J Infect Chemother 22 (2016) 770–773

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Case report

Diagnosis of imported Ugandan typhoid fever based on local outbreak information: A case report

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ARTICLE INFO

Article history:
Received 25 January 2016
Received in revised form
11 May 2016
Accepted 12 May 2016
Available online 11 June 2016

Keywords:
Salmonella enterica
Typhoid fever
Multidrug resistance
Fluoroquinolone
Uganda

ABSTRACT

Re-emerging multidrug-resistant typhoid fever is becoming a worldwide threat, especially in East Africa. At the beginning of 2015, an outbreak of typhoid fever started in the capital city of Uganda, and 1940 suspected cases were reported by 5 March 2015. In this report, we describe a case of typhoid fever caused by a MDR strain with HIV infection and hemoglobin S-syndrome thalassemia in an Ugandan from Kampala City. It is essential to consider MDR strains of *Salmonella enterica* serovar Typhi infections, including fluoroquinolone-resistant strains, in patients from Africa and Southeast Asia.

1. Introduction

Typhoid fever is a systemic, Gram-negative bacterial infection caused by *Salmonella enterica* serovar Typhi (*S.* Typhi), which is characterized not only by fever and headache, but also unremarkable physical symptoms including gastrointestinal symptoms or a faint rash at the end of the first week of illness. An estimated 22 million new cases of typhoid fever occur each year worldwide and it is fatal in around 200,000 patients [1]. In the last decade, there has been a progressive decline in morbidity and mortality due to malaria infection in East Africa, and the numbers of people living with HIV and tuberculosis have decreased worldwide since 2000 [2]. Bacteria, including *S.* Typhi, have therefore become important common causes of febrile illness [3]. Since 2008, the re-emergence of multidrug-resistant (MDR) typhoid fever, defined as disease that is resistance to ampicillin, chloramphenicol, and co-trimoxazole, has been reported in East African countries including Malawi [4], Uganda [5], Zimbabwe [6], and Zambia [7], forewarning the emergence of fluoroquinolone-resistant *S.* Typhi. Most recently, an outbreak of typhoid fever started in Kampala City, the capital of Uganda, at the beginning of 2015. As of 5 March 2015, 1940 suspected cases had been reported [8], but up-to-date information on antimicrobial susceptibility, especially to fluoroquinolones, is unfortunately limited.

In this report, we describe a case of typhoid fever caused by an MDR *S.* Typhi strain, which has low susceptibility to fluoroquinolones, with HIV infection and hemoglobin S-syndrome thalassemia in an Ugandan from Kampala City who visited Japan in 2015.

2. Case report

A 44-year-old Ugandan woman was admitted to our hospital with more than a week-long history of high-grade fever, diarrhea and reduced dietary intake during a trip to Japan from Kampala City, the capital of Uganda (Fig. 1). She had been in Japan for 10 days when she became ill. Her medical history revealed

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http://dx.doi.org/10.1016/j.jiac.2016.05.004
1341-321X/

Fig. 1. Map of Uganda showing the location of Kampala City, the capital of Uganda, and the affected districts.

significant habitual alcohol intake. On arrival at the hospital, she was febrile at 38.1 °C and moderately pale with a pulse of 93 beats per minute, dehydrated, and displayed slight confusion. No systemic lymphadenopathy was observed, but her liver and spleen were both quite enlarged. There was no skin rash over the patient's trunk or extremities. The initial laboratory findings are shown in Table 1; detailed red blood cell parameters did not reveal the cause of anemia (Table 2). Rapid diagnostic tests for malaria (The NOW® Malaria Test, Binax, Inc., Portland, ME) and dengue fever (Dengue NS1 Detect Rapid Test, InBios, Seattle, WA) were negative, and microscopic examination of blood smears using Giemsa stain confirmed the absence of plasmodium parasites even though the red cells showed marked target cells (Fig. 2). She was unaware of her HIV-1 seropositivity until the diagnosis on admission. Her viral load was 56,000 copies/mL and CD4 count 224 cells/μL. An abdominal computed tomography (CT) scan was performed and the results revealed hepatosplenomegaly and gallbladder enlargement with increased wall thickness and gallstones. There was no evidence of any other HIV-1-related opportunistic infections, including those in the central nervous system.

Table 1
Laboratory data on admission.

Peripheral blood			Blood chemistry					
WBC	10,400	/μL	T-Bil	1.5	mg/dL	Na	131	mEq/L
RBC	280×10^4	/μL	AST	275	IU/L	K	3.7	mEq/L
Hb	8.6	g/dL	ALT	57	IU/L	Cl	102	mEq/L
PLT	23.0×10^4	/μL	LDH	307	IU/L	CRP	10.1	mg/dL
Seg	83.0	%	ALP	466	IU/L	Fe	66	μg/dL
Eos	0.0	%	γGTP	749	IU/L	TIBC	146	μg/dL
Ly	11.0	%	Amy	138	IU/L	UIBC	80	μg/dL
Mo	6.0	%	BUN	39.0	mg/dL	Ferritin	474.6	ng/mL
			Cr	1.37	mg/dL	Transferrin	122	mg/dL
			CPK	54	IU/L	Haptoglobin	100	mg/dL

The patient was initially treated with empirical intravenous cefmetazole (1 g twice daily) for acute cholecystitis, according to the national protocol [9]. On the second day of admission, blood and stool cultures yielded growth of *S.* Typhi O9 and Hd, and these isolates were found to be MDR (resistant to chloramphenicol, ampicillin, and cotrimoxazole) but susceptible to levofloxacin (LVFX) [minimum inhibitory concentration (MIC) 1 μg/mL] and minocycline (MIC $\leq$ 1 μg/mL). Drug susceptibilities were determined by the Clinical and Laboratory Standards Institute (CLSI)-S19 using MicroScan WalkAway NC6.11 J panel. Ultimately, antibacterial therapy was switched to intravenous ceftriaxone (CTRX) 1 g twice daily for 14 days for the treatment of *S.* Typhi, plus intravenous LVFX 500 mg twice daily for 7 days, because the possibility of Grade III (*severe*) cholecystitis and cholangitis with neurological dysfunction could not be excluded [10]. The patient demonstrated an excellent clinical response and she left our hospital fully recovered 16 days after admission, including resolution of the hepatosplenomegaly. We also advised her to seek treatment for HIV infection after returning home.