Tuberculosis screening in a dialysis unit: detecting latent tuberculosis infection is only half the problem


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SUMMARY
Patients with chronic kidney disease are at increased risk of tuberculosis. We describe the events that occurred when we encountered a patient receiving haemodialysis with pulmonary tuberculosis. Nine (of 41) patients dialysing at the same time as the index case had a positive interferon-gamma release assay (IGRA) and were offered therapy for latent tuberculosis infection (LTBI). Patients with an initial negative IGRA were rescreened at six months, identifying a further three IGRA-positive patients. All patients were then rescreened at 12 months. No new IGRA-positive cases were identified and no staff or patients developed active disease. Only five of the 12 IGRA-positive patients completed LTBI therapy.

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Introduction

Patients with chronic kidney disease (CKD) are at increased risk of developing tuberculosis, which may be due to altered T-cell immunity or to immunosuppressive therapy.1 The prevalence of CKD is also higher in ethnic minority groups at increased risk of latent tuberculosis infection (LTBI).2

Evidence to guide protocols for active case-finding and treatment of LTBI in haemodialysis patients is limited.2 This report describes the events that occurred on encountering a clinical case of tuberculosis in a patient receiving haemodialysis.

Events leading to the investigation

Hospital setting

Peterborough City Hospital is a general hospital with 612 beds. The hospital hosts a satellite dialysis unit run by Leicester Hospitals with 15 stations and two side-rooms. The unit operates Monday–Saturday with three shifts per day.

Index case

A 56-year-old man from India arrived in the UK in April 2011. He had a background of haemodialysis-dependent CKD secondary to systemic lupus erythematosus and initially dialysed in London. In July 2011 he relocated to Peterborough and dialysed in Corby until December 2011 when he transferred to Peterborough. He dialysed three times per week for an average of 4 hours per episode. He was seen in the respiratory clinic following a positive interferon-gamma release assay (IGRA) test performed while investigating weight loss. Computed
tomography (CT) thorax/abdomen was unremarkable. Echocardiography revealed an ejection fraction of <30%. His weight loss was thought to reflect cardiac cachexia and improving fluid balance. He was reviewed in December 2011 and clinically and radiologically there was no evidence of tuberculosis. By February 2012 he had achieved euvolaemia and was clinically improving.

In May 2012 he presented with a productive cough and breathlessness. He had not been noted as actively coughing while on the dialysis unit. He denied night sweats but was febrile (38.9°C) with respiratory crackles on examination. Inflammatory markers were raised. Chest radiography revealed new bilateral upper lobe infiltrates. He was admitted for intravenous co-amoxiclav but failed to improve. A respiratory opinion was sought six days after admission: tuberculosis was suspected. Transfer from a four-bedded bay to respiratory isolation was suggested. Sputum was sent and was acid-fast bacilli (AFB) smear positive (day 1), and nucleic acid amplification test (NAAT) for tuberculosis was positive the following day.

He was commenced on anti-tuberculous therapy (ATT). High-resolution CT thorax confirmed bilateral upper lobe cavitating lesions. Mycobacteria were detected on day 14, confirmed as Mycobacterium tuberculosis at day 38 and fully susceptible tuberculosis (mycobacterial reference laboratory) at day 81. He completed six months of standard ATT and remained well 12 months after stopping therapy.

A contact-tracing meeting was convened involving staff from Peterborough and Leicester Hospitals and the Health Protection Agency (HPA).

Bacteriology methods

Samples for tuberculosis are stained for AFB using auramine stain and cultured using the Bactec MGIT960 Mycobacterial Detection System (Becton Dickinson, Franklin Lakes, NJ, USA). Smear-positive samples are subjected to NAAT for detection of M. tuberculosis (GeneXpert, Cepheid, Sunnyvale, CA, USA). IGRA are performed using QuantiFERON-TB Gold (QFT-GIT; Cellestis, Chadstone, Victoria, Australia).

Infection control measures

Patients with suspected pulmonary tuberculosis are placed in source isolation and FFP3 masks are made available for staff.

Results

Actions taken by the contact-tracing committee (Table 1)

Identification of exposed/ward patients

Six patients were identified who spent ≥8 h with the index case in the ward prior to him being isolated. Letters were sent to these patients and their general practitioners (GPs) to inform them of possible exposure.

Advice to staff

All ward and haemodialysis staff members were advised by letter of possible exposure and to seek medical attention if they had any features of active tuberculosis. Pregnant staff members were advised not to attend the index case while he was considered contagious.

Staff were not offered screening with IGRA testing. Only one member of staff contacted the community tuberculosis team. Their symptoms were not suggestive of active tuberculosis but screening was undertaken (chest X-ray and Mantoux as per local policy) and found to be negative. The community tuberculosis team screened six household contacts as per UK guidelines. One child was offered treatment for LTBI.

Screening haemodialysis patients

The index case was considered unlikely to have been infectious in Corby when he had a normal CT scan.

Identification of at-risk members of the public

The HPA contacted the drivers who transported the index case to hospital for haemodialysis, and wrote to their GPs advising of possible exposure.

Results of contact screening

Fifteen patients received haemodialysis in the same session as the index case since the index case commenced haemodialysis in Peterborough, one of whom had been transferred for transplantation. Dialysis patients within Peterborough typically spend 5–6 hours per session on the unit from arrival until discharge. Twelve patients underwent IGRA testing and a chest X-ray. Two of these had positive IGRA tests (one an Indian-born Asian, the other a UK-born Caucasian). Three patients were not screened; one of these underwent transplantation, and two died prior to testing of end-stage kidney disease.

At the following contact-tracing meeting, screening was extended to all patients dialysing on the same day as the index case, identifying a further 26 patients. Two of these had died (from non-tuberculosis-related causes) and two transplant recipients had been transferred. Seven of the remaining 22 patients screened (12 weeks after smear positivity) were IGRA positive (five UK-born Caucasians; two Asians born in India and Pakistan respectively). Seven abnormal chest X-rays were reviewed but tuberculosis was not suspected or diagnosed in any patient. All nine were offered ATT for LTBI; only five completed therapy.

Repeat IGRA and chest X-ray (or CT) screening were performed six months later on the 27 patients with negative IGRA. Three patients tested IGRA positive (two UK-born Caucasians and one Asian born in Pakistan) and were offered ATT for LTBI; one completed therapy.

A final screen was conducted 12 months after smear positivity of all exposed patients. No further IGRA-reactive patients were detected and no contacts developed symptoms of active tuberculosis in this time. Seven of the nine patients positive on first screen were rescreened at 12 months; four were negative. Further investigation of these four patients suggested that they had IGRA levels between 0.35 and 0.91 IU/mL. Those that remained positive had IFN-γ concentrations >3 IU/mL.

Financial and clinical impact

Overall, 91 IGRA tests (at ~£70 each; totalling £6370), 103 chest radiographs (~£27; £2,781) and three CT chests (~£82; £246) were performed (requiring interpretation). Eleven
courses of LTBI therapy were administered (≈ £90; two tablets of Rifinah 300 once daily and pyridoxine 10 mg (once daily; £990)) and 32 extra outpatient consultations were required (at ≈ £200 per consultation; £6,400), yielding an approximate total cost of at least £16,787.

Discussion

We describe an isolated case of smear-positive pulmonary tuberculosis in a haemodialysis patient, the measures taken to reduce the risk of nosocomial transmission, and some of the costs incurred. A multidisciplinary team was set up to consider the ill-defined period of infectivity, screening (who, how, when), whether to treat, and to co-ordinate patient and staff information.

Tuberculosis outbreaks are well described, and have often been due to healthcare workers and other patients. Previous outbreaks have used tuberculin skin testing (TST) and chest X-ray. Recent studies suggest that IGRA testing is superior to TST. Serial IGRA testing has only been assessed in small cohorts of patients. Seroconversion/seroconversion is not uncommon. Three patients converted from IGRA negative to positive at six months, all with low concentrations of interferon-gamma (IFN-γ) (<1.50 IU/mL). In our cohort, persistently positive IGRA was found to occur in patients with higher concentrations of IFN-γ. Those who displayed reversion had lower concentration reactions (<1.50 IU/mL), suggesting that discrepancies in serial IGRA testing are increased at low concentrations, as described previously. The clinical significance of reversions is uncertain. Variations in host immunity and transient responses to infection, reproducibility of the QFT-GIT assay and use of a single cut-off value are likely to be contributory factors; however, without a gold standard LTBI diagnostic test, distinction between true- and false-positive results cannot be determined. A study of healthcare workers who underwent serial QFT-GIT testing concluded that adding a borderline zone (0.35–2.0 IU/mL) would aid interpretation. Our limited data support this.

There was an opportunity to treat the index case when he had LTBI and no clinical or radiological evidence of pulmonary
tuberculosis. However, in this group of patients, successful completion of ATT for latent therapy was low (5/9; 55.6%) despite high patient anxiety in the setting of a potential outbreak. Patient selection and when to screen for latent tuberculosis in the course of advanced CKD remains challenging.

A risk assessment was undertaken by the contact-tracing meeting regarding screening staff members. It was felt that the amount of contact with the index case was highly variable but it was crudely estimated that 16 dialysis nurses spent between 20 and 260 min in close clinical contact with the index case prior to barrier nursing being undertaken. A decision was made that potentially exposed staff members would not be formally screened, especially as the initial screening of close contacts revealed latency in only one of the index case’s children.

We provide approximate costs for each aspect of the investigation, which totalled more than £16,000. Clearly there are further costs not included in this estimate (discussions with patients/relatives, meetings, teleconferences, writing reports, etc.).

IGRA and chest X-ray are appropriate tools to screen for LTBI in a haemodialysis population. A multidisciplinary approach is essential to co-ordinate actions. In our experience, treatment for LTBI is poorly tolerated in haemodialysis patients. Further work is required to determine more accurately who requires screening and the timing thereof.

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Conflict of interest statement
None declared.

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References


