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REVIEW

Successful treatment of multi-focal XDR tuberculous osteomyelitis

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Summary We herein describe the nosocomial transmission of a pre-XDR or MDR case of pulmonary tuberculosis in a HIV-negative health care worker in an area endemic for MDR and XDR tuberculosis. Following inadequate therapy and non-compliance, he presented with extra-pulmonary XDR tuberculosis in the form of multi-focal osteomyelitis and encysted pleural effusion. He was cured after two years of treatment with various anti-tuberculous drugs in addition to interferon gamma.

Contents

Case presentation 409
Case discussion 411
Conclusion 413

Abbreviations: XDR, extensively drug resistant; MDR, multi-drug resistant; MRI, magnetic resonance imaging.

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Funding 413
Competing interests 413
Ethical approval 413
Acknowledgment 413
References 413

Case presentation

The case was a 30-year-old Saudi physician who studied medicine for six years in the Ukraine from 1992 until 1997. He denied direct contact with patients who had extensively drug-resistant tuberculosis. He described having indirect contact with these patients in January 2006. These patients were waiting in the radiology department for chest X-rays. In August 1996, he developed a fever and cough that did not respond to one week of treatment with moxifloxacin. His CT chest revealed a right apical cavity. He was admitted to a hospital in Riyadh and was started on isoniazid, rifampin, ethambutol and pyrizinamide for smear-positive tuberculous cavitary pulmonary disease. He did not improve after one month of therapy. Moxifloxacin, amikacin and cycloserine were therefore added. His sputum *Mycobacterium tuberculosis* [isolate A] was sensitive to ethambutol and resistant to isoniazid, rifampin and streptomycin. Second-line drug susceptibility information was not available (Table 1). He improved clinically but his sputum cultures continued to be positive for *M. tuberculosis* in September and October 2006. He returned to the Ukraine in November 2006 and continued on isoniazid, rifampin, ethambutol, pyrizinamide, moxifloxacin and cycloserine for six months. He stopped his therapy in April 2007 and developed a recurrent fever and cough in May 2007. He graduated in July 2007 and returned to Saudi Arabia to be admitted for pleura-pulmonary tuberculosis. His sputum was smear-positive and his pleural effusion was also positive for *M. tuberculosis*. His tuberculous empyema required chest tube drainage. He was re-started on isoniazid, rifampin, pyrizinamide, ethambutol, moxifloxacin, cycloserine and amikacin. In July 2007, second-line drug susceptibility testing was performed by the National Tuberculosis Reference Laboratory, London, UK. His sputum *M. tuberculosis* [isolate B] was resistant to isoniazid (high level resistance), rifampin, ethambutol, pyrazinamide, ofloxacin, streptomycin, amikacin, capreomycin and ethionamide. It was only sensitive to linezolid, clofazimine and cycloserine (Table 1). He had no medical follow-up from September 2007 until July 2008. He sought a second opinion in Jordan. He felt better on alternative medicine and his respiratory symptoms improved. He was receiving moxifloxacin, ethambutol and cycloserine in August 2008 when he experienced left ankle pain, swelling and limitation of movement. MRI confirmed left ankle osteomyelitis (Fig. 1) and he underwent debridement. Bone histopathology showed caseating granuloma with negative acid-fast bacilli. A tissue sample from the ankle bone was emulsified in sterile normal saline using a sterile mortar and pistol. Both samples were inoculated in BACTEC-MGIT TB liquid culture tubes (BD Biosciences, Sparks, MD) and incubated in the BACTEC-MEGIT 960 instrument (BD Biosciences) until there was positive detection by the machine. The isolate was confirmed to be *M. tuberculosis* by PCR using the gene GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA). Sensitivity testing to isoniazid, rifampin, ethambutol and streptomycin were performed on a MEGIT 960 instrument (BD Biosciences) according to manufacturer's instructions. The drug concentrations were as follows: isoniazid 0.4 mg/ml, rifampin 1 mg/ml, ethambutol 5 mg/ml and streptomycin 4.0 mg/ml. The organism was resistant to all first-line drugs. The sample was referred

Table 1 Tuberculosis drug susceptibilities for the three isolates sputum and bone (R: resistant, S: sensitive, NP: not performed).

Tuberculosis drug sensitivities	Isolate A sputum	Isolate B sputum	Isolate C bone
Rifampin	R	R	R
Isoniazid	R	R	R
Pyrizinamide	R	R	R
Ethambutol	S	R	R
Streptomycin	R	R	R
Amikacin	NP	R	R
Capreomycin	NP	R	R
Kanamycin	NP	NP	R
Ethionamide	NP	R	R
Ofloxacin	NP	R	R
Moxifloxacin	NP	NP	R
Linezolid	NP	S	S
PAS	NP	NP	R
Cycloserine	NP	S	NP
Clarithromycin	NP	NP	NP
Clofazimine	NP	S	NP