A rare case of empyema necessitatis sustained by *Nocardia farcinica* in a kidney transplant recipient

Zohreh Rostami [a], Luca Cegolon [b,c], Ensieh Vahedi [d], Mandana Kashaki [e], Reza Kachuei [f], Ramezan Jafari [g], Mohammad Javanbakht [a,*]

[a] *Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[b] *University of Trieste, Department of Medical, Surgical & Health Sciences, Trieste, Italy*
[c] *University Health Agency Giuliano-Isontina (ASUGI), Public Health Departmnent, Trieste, Italy*
[d] *Chemical Injuries Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Molla Sadra Street, Tehran, Iran*
[e] *Shahid Akbarabadi Clinical Research Development, Unit (ShACRDU), School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[f] *Molecular Biology Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[g] *Department of Radiology, Baqiyatallah University of Medical Sciences, Tehran, Iran*

ARTICLE INFO

Keywords
Empyema necessitatis
Nocardia nova
Kidney

A 55-year-old man from Northern Iran was admitted to accident & emergency service (A&E) of Baqiyatallah university hospital of Teheran (Iran) in August 2019 for asthenia, night sweats, 12 kg weight loss, shortness of breath, productive cough, a left hemithoracic painful mass and dark yellow urine discoloration for the past four months. The patient had received kidney transplantation 16 months before and was under immunosuppressive treatment with cyclosporine 75 mg twice per day, mycophenolic acid 720 mg twice per day and 5 mg daily prednisolone. The patient had diabetes mellitus and hypertension, no history of alcohol consumption, nor smoking nor lung disease. He was a taxi driver, sometimes gardening his backyard. Over the last 4 months the patient had been hospitalized several times with the same symptoms (fever, productive coughing and dyspnea).

A rapidly growing erythematous verrucous skin plaque on the back of the 4th finger of his left hand had developed 5 months before admission (Fig. 1). An excisional biopsy was undertaken for diagnostic purposes. The microscopical examination of the specimen revealed papillomatosis hyperkeratosis, rete-ridges irregularities of the epidermis and aggregation of leukocytes, histiocytes, plasma cells, neutrophils and multi-nucleated giant cells in the upper dermis, especially around dilated thin wall vessels. Since there was no evidence of malignancy, the pathologist reported pseudo-epitheliomatous hyperplasia with mixed inflammatory dermal reaction and vague suppurative granuloma.

Although the purified protein derivative (PPD) test for tuberculosis (TB), serologic test for leishmaniasis were both negative and direct microbiological examination as well as culture of the skin specimen had never been performed, the patient had always been diagnosed with bacterial pneumonia at each previous hospital admission, treated with antibiotics and discharged upon fever cessation.

During the present hospital admission diffuse fine crackles could be auscultated, with no respiratory sounds from his right hemithorax. A 3 × 4 cm non-tender mass with undefined borders on the right side of his neck and another 4 × 8 cm painful erythematosus mass in the left lateral chest wall could be palpated. A subsequent chest X-ray showed massive pleuro-pericardial effusion, confirmed at chest computerized tomography (CT) scan, which also showed that the pleuro-pericardial effusion extended outside the thorax into the surrounding tissues (thyroid and abdominal cavity) (Fig. 1 dD-dE). Since ultrasonography (US) revealed a large heterogeneous lobulated focus in the sub-cutaneous area of his left hemithorax, extending to the lower areas and expanding also to the pericardial space, a fluid aspiration was undertaken.

Concentrated and purulent fluid was drained and sent for biochemical analysis, direct smear and microbiological culture. The pleural fluid aspirated resulted exudative and the fluid specimen smear was positive for white blood cells (WBC: 20–30/high power field) and negative for red blood cells (RBC) as well as for epithelial cells. The patient was

* Corresponding author.
E-mail address: mhmjvbt81@gmail.com (M. Javanbakht).

frankly anemic (Hb = 8.8 g/dl) with leucocitosis (WBC count: 14,400/μL); the erythrocyte sedimentation rate (ESR) was 105 mm/h and C reactive protein (CRP) was 65.4 mg/L. Plasma concentrations of the main electrolytes (Sodium: 135 mEq/L; Potassium: 4.6 mEq/L, Calcium: 10.2 mg/dl; Phosphate: 4.2 mg/dl; Magnesium: 1.6 mg/dl) were all within their normal range as well as aspartate aminotransferase (AST: 36 U/L) and alanine aminotransferase (ALT: 20 U/L). By contrast, plasma concentration of alkaline phosphatase (ALP: 779 U/L) was rather elevated. An abdominopelvic US scan showed a large cystic lesion in the cortical part of the transplanted kidney. Blood culture was negative, plasma DNA PCR (QNAT) was positive for CMV (44,685 IU/ml).

Initially the patient was treated with ganciclovir (for CMV infection) and ampicillin (for possible actinomycosis). Microbiological staining of the pleural fluid specimens in fact revealed beaded Gram-positive branching bacilli, indistinguishable from Actinomyces at Gram stain. Nonetheless, modified acid-fast staining showed acid-fast bacilli, thereby confirming Nocardiosis. On the other hand, Actinomycosis-producing actinomycetes can be distinguished from aerobic,

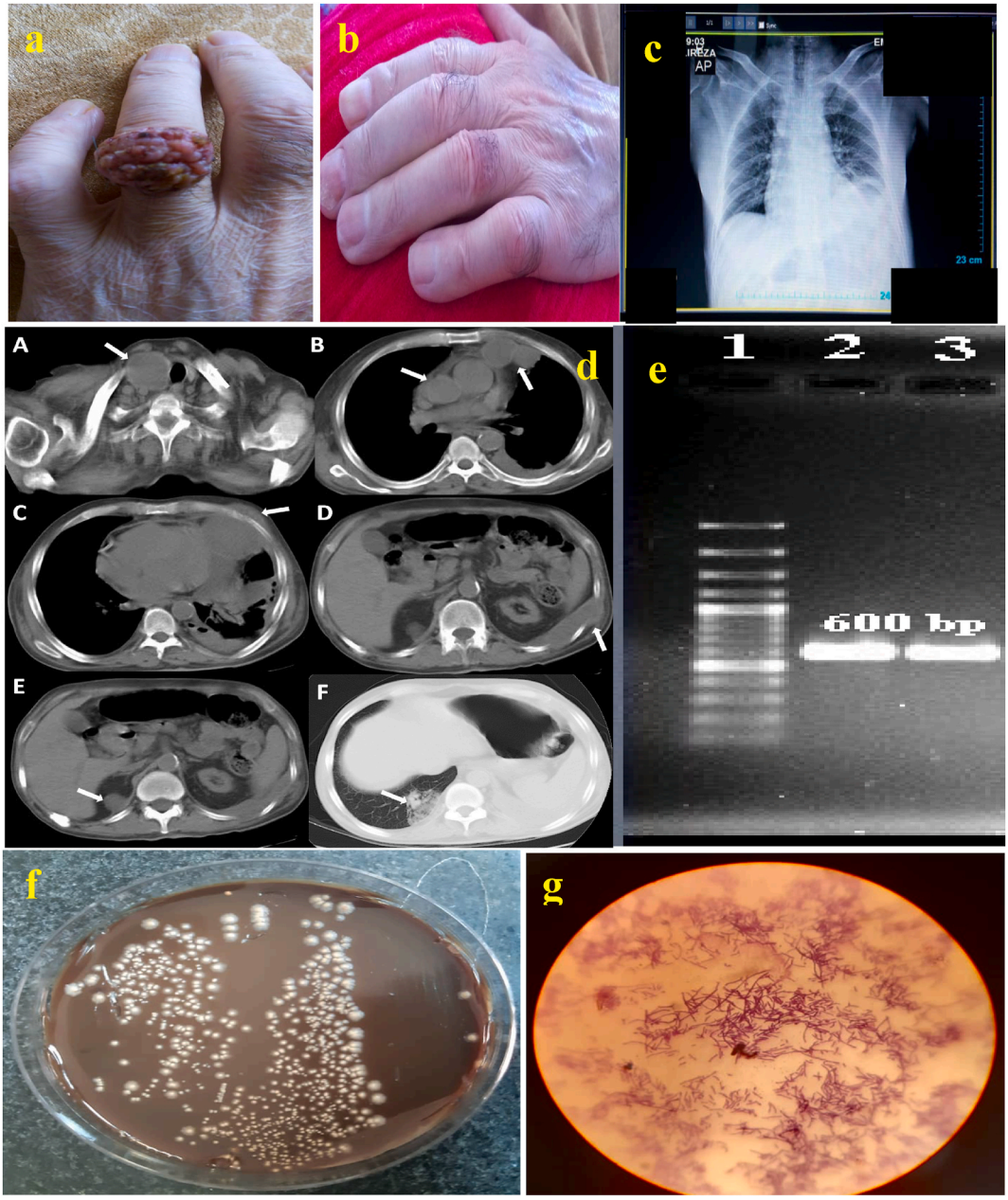

Fig. 1. Clinical, imaging and laboratory findings of *Nocardia* in a kidney transplant recipient.
a: Cutaneous lesion before treatment showing erythematous verrucous skin plaque on the back of the third finger. **b: Cutaneous lesion after treatment. c: Chest X ray after treatment. d**: **Chest radiological imaging:** Axial computerized tomography scan (CT) without contrast (A–E) and chest X-Ray (F) images: **(A)** Cystic mass in the right thoracic inlet with irregular wall and mass effect on trachea; **(B)** Multiple irregular cystic masses in the anterior and middle mediastinum, with left pleural effusion; **(C)** Large anterior mediastinal cystic mass with invasion to rib, chest wall and sub-cutaneous soft tissue beyond the rib; **(D)** Left pleural involvement (thickening and effusion) with extension to chest wall and sub-cutaneous soft tissue (empyema necessitatis); **(E)** Right sub-diaphragmatic retroperitoneal cystic mass; **(F)** Sub-pleural consolidation and alveolar opacity in the right lower lobe after treatment. **e: Agarose gel electrophoresis and PCR products of *Nocardia* spp. using NG1 & NG2 primers**. **Lane 1**: 100bp DNA ladder; **Lane 2:** *N. brasiliensis* NCIMB12083; **Lane 3:** *N. farcinica* (present isolate) NG1 primer: 5′-ACCGACCACAAGGGGG-3′ ; NG2 primer: 5′-GGTTGTAAACCTCTTTCGA-3′ **f: Colonial morphology of Nocardia species on blood agar**: whitish chalky adherent colonies of Nocardia species. g: Gram positive branching, filamentous rods on Gram's stain.

filamentous bacteria such as Nocardia species. Therefore, the specimen fluid was placed in aerobic and anaerobic culture medium at 35–36C for two weeks. Whilst no bacteria grew in the anaerobic environment over the course of 3 weeks, aerobic Gram-positive filamentous organisms were identified. Primers NG1 (5′-ACCGACCACAAGGGGG-3′) and NG2 (5′-GGTTGTAAACCTCTTTCGA-3′) were used to amplify a *Nocardia* genus-specific 598-bp fragment of 16S rRNA, as previously described [1]. Agarose gel electrophoresis-purified PCR products were sequenced, confirming infection by *N. farcinica*.

Following diagnosis of Nocardiosis at molecular analysis, the treatment plan of the patient was modified to 160 mg trimethoprim-800 mg sulfamethoxazole twice a day. After 4 weeks of the latter treatment scheme the patient's conditions improved, fever and cough resolved and the fluid drainage from the thoracentesis site normalized. The above treatment regimen was extended for up to 12 months.

In conclusion, this is the first reported case of empyema necessitatis sustained by *N. farcinica*, occurring in a kidney transplanted patient. Clinicians should be aware of the possibility of complications (as empyema necessitatis) when dealing with immunocompromised patients, for a prompt collecton of appropriate specimen to be examined. A rapid diagnosis of empyema necessitatis in fact allows to start appropriate antimicrobial therapy and surgical drainage, thereby reducing morbidity and mortality.

Funding

None.

Consent for publication

A written informed consent to publish this case report was obtained from the patient.

Declaration of competing interest

None.

Acknowledgments

Thanks to guidance and advice from "Clinical Research Development Unit of Baqiyatallah Hospital".

Reference

[1] Laurent FJ, Provost F, Boiron P. Rapid identification of clinically relevant Nocardia species to genus level by 16S rRNA gene PCR. J Clin Microbiol 1999;37(1):99–102.