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Latent introduction to the Netherlands of multiple antibiotic resistance including NDM-1 after hospitalisation in Egypt, August 2013

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We describe the introduction of various multi-drug resistant bacterial strains, including an NDM-1-producing *Klebsiella pneumoniae*, through a traveller returning from Egypt, where they had been admitted to a private hospital. All family members of the patient were colonised with one or more extended-spectrum beta-lactamase producing strains. These findings emphasise the importance of adherence to isolation precautions for returning patients and suggest the need for inclusion of *Enterobacteriaceae* in admission screening.

We here report of a patient who had been hospitalised in Egypt for appendicitis in July 2013, and was colonised with various multiresistant *Enterobacteriaceae* including strains producing NDM-1, oxacillinase-48 (OXA-48) and extended spectrum beta-lactamase (ESBL). Explorative screening for multiresistant microorganisms among the patient's family members also yielded several ESBL-producing microorganisms. This report addresses the need for heightened awareness of patients and family members who have recently been exposed to healthcare environments in countries with high levels of antibiotic resistance.

Patients repatriated after hospitalisation abroad are a risk for introducing multiresistant microorganisms into hospitals in their home countries. In 2008, New Delhi metallo-beta-lactamase (NDM), which hydrolyses last-line carbapenem antibiotics, has been for the first time described in a Swedish patient returning from India [1]. Most reports on NDM are related to travellers returning from Pakistan and India. However, the global dispersal of NDM is of growing concern [2]. In the past two years, NDM-producing strains have been reported in patients returning from the African continent without obvious links to the Indian subcontinent [3,4].

Case description

A Dutch patient in their 40s was admitted to our hospital for fever and abdominal pain. On admission, computed axial tomography showed a periappendicular abscess. Four days earlier, the patient had returned from holidays in Egypt with his spouse and two children. One week into their holidays (two weeks before presentation at our hospital) the patient had complained about right lower abdominal pain and was admitted to a private hospital in Egypt where 400 mg ciprofloxacin twice a day and 500 mg metronidazole three times a day were given intravenously for two weeks. The patient was discharged after 13 days without having undergone any surgical intervention, and subsequently returned to the Netherlands.

In our hospital, the abscess was drained and the patient was treated with piperacilin/tazobactam 4,500 mg three times a day intravenously for five days with good clinical response.

A perianal screening swab taken on admission grew *Klebsiella pneumoniae*, which was resistant to meropenem (minimum inhibitory concentration: 32 mg/L). Molecular testing of the strain by PCR and sequencing of the PCR product revealed that the strain harboured the gene encoding NDM-1. Molecular testing of faeces detected OXA-48, and culture of this sample grew *Escherichia coli* and *K. pneumoniae* positive for OXA-48.

We also screened the patient's spouse and children, who had been visiting the patient in the hospital in Egypt. Stool samples were obtained 14 days after admission of the index patient. The Table shows an overview of the screening results for multiresistant microorganisms of the family. The patient, his spouse and the youngest child carried ESBL-producing strains with CTX-M1. The older child carried two different ESBL-producing *E. coli* strains positive for CTX-M9. A gene encoding *K. pneumoniae* carbapenemase (KPC) was detected by molecular tests from faeces of the youngest child. The culture of this sample remained negative for carbapenemase-producing strains. Screening of contact patients on the ward where the index patient was treated did not reveal further dissemination of any resistant strains.

Table

Carbapenemase and/or extended-spectrum beta-lactamase-producing strains from samples of a family returning to the Netherlands from Egypt, August 2013

Strain/resistance encoding genes[a]	Index patient	Spouse	Older child	Younger child
Klebsiella pneumoniae/ NDM1, CTX-M1, all TEMs[b]	+			
Escherichia coli/OXA-48, CTX-M1	+			
K. pneumoniae/OXA-48, SHV	+			
E. coli/CTX-M1, all TEMs[b]	+			
E. coli/CTX-M1, all TEMs[b] except for TEM 104				+
E. coli/CTX-M1 (no TEM)	+	+		
E. coli/CTX-M9		+	+, +[c]	
Resistance genes detected directly on stool samples[d]				
OXA-48	+			
KPC				+

[a] Strains phenotypically non-susceptible to third generation cephalosporins and/or carbapenems were tested for resistance genes by microarray Checkpoint chip CT103 (Checkpoints, Wageningen, the Netherlands). Detected ESBL-encoding genes (TEM-104, TEM-164, TEM-238, SHV, CTX-M) and carbapenemase-encoding genes (KPC, NDM, OXA-48, VIM, IMP) are reported.

[b] 'All TEMs' refers to detection of TEM-104, TEM-164 and TEM-238.

[c] Two CTX–M9 producing *E. coli* strains were found, which were phenotypically different and had distinct antimicrobial resistance patterns.

[d] Stool samples of all family members were tested for carbapenemase-encoding genes (KPC, OXA-48, VIM, NDM) by the microarrays Check-Direct CPE (Checkpoints, Wageningen, the Netherlands) and Hyplex Superbug ID (Amplex Biosystems GmbH, Gießen Germany).

Discussion

High prevalence of ESBL-producing bacteria with rates of over 60% in Egyptian hospitals has been reported [5,6]. Also outbreaks involving OXA-48- and VIM-1 carbapenemase-producing strains have been described in the southern Mediterranean region including Egypt [7]. The occurrence of an NDM-1-producing *Acinetobacter* in Egypt has previously been reported, but so far no reports of NDM-1-producing *Enterobacteriaceae* could be found in the literature [8]. This is in contrast to other countries in the area such as Morocco and the United Arab Emirates where these bacteria have already been isolated [9-11].

Highly sensitive and rapid screening methods are the mainstay to prevent introduction of multiresistant microorganisms in hospitals in low prevalence countries by repatriated patients. Molecular tests that allow detection of carbapenemase-encoding genes directly from clinical samples are promising when used in addition to conventional culturing [12].

In the youngest child, we detected a KPC gene by two molecular testing methods directly from faeces, but we were not able to confirm these findings by culture. The bacterial load of the KPC- producing strain was probably too low to be cultured.

It is well recognised that repatriated patients are a risk for introducing multiresistant microorganisms. Family members attending patients hospitalised abroad may also be at risk of acquiring multiresistant bacteria, as our case illustrates. Although we cannot be sure that the family members picked up all strains in the hospital in Egypt, the diversity of multiresistant microorganisms including strains rarely found in the Netherlands makes this highly plausible. Neither can we rule out that the strains were acquired in Egypt outside the hospital, since travelling to African countries has been described as a risk factor for ESBL carriage [13].

Based on these findings, we recommend alertness and compliance with isolation precautions. Infection control guidelines may need to be expanded to include admission screening for resistant *Enterobacteriaceae* in low prevalent counties for a growing number of international travellers, including family members who have visited a patient abroad.

Conflict of interest

None declared.

Authors' contributions

EB collected the data and drafted the manuscript; AWF participated in the coordination and concept of the manuscript; KZ performed and analysed the molecular tests; JPA participated in the coordination and concept of the manuscript and helped with the draft of the manuscript; DB organised the sample collection and participated in the concept of the manuscript; HG coordinated and edited the manuscript; JWR supervised the molecular research and analysis.

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