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A patient with central nervous system tuberculomas and a history of disseminated multi-drug-resistant tuberculosis

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ABSTRACT

Tuberculosis (TB) is one of the leading causes of death worldwide, particularly in low- and middle-income countries. The global rates and numbers of drug resistant TB are rising. With increasing globalization, the spread of drug-resistant strains of TB has become a mounting global public health concern. We present a case of a young man previously treated for multi-drug resistant (MDR) TB in India who presented with neurological symptoms and central nervous system TB in the United States. His case highlights unique diagnostic and treatment challenges that are likely to become more commonplace with the increase of patients infected with drug-resistant TB and complicated extrapulmonary disease.

1. Introduction

Tuberculosis (TB) remains one of the top ten causes of death worldwide. In 2015, an estimated 10.4 million people worldwide developed TB and 1.8 million died; over 95% of these deaths occurred in low- and middle-income countries [1]. Resistance to standard anti-TB regimens is becoming widespread in the form of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis. MDR-TB is defined as resistance to isoniazid and rifampin, two of the most potent first-line TB drugs; XDR-TB is resistance to isoniazid, rifampin, the fluoroquinolones, as well as any of the second line injectable agents [1]. Globally, MDR-TB and XDR–TB notifications are both increasing. There were an estimated 480,000 people globally who developed MDR-TB in 2015; the largest numbers of these cases were reported in India, China, and Russia, and 9.5% of MDR cases met the definition of XDR-TB [1]. While TB most commonly infects the lungs, TB can occur in any organ in the body, including the central nervous system (CNS). CNS TB occurs in approximately 1% of patients with TB disease and is associated with major morbidity and mortality.

We present a complicated case of CNS TB in a young man with a history of previously treated MDR-TB. The diagnosis and treatment of this patient presented unique challenges to the treatment team. While MDR and XDR-TB are presently uncommon in patients treated in the United States, rising numbers of cases of drug resistant TB globally and increasing globalization and international travel raise concerns that such cases could be encountered more frequently both in the US and worldwide.

2. Case history and presentation

The patient's TB history is illustrated in Fig. 1 and Table 1 and is summarized here. The patient is a 28-year-old man from India who moved to the United States to attend university in 2004. In 2009, he developed night sweats, fever, weight loss, and cough. He returned to India shortly afterwards, where he was diagnosed with pulmonary and extrapulmonary TB with cervical lymphadenitis. Initial drug susceptibility testing from a lymph node aspirate revealed resistance to pyrazinamide. He was initially treated with a reportedly standard regimen (records not available) but his symptoms did not improve. Two months after start of treatment, he was diagnosed with disseminated TB involving the lungs, spine, and lymph nodes, and required surgery for stabilization of the spine. He was presumed to have MDR-TB, and was

Abbreviations: AFB, acid-fast bacilli; BAL, bronchoalveolar lavage; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computerized tomography; DOT, directly observed therapy; DST, drug susceptibility testing; FDA, Food and Drug Administration; IV, intravenous; LUL, left upper lobe; MDR-TB, multidrug-resistant tuberculosis; MRI, magnetic resonance imaging; TB, tuberculosis; WHO, World Health Organization; XDR-TB, extensively drug-resistant tuberculosis

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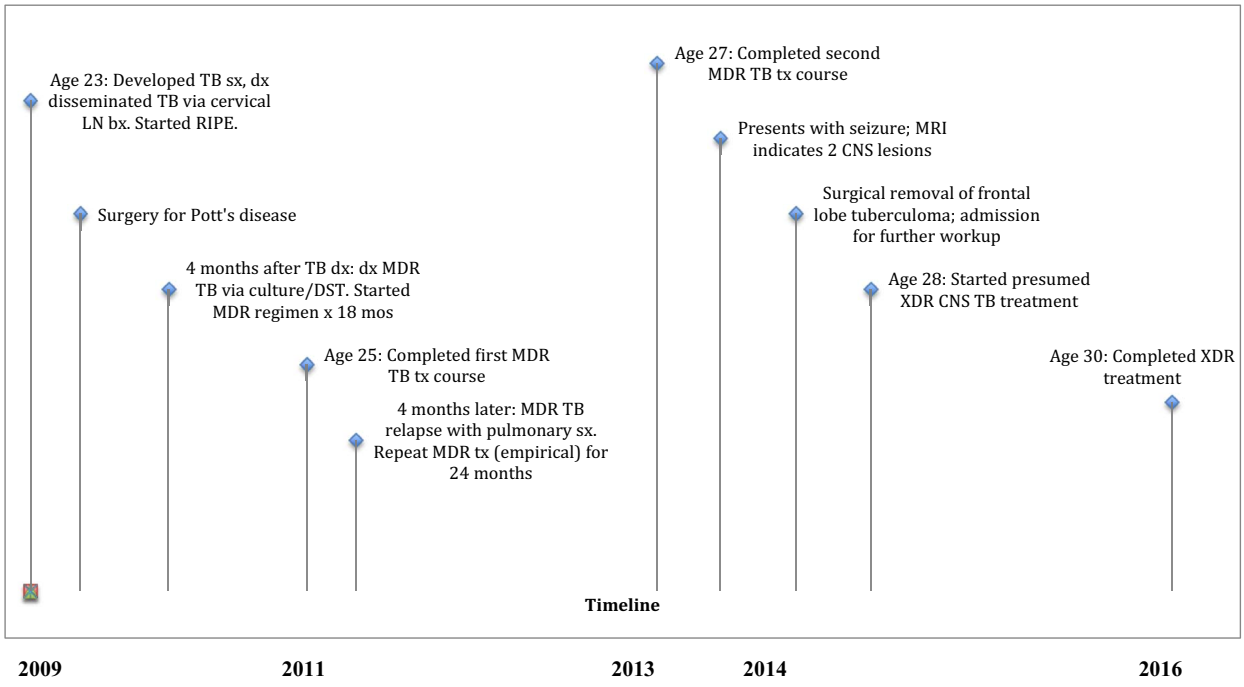

bx: biopsy; CNS: central nervous system; DST: drug susceptibility testing; dx: diagnosed; LN: lymph node; MDR: multi-drug resistant; mos: months; MRI: magnetic resonance imaging; RIPE: rifampin / isoniazid / pyrazinamide / ethambutol; sx: symptoms; TB: tuberculosis; XDR: extensively drug-resistant

Fig. 1. Case narrative timeline.

Table 1
Categories of antituberculous drugs and patient's TB treatment and drug susceptibility testing history, adapted from the 2016 WHO TB Treatment Guidelines [2].

WHO classification		Drug	Presumptive MDR regimen, 2009 (4 months, pre-DST)	MDR regimen (2 courses)[a]	Total # of months from previous regimens	Resistant on previous DST?	# Of months in "XDR" regimen[b]
First-line agents (drug-sensitive TB)		Isoniazid	x	x	46	x	
		Rifampin	x		4	x	
		Ethambutol	x	x	46		
		Pyrazinamide	x		4	x	
Group A: fluoroquinolones		Levofloxacin			0		
		Moxifloxacin	x		1		24
		Gatifloxacin			0		
		(Ofloxacin)			0	x	
Group B: Second-line injectable agents		Amikacin			0		
		Capreomycin			0		24
		Kanamycin	x	x	8		
		(Streptomycin)			0	x	
Group C: Other core second-line agents		Ethionamide/ Protionamide	x	x	43		
		Cycloserine/Terizidone	X	x	43		
		Linezolid			0		24
		Clofazimine		x	42		
Group D: Add-on agents	D1	Pyrazinamide	x		4	x	15[c]
		Ethambutol	x	x	46		
		High-dose isoniazid	x	x	46	x	15[c]
	D2	Bedaquiline			0		18
		Delamanid			0		
	D3	p-aminosalicylic acid		x	42		
		Imipenem-cilastatin			0		
		Meropenem			0		24
		Amoxicillin-clavulanate			0		24
		(Thioacetazone)			0		

DST: drug susceptibility testing; MDR: multi-drug resistant; TB: tuberculosis; WHO: World Health Organization; XDR: extensively-drug resistant.

[a] Prescribed in 2009 and 2011, before some of the agents in this table were available.

[b] Prescribed in 2014, before some of the agents in this table were available.

[c] Added seven months into treatment course for increased CNS penetration.