, 2010; Volleková *et al.*, 2008), cerebral vasculitis (Pichon *et al.*, 2008) and endocarditis (de Diego Candela *et al.*, 2010). To our knowledge, this is the first reported case of severe pulmonary infection caused by *A. kalrae*. In the majority of the reported cases the source of *A. kalrae* was unknown. However, *A. kalrae* has been isolated from natural and commercially available soils and compost (Sugiura & Hironaga, 2010). It enters the human body through the respiratory tract or by inoculation due to trauma (Pichon *et al.*, 2008). The patient may have acquired the infection while gardening after contact with contaminated soil.

Fig. 2. *A. kalrae* colony on Sabouraud agar displaying a small dense cream–yellow morphology and slight fissuring into the agar.

One of the questions that arose was whether the isolated *A. kalrae* was acting as a pathogen or only as a colonizer of the thoracic cavity. Because a lobectomy was performed without opening of the cavity during the first operation, no material was sent for culture; however, pathology provided no evidence of *Aspergillus* or other fungi. Sputum cultures during this admission period contained an *Arthrographis* species but these were regarded as contaminants. During the second operation, unfortunately no tissue was sent for histopathological investigation because there was no suspicion of malignancy. We have regarded *A. kalrae* as an opportunistic pathogen because it was consistently isolated after two operations that were separated by a year, because the clinical picture was typical of that of a fungal pulmonary infection and because no other pathogens were isolated. Apparently, *A. kalrae* is an opportunistic human pathogen that may cause a severe pulmonary infection in patients with an immune-compromised lung after radiotherapy on the chest.

In most reported cases, *A. kalrae* was treated with itraconazole because of its known susceptibility to this antifungal (Biser *et al.*, 2004; Chin-Hong *et al.*, 2001; Degavre *et al.*, 1997; Sugiura & Hironaga, 2010; Volleková *et al.*, 2008). Susceptibility to terbinafine, miconazole and amphotericin B has been reported also (Biser *et al.*, 2004; Sugiura & Hironaga, 2010). Generally a treatment period of 3–12 months is advocated; however, in our case, treatment with itraconazole for only 2 weeks, in addition to surgical resection, proved to be effective. Apparently, a definitive cure can be obtained by radical surgical resection followed by a short interval of antifungal therapy, such as seen with aspergillomas, for example. However, the precise additional value of itraconazole next to surgery in this case remains unclear. Retrospectively, aggressive antifungal therapy given during the first admission and after the lobectomy might have

prevented the following further surgical interventions and complications.

In conclusion, we report the first case of a pulmonary infection caused by *A. kalrae*. The patient was cured after surgical resection and a short course of antifungal therapy. This case illustrates that irradiated lung tissue is susceptible to opportunistic infections with uncommon pathogens.

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