Respiratory Medicine Case Reports 27 (2019) 100855

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Pulmonary actinomycosis and tracheal squamous cell carcinoma: A rare simultaneous presentation of both in a single patient

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A B S T R A C T

A 57-year-old male with schizophrenia and a 37 pack-year smoking history presented with cough productive of purulent sputum associated with hemoptysis and worsening shortness of breath. Computed tomography (CT) scan revealed multiple masses in the right upper and lower lobes with a small distal tracheal mass and significant mediastinal lymphadenopathy. CT guided biopsy of the largest lung mass in the right lower lobe confirmed a diagnosis of pulmonary actinomycosis. The patient received appropriate antibiotic therapy for four weeks, but his condition did not improve. A repeat CT scan showed worsening of the right lung consolidation with increasing occlusion of the trachea. Bronchoscopy was performed which revealed a friable necrotic mass occupying 70% of the tracheal lumen. Histopathology showed squamous cell carcinoma of the trachea likely of primary origin. Unfortunately, the patient was not a candidate for any surgical intervention or oncologic treatment, and he died few days later. This patient had a rare simultaneous presentation of both pulmonary actinomycosis and tracheal squamous cell carcinoma. To the best of our knowledge, this is the first reported case of simultaneous diagnosis of both conditions in the same patient. This case illustrates the importance of looking for an alternative diagnosis in patients with actinomycosis who do not respond well to appropriate therapy.

1. Introduction

Pulmonary actinomycosis is a rare condition that often mimics lung cancer, abscess or tuberculosis. Definitive diagnosis depends on histopathological features. It usually responds well to treatment with proper antibiotics, but a prolonged course is needed to prevent relapse [1]. This case describes a patient who was diagnosed with actinomycosis but did not respond to treatment and was ultimately diagnosed with tracheal cancer on further workup.

2. Case presentation

A 57-year-old male with schizophrenia and a 37 pack-year smoking history presented with cough productive of purulent sputum, mixed with occasional hemoptysis and increasing shortness of breath over a few weeks' duration. The clinical examination was significant for cachexia with poor oral hygiene. The patient had decreased air entry with wheezes and coarse crepitations in the right lung fields with no audible stridor. Initial laboratory testing revealed leukocytosis (white blood cell count 21,000/UL). Computed tomography (CT) scan of the chest revealed multiple masses in the right lung, largest of which in the right lower lobe measuring 7 cm in largest diameter. In addition, there was a small distal tracheal mass and a significant mediastinal lymphadenopathy (Figs. 1 and 2). CT guided lung biopsy of the largest lower lobe mass revealed necrotizing acute and chronic inflammation with granulomatous features and associated sulphur granules with radiating bacterial organisms consistent with actinomycosis (Fig. 3). No visible malignant cells were identified. Unfortunately, the patient was lost to follow up and did not receive antibiotic therapy at that time. He presented to the hospital three weeks later with deterioration in his condition. Although he was started on intravenous clindamycin due to a penicillin allergy, his condition did not improve after four weeks of therapy. Repeat CT scan eight weeks after initial imaging revealed worsening of the right lung masses and consolidation with a significant increase in the size of the distal tracheal mass (Figs. 4 and 5). Therefore, bronchoscopy was performed which showed a friable necrotic mass on the posterior wall of the trachea involving about 70% of the tracheal lumen. Biopsy results revealed an invasive squamous cell carcinoma of the trachea most likely of primary origin (Figs. 6 and 7). The patient was not a candidate for any surgical intervention or oncologic treatment because of his critical condition. He deteriorated quickly and died a few days later.

3. Discussion

This patient had a rare simultaneous presentation of pulmonary actinomycosis and invasive squamous cell carcinoma of the trachea, which is absent from the reported literature. The diagnosis of

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https://doi.org/10.1016/j.rmcr.2019.100855
Received 1 February 2019; Received in revised form 5 April 2019; Accepted 13 May 2019

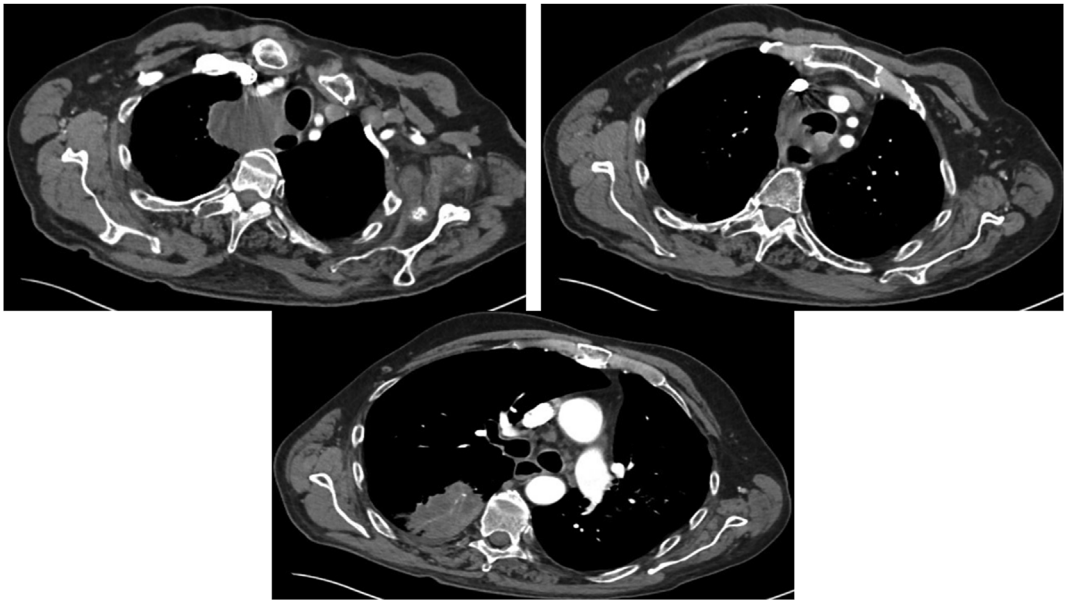

Fig. 1. Initial chest CT scan with mediastinal window showing multiple lung masses in the right lung filed with mediastinal lymphadenopathy and small distal tracheal irregular mass.

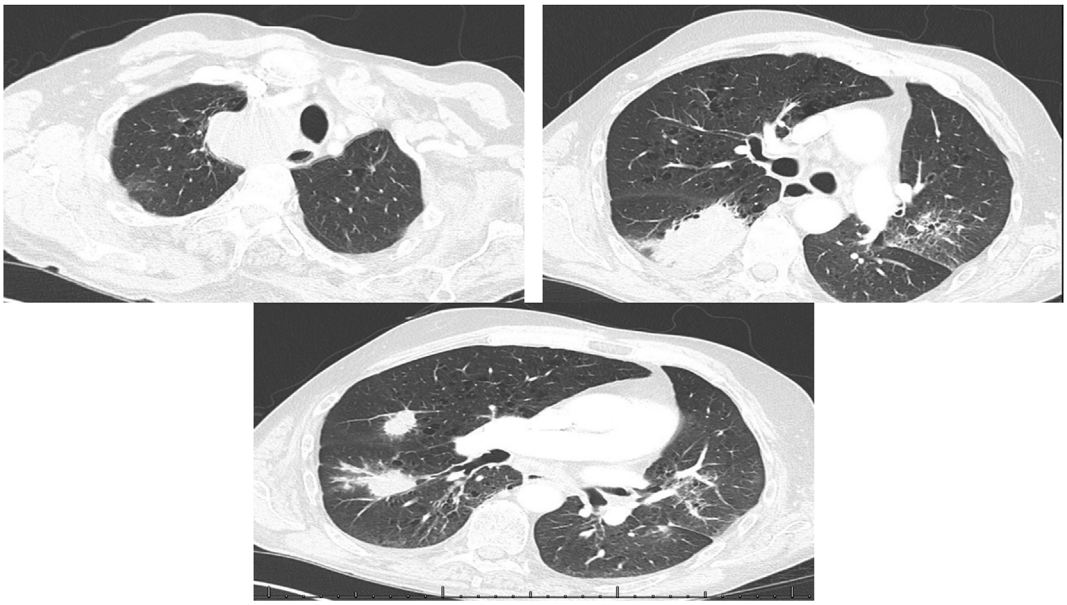

Fig. 2. Initial chest CT scan with lung window showing multiple lung masses in the right lung field the largest of which measuring 7 cm in diameter in the right lower lobe.

actinomycosis was confirmed by tissue biopsy of the largest mass in the right lower lobe seen in Figs. 1 and 2, which showed granulomatous inflammation, organism filaments, and sulfur granules. However, this does not exclude malignancy as only one mass was biopsied and endobronchial ultrasound was not performed initially for mediastinal lymph nodes biopsy. Although he received appropriate therapy, he continued with shortness of breath and fever. A repeat CT scan done 8 weeks after his initial presentation, showed an increase in the distal tracheal mass, which was thought on the initial CT scan to represent extension of actinomycosis. Subsequent bronchoscopy was performed, and tissue pathology revealed findings of squamous cell carcinoma of the trachea, most likely of primary origin. To the best of our knowledge, this is the first reported case of simultaneous diagnosis of invasive squamous cell carcinoma of the trachea and pulmonary actinomycosis in the same patient. The increasing size of the distal tracheal mass over a period of 2 months was initially attributed to actinomycosis invasion, but in retrospect was due to the tracheal malignancy which ultimately led to a fatal outcome in this patient.

Actinomyces species are anaerobic filamentous, branching, gram-positive bacilli that colonize the mouth, gastrointestinal and female genital tracts as well as the bronchi of humans and can cause a range of clinical disease including cervicofacial, pulmonary and abdominal disease [1]. Pulmonary actinomycosis is a rare condition now in the antibiotic era, but has been associated with several factors including poor oral hygiene and alcohol intoxication as well as disruption of the mucosal lining of the oral cavity and airway from cigarette smoking. Other risk factors include diabetes, radiation, malnutrition, malignancy, and immunosuppression. Actinomycosis is often misdiagnosed as lung cancer on imaging studies when it presents as a mass, nodule or as a consolidation with adenopathy [2]. CT chest could show a range of

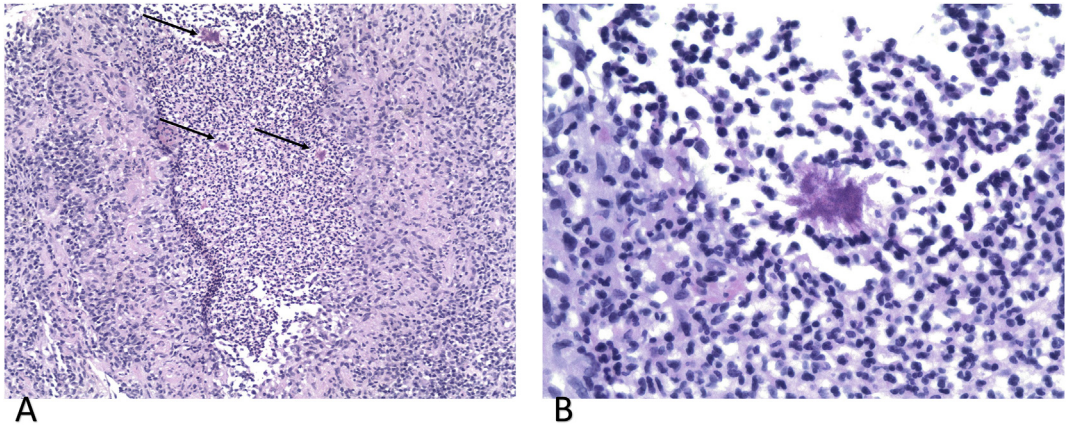

Fig. 3. Lung biopsy of the right lower lobe mass. A: tissue magnified by electron microscopy (100X) showing necrotizing acute and chronic inflammation with granulomatous features and associated sulphur granules with radiating bacterial organisms and three foci of actinomycosis (arrows). B: tissue magnified by electron microscopy (400x) showing a focus of actinomycosis with acute and chronic inflammation.

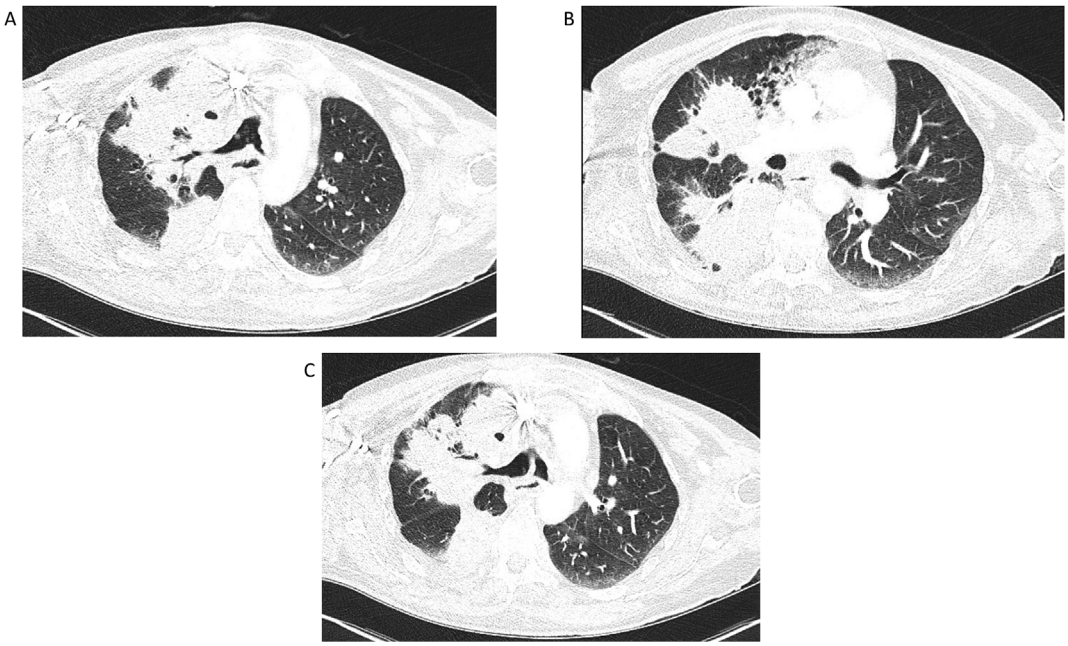

Fig. 4. Repeat chest CT scan 8 weeks later with lung window showing worsening right sided lung masses.

findings in pulmonary actinomycosis including patchy air-space consolidation, cavitation, multifocal nodular appearance, pleural thickening and effusion, and hilar and mediastinal lymphadenopathy [3]. It is well known to extend across tissue planes leading to sinus tracts or infection outside the lung parenchyma [1]. Other differential diagnoses include aspergilloma, endemic mycoses, nocardiosis, abscess/empyema or tuberculoma [2]. However, growth of the organism alone does not prove disease, as *Actinomyces* are commensal flora. Definitive diagnosis depends on the histopathological findings of granulomatous inflammation with organism filaments and sulphur granules in accordance with growth of *Actinomyces* in respective tissue cultures. Sulphur granules are highly suggestive but not specific for the diagnosis of actinomycosis. *Actinomyces* isolation from sputum culture and bronchial lavage fluid is difficult to achieve due to prolonged anaerobic growth requirements [2,4]. Penicillin is the drug of choice for actinomycosis, but in those who are allergic, clindamycin and tetracyclines have a good activity [5]. Response to antibiotics is typically observed in the first few weeks of therapy but treatment must be prolonged (often months) in extensive disease to prevent relapse [1]. Medical therapy with intravenous antibiotics is considered the first line of therapy as actinomycosis typically responds well to antibiotics. However, surgical interventions should be considered in cases of antibiotics failure, severe extensive disease with invasion to vital structures, lack of clear diagnosis, and severe hemoptysis. Therefore, those who respond poorly to antibiotic therapy generally should have further specimens obtained to rule out other infectious causes and/or malignancy [6].

Primary tracheal tumors are very rare, with squamous cell carcinoma being the most frequently diagnosed tracheal cancer followed by adenoid cyst carcinoma [7]. Smoking, exposure to carcinogens such as inhaled hydrocarbons, and history of prior lung cancer are considered risk factors for tracheal squamous cell carcinoma [7,8]. It is more common in males and is usually diagnosed in the sixth and seventh decades. Common presenting symptoms are dyspnea, hemoptysis, cough, wheezing, stridor, and recurrent pneumonia. It is usually diagnosed four to six months after symptom onset. Because of overlapping symptomatology with more common diseases, this condition is often missed, and patients are treated for other conditions such as chronic obstructive pulmonary disease, pneumonia or asthma. Additionally, the trachea has a significant reservoir and symptoms of upper airway obstruction do not occur until the tumor occupies 50–75% of the tracheal

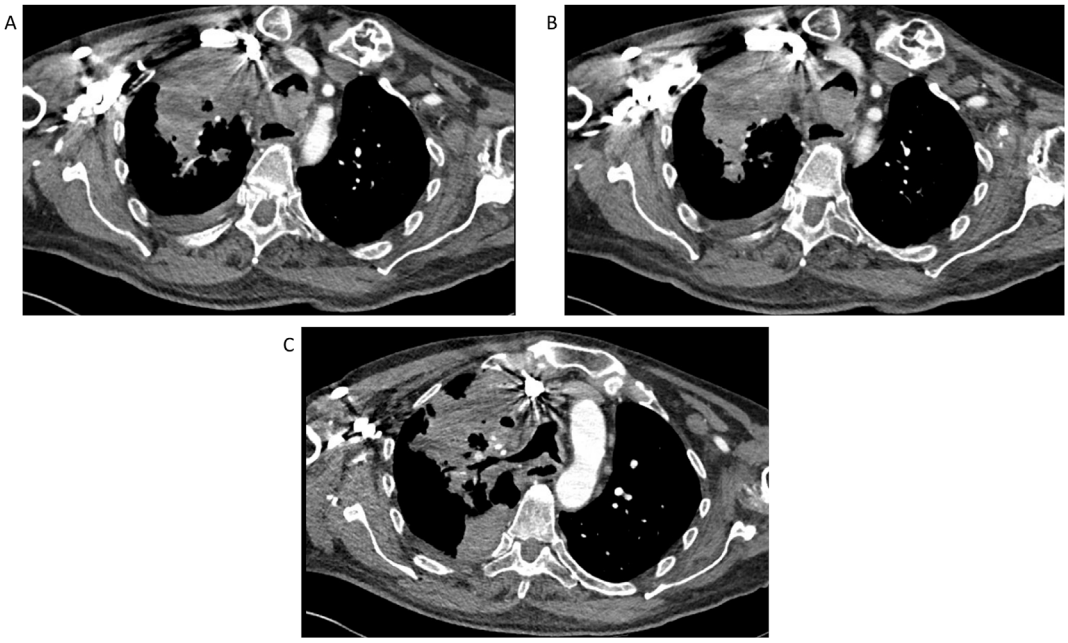

Fig. 5. Repeat chest CT scan 8 weeks later with mediastinal window showing right sided lung masses and increased size of distal tracheal mass involving the posterior wall.

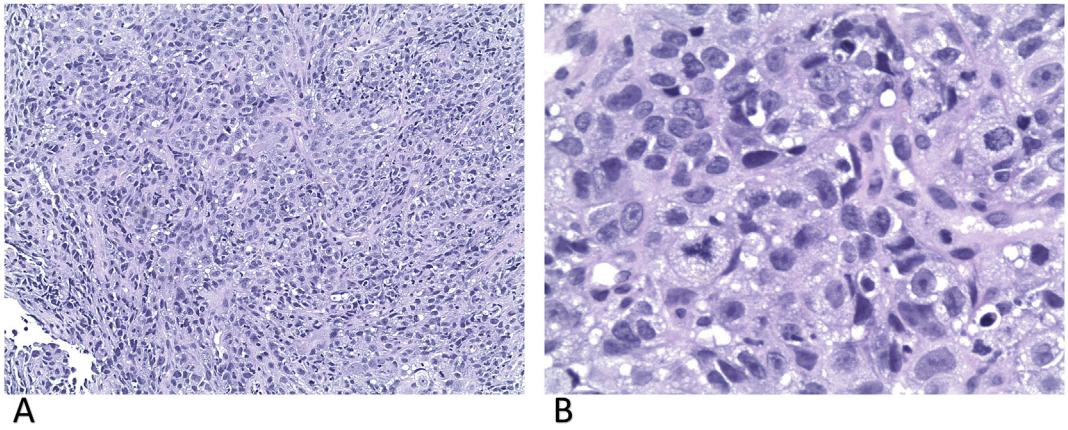

Fig. 6. Tracheal tissue biopsy showing poorly differentiated squamous cell carcinoma magnified by electron microscopy by (100X - A) and (400X – B).

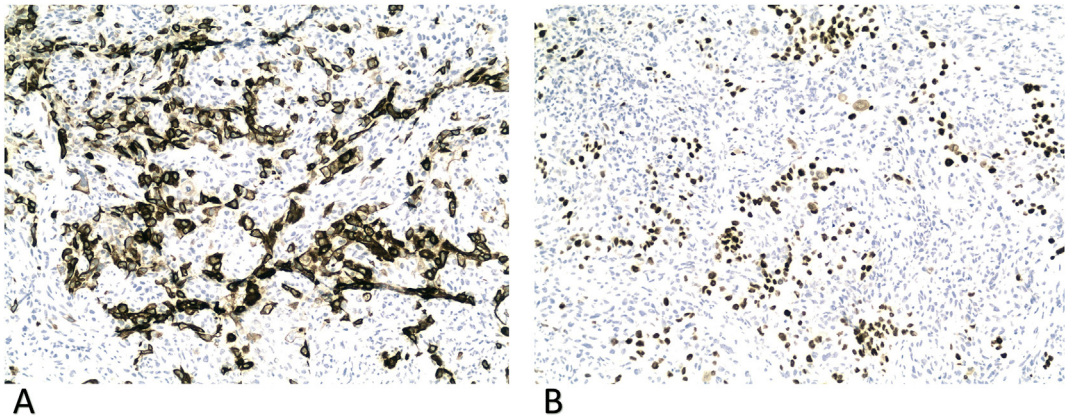

Fig. 7. Poorly differentiated squamous cell carcinoma staining positive for CK 5/6 (A) and P40 (B) from tracheal tissue biopsy.

lumen, which delays the diagnosis until advanced stages [7,8]. A third of patients with tracheal squamous cell carcinoma have lung or mediastinal metastasis at the time of diagnosis. Staging of tracheal cancer is based on TNM (tumor size, lymph nodes, and metastasis) [7]. Surgical resection followed by radiotherapy is associated with a significant increase in five-year survival and should be considered in all patients if there are no contraindications. Those include: 1) involvement of more than 50% of tracheal length 2) chronic respiratory failure 3) dependence on oral corticosteroids 4) invasion of the heart or aorta or 5) distant metastasis [9,10].

It is unclear in this patient which disease came first and if one disease precipitated the development of the other. An association between pulmonary actinomycosis and tracheal cancer has not been described in the literature. *Actinomyses* species can colonize necrotic tissue associated with lung cancer, tuberculosis, bronchiectasis or aspergillosis, however this patient demonstrated histopathological changes indicative of more than colonization [1]. There are several reported cases of concurrent actinomycosis infection and squamous cell lung cancer, as well as a few cases reported with adenocarcinoma or small cell carcinoma [11–13]. However, actinomycosis is not reported with tracheal cancer and it is unclear if there is an association between both conditions.

This case illustrates the importance of looking for other alternative diagnoses in the absence of treatment response in patients with pulmonary actinomycosis. Furthermore, tracheal cancers are rare and present with nonspecific respiratory symptoms, so a high index of suspicion is required.

4. Learning points

- Pulmonary actinomycosis, which can mimic lung cancer, is a rare condition diagnosed based on microbiologic and histopathological findings. It usually responds to medical treatment alone with appropriate antibiotics although treatment courses are lengthy to prevent relapse.
- In pulmonary actinomycosis, poor response to treatment should prompt clinicians to look for an alternative diagnosis. This patient was diagnosed with tracheal squamous cell carcinoma on further work up.
- Primary tracheal carcinoma is a rare condition, which is often missed due to nonspecific symptoms that overlap with more common conditions such as chronic obstructive pulmonary disease (COPD), pneumonia or asthma. Failure to respond to treatment of these conditions should raise the suspicion of this condition.
- To the best of our knowledge, this is the first case of simultaneous diagnosis of pulmonary actinomycosis and primary tracheal cancer in the same patient. The association of between both conditions is yet to be determined as literature is lacking.

Conflict of interest

The authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100855.

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