Pulmonary actinomycosis and polymicrobial empyema in a patient with ABPA and bronchocoele

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Abstract
We present a 43-year-old woman, with a history of allergic bronchopulmonary aspergillosis and a chronic bronchocoele, who was admitted to hospital with an infection of the bronchocoele, progressing to a pulmonary abscess and polymicrobial empyema, following dental extraction and regular Lactobacillus probiotic ingestion. Interval chest imaging following this procedure demonstrated worsening right upper lobe opacities and a right-sided pleural effusion. Bronchoscopies identified copious mucoid secretions and an infected bronchocoele with a right upper lobe airways impaction. Oral cavity organisms including Actinomyces odontolyticus were cultured on bronchial washings. Streptococcus mitis and Lactobacillus rhamnosus were cultured in pleural fluid. Treatment with endoscopic mucoid secretion suctioning; intercostal catheter insertion and therapeutic drainage; and antibiotic, glucocorticoid and anti-IgE therapy resulted in clinical and radiological improvement. Our case illustrates the potential pulmonary complications from oral cavity organisms following tooth extraction and probiotic use in patients with chronic lung disease associated with mucoid lesions and airways obstruction.

KEYWORDS
ABPA, Actinomyces odontolyticus, bronchiectasis, Lactobacillus rhamnosus, Streptococcus mitis

INTRODUCTION
Actinomyces odontolyticus, Lactobacillus rhamnosus and Streptococcus mitis are rare causes for pulmonary infections and are mostly reported in immunocompromised patients or those with a history of untreated periodontal disease. To our knowledge, we describe the first case of a patient with a history of allergic bronchopulmonary aspergillosis (ABPA) and a chronic bronchocoele, who subsequently developed an infected bronchocoele, complicated by pulmonary actinomycosis and L. rhamnosus and S. mitis empyema following tooth extraction and regular Lactobacillus probiotic use.

CASE REPORT
A 43-year-old woman was hospitalized after presenting with fevers, right-sided pleuritic chest pain and productive cough. Her medical history included previously treated pulmonary tuberculosis; childhood atopic asthma; and right upper lobe, right middle lobe and lingula lobe bronchiectasis. Prior spirometry and transfer factor for carbon monoxide (TLCO) were within normal limits with no significant bronchodilator response. Chest imaging performed 4 years prior to her admission (Figure 1A) demonstrated bronchiectasis and an uncomplicated bronchocoele in the right upper lobe. Twelve months prior to admission, eosinophil count was $1.02 \times 10^9/\text{L}$, total immunoglobulin E (IgE) level was 1070 IU/ml and radioallergosorbent (RAST) test to Aspergillus was positive. Her background symptoms (i.e., cough and exertional dyspnoea) were generally well controlled on regular combined fluticasone propionate/salmeterol 250 μg/50 μg inhaler. She denied any history of immunodeficiency, alcoholism, aspiration or gastroesophageal reflux disease.

The hospitalization followed a dental extraction 4 months prior for a cracked tooth. She was also regularly...
ingesting *Lactobacillus* probiotic capsules. Chest imaging demonstrated significant enlargement of the known right upper lobe opacity, with another small bronchocoele in the lingula (Figure 1B,C). She was admitted for 2 days and treated with 9 days of empiric cephalosporins and discharged home for an urgent outpatient bronchoscopy with a weaning regimen of prednisolone, commencing at a dose of 37.5 mg daily over a 2-week period. The bronchoscopy performed 7 days following her hospital discharge identified impacted mucoid plugs in the right upper lobe and lingula. The lingula plug was successfully aspirated endoscopically with drainage of purulent secretions. The tenacious right upper lobe mucoid plug was unable to be aspirated. A right upper lobe endobronchial biopsy was performed. *Aspergillus fumigatus* was cultured on bronchial washings and *Aspergillus niger* complex and *A. odontolyticus* were cultured from the tissue sample.

Eight days following bronchoscopy, she represented to the emergency department with recurrent productive cough, pleuritic chest pain and fevers. She was afebrile, haemodynamically stable and had a respiratory rate of 18 breaths per minute with oxygen saturations of 96% on room air. Chest examination was unremarkable. Follow-up chest x-ray demonstrated persistence of the right upper lobe opacity, unchanged from her chest imaging performed at the time of initial presentation. Laboratory investigations...
TABLE 1 Summary of data on reported cases of intrathoracic *Actinomyces odontolyticus*, *Lactobacillus rhamnosus* and *Streptococcus mitis* infection

| Reference | Disease(s) | Age (years)/sex | Underlying condition(s) | Presentation | Chest radiograph finding(s) | Diagnostic procedure |
|-----------|------------|-----------------|--------------------------|--------------|-----------------------------|----------------------|
| 8         | Lung abscess | 61/F            | Rheumatoid arthritis, corticosteroid therapy | Fever, chest pain, dyspnoea | Pleural effusion, cavitating lesion | Abscess culture |
| 9         | Pneumonia   | 61/M            | Lung transplant, immunosuppression | Chest pain | LUL infiltrate | Bronchoscopy brush culture |
| 9         | Mediastinitis | 43/M          | Heart-lung transplant, immunosuppression | Post-operative sternal wound | Bi-basilar infiltrate | Wound culture |
| 10        | Empyema     | 38/F            | Periodontal disease | Weight loss, fever, chest pain, cough, dyspnoea | Pleural effusion | Pleural fluid culture |
| 11        | Pneumonia   | 52/F            | Bronchiectasis | Weight loss, fever | LUL infiltrate with cavitating lesion | Sputum culture, lung granule |
| 12        | Pneumonia, skin abscess | 52/M        | Alcoholism, periodontal disease | Weight loss, fever, cutaneous drainage | B/L cavitating apical infiltrates, pleural thickening | Abscess culture |
| 12        | Empyema necessitates | 50/M        | S/P pneumonectomy for aspergiloma, ETOH use, pulmonary TB | Fever, chest pain, dyspnoea | Left pleural empyema | Pleural fluid culture |
| 14        | Pericardial + pleural effusion | 68/M | S/P resection of gastric polyp | Dyspnoea, fever | Pericardial + pleural effusion | Pericardial fluid culture |
| 14        | Chest wall erosion, spinal and calf abscesses, pleural effusion | 58/F | Dental plate | Weight loss, fever, chest pain | Left anterior mid-lung shadow | Chest wall biopsy culture |
| 14        | Pneumonia, empyema | 40/M        | Alcoholism, smoker | Fever, chest pain, productive cough | RUL infiltrate, pleural effusion | Pleural fluid culture |
| 15        | Lung abscess | 49/M            | Alcoholism, smoker | Dyspnoea | Pleural effusion | Pleural fluid culture |
| 16        | Lung abscess | 37/F            | Sarcoidosis, PNL, newly diagnosed diffuse large B-cell lymphoma | Dyspnoea, fever, dry cough | LLL infiltrate, right lung mass, right hilar mass | Abscess culture |
| 17        | Lung abscess | 64/F            | Periodontal disease, appendicitis (age 33) | Fever, chest pain, dry cough | RML nodular shadow | Pleural fluid culture |
| 18        | Pneumonia   | 34/M            | S/P gastric polypectomy, dental caries | Cough, sputum | LUL cavitating lesion | Bronchial washings |
| 19        | Pleural effusion | 65/M         | Smoker, periodontal disease, alcoholism | Cough, sputum, fever, dyspnoea | Pleural effusion, RUL + LUL consolidation | Bronchial washings |
| 20        | Lung abscess | 60/M            | Smoker, newly diagnosed lung squamous cell carcinoma | Hoarseness | Left hilum mass, LUL cavitating lesion, mediastinal lymphadenopathy | Bronchial washings |
| 21        | Pneumonia   | 69/M            | Periodontal disease, renal transplant | Unknown | Unknown | Bronchial washings |
| 22        | Pneumonia   | 43/M            | Asthma, chronic eosinophilic pneumonia | Cough, dyspnoea | Pulmonary infiltrates, left pleural effusion | Endobronchial biopsy culture, bronchial washings |
| 23        | Pneumonia   | 38/M            | Smoker, newly diagnosed Hodgkin’s lymphoma | Sputum, cough | LUL infiltrate | Bronchial washings |
| 24        | Empyema     | 68/M            | Smoker, periodontal disease, alcoholism | Fever, chest pain, dyspnoea, sputum, cough | Right-sided consolidation, pleural effusion | Pleural fluid culture |
| 25        | Empyema     | 59/M            | Pulmonary TB, asthma, obesity, periodontal disease | Cough, sputum chest pain, fever | Pleural effusion | Pleural fluid culture |

(Continues)
revealed a C-reactive protein (CRP) of 102 mg/L and white blood cell (WBC) count of $14.7 \times 10^9/L$ with neutrophilia of $12.4 \times 10^9/L$. She was hospitalized and commenced on intravenous ceftriaxone and azithromycin and maintained on oral prednisolone 25 mg.

Repeat computed tomography (CT) of the chest demonstrated significant enlargement of the obstructed bronchocoele in the right upper lobe with radiological evidence of a lung abscess, complicated by a right-sided empyema (Figure 1D). Treatment was broadened to piperacillin-tazobactam after several days with persistent fevers and elevated inflammatory markers (peak CRP of 451 mg/L and WBC count of $15.7 \times 10^9/L$). A small-bore intercostal catheter was inserted for therapeutic drainage of the right pleural effusion. Approximately 300 ml of brown pus was drained. Oral organisms, *L. rhamnosus* and *S. mitis*, were cultured on the pleural fluid. Biochemistry post-procedure revealed a CRP of 102 mg/L and WBC count of $10.0 \times 10^9/L$. Repeat bronchoscopy performed on day 12 of admission following a longer course of steroids showed that the previously impacted right upper lobe mucoid plugs were no longer occlusive and mucopurulent secretions were now draining from the right upper lobe. The oral cavity organism, *A. odontolyticus*, was again cultured on bronchial washings and antimicrobial therapy was subsequently changed to intravenous benzylpenicillin and teicoplanin. As *Aspergillus* species was previously cultured on bronchial washings and tissue sample, empiric voriconazole was also commenced. A third bronchoscopy was performed on day 19 of admission due to poor radiological resolution of the right upper lobe abscess. During this procedure, the previously occluded right upper lobe segment remained patent and only normal upper respiratory flora were cultured from these bronchial washings. Interval chest CT imaging performed on day 22 of admission revealed the right upper lobe lung abscess had reduced in size with a smaller recurrence of the right-sided pleural effusion. A second intercostal catheter (14 Fr) was inserted for therapeutic drainage and 90 ml of cloudy amber-coloured fluid was drained. *Lactobacillus rhamnosus* was again cultured on the pleural fluid. Laboratory investigations revealed a CRP of 51 mg/L and WBC count of $5.4 \times 10^9/L$. Steady clinical, biochemical and radiological improvement occurred over a 4-week inpatient stay from a combination of a prolonged course of intravenous antibiotics, oral prednisolone and antifungal therapy in combination with endoscopic aspiration of impacting mucoid plugs and therapeutic drainage of the right-sided empyema. She was subsequently discharged home with a further 2-week course of intravenous antibiotics, oral prednisolone and antifungal therapy.

She was followed up over a 12-month period. Voriconazole was ceased at 6 months due to side effects of liver function derangement, blurred vision, lethargy, skin and nail discolouration and hair loss. Prednisolone was weaned to 5 mg daily with elevation in blood eosinophil counts and increased cough and breathlessness when further weaning was attempted. Due to the requirement for maintenance oral corticosteroids, she was commenced on omalizumab (anti-IgE monoclonal antibody). Following four doses of omalizumab, she reported significant improvements in her respiratory symptoms. Her prednisolone has subsequently been ceased. At 12 months, there was significant clinical and radiological resolution of the right upper lobe lesion with no residual day-to-day respiratory symptoms (Figure 1E).
DISCUSSION

Aspergillus rarely causes infection in individuals with normal immunity and bronchial architecture. Abnormal airway anatomy and a predisposition to airway hypersensitivity reactions are key aspects in the pathogenesis of ABPA. Aspergillus can colonize the bronchial airways in susceptible individuals, causing bronchial inflammation, mucus impaction and inflammation resulting in further bronchiectasis, fibrosis and respiratory compromise.\(^1\) Mucocoele formation may result from chronic mucous impaction. Our patient met the International Society for Human and Animal Mycology (ISHAM) 2013 Diagnostic Criteria for ABPA on the basis of her childhood asthma, positive RAST test to Aspergillus, elevated total IgE and presence of pulmonary opacities on chest radiograph and eosinophilia.\(^2\) Oral antifungal agents and corticosteroids may be used in the treatment of an acute exacerbation of ABPA.\(^3\) Anti-IgE therapy, such as omalizumab, has also been shown to improve outcomes in patients with ABPA and severe asthma.\(^4\)

Actinomyces odontolyticus, L. rhamnosus and S. mitis are microorganisms that have all been individually identified as a part of the normal oropharyngeal flora and considered to have low pathogenicity in humans.\(^5\)–\(^7\) A structured search of the medical literature (Ovid MEDLINE and EMBASE) from January 1966 to December 2021 was conducted to identify English-language articles that reported on pulmonary infections caused by A. odontolyticus, L. rhamnosus and S. mitis. The findings of our literature review are summarized in Table 1. Twenty-one cases of pulmonary actinomycosis caused by A. odontolyticus,\(^8\)–\(^25\) one case of empyema caused by L. rhamnosus\(^26\) and 89 cases of empyema caused by S. mitis were identified.\(^27\)–\(^30\) Of these cases, 84 were identified as a part of a retrospective audit examining the aetiology of community-acquired lung abscesses diagnosed at one Japanese healthcare service.\(^29\) Only one case of pulmonary actinomycosis has been reported in a patient with a past history of bronchiectasis of unclear aetiology.\(^11\) None of these microorganisms have been previously been identified in patients with ABPA.

A history of periodontal disease, aspiration and being immunocompromised were the most commonly reported risk factors identified in patients who developed pulmonary infections secondary to A. odontolyticus,\(^8\)–\(^16\) L. rhamnosus\(^3\) or S. mitis.\(^32\)

We propose a plausible case where obstructive mucus impaction due to ABPA led to the formation of a chronic mucocoele in the right upper lobe, which acted as a nidus for infection and abscess formation from organisms originating in the oral cavity in which dental extraction may have acted as a seeding event based on the temporal proximity of these events and identified organisms. Silent aspiration could have also triggered this infection, although we had no reason to suspect this based on this patient’s clinical history. A secondary empyema was additionally colonized by Lactobacillus species perhaps made more likely from high loads of this organism due to regular ingestion of Lactobacillus-containing probiotics. Our case study raises the need for discussion regarding the role of preventative antibiotic therapy in conjunction with dental procedures for at-risk patients with chronically occluded airways and presence of mucocoele. Aspiration risk should also be assessed in those who regularly consume Lactobacillus-containing probiotics. In addition, our case highlights the potential for ABPA patients to develop severe complications when mucoid impaction prevents drainage post infection.

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for publication of this case report and accompanying images.

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