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NDM-1- or OXA-48-producing Enterobacteriaceae colonising Polish tourists following a terrorist attack in Tunis, March 2015

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We describe the introduction of NDM-1-producing *Klebsiella pneumoniae* ST147 and *Escherichia coli* ST410, and OXA-48-producing *K. pneumoniae* ST101 strains to Poland by two patients transported to the country after hospitalisation in Tunisia. The patients had gunshot wounds following the terrorist attack in the Bardo National Museum in Tunis in March 2015. Our report reinforces the need for microbiological screening of patients returning from travel on admission to healthcare institutions, especially following hospitalisation in countries where carbapenemase-producing *Enterobacteriaceae* are endemic.

We describe two patients colonised by carbapenemase-producing *Enterobacteriaceae* (CPE), which were identified on and following admission of the patients to a hospital in Warsaw, Poland, in March 2015. The patients had gunshot wounds as a result of a terrorist attack in Tunis, Tunisia, and were transferred to Warsaw directly from a hospital in Tunis.

following the terrorist attack

On 18 March 2015, visitors at the Bardo National Museum in Tunis were attacked by a group of armed terrorists. A total of 24 people from different countries were killed and around 50 were injured by gunshot. According to the Poland's Ministry of Foreign Affairs, three Polish citizens died and 10 others were wounded, who were treated in several clinical centres in Tunis [1]. On 20 March, eight of the 10 less seriously injured Polish patients were transferred to a hospital in Warsaw (Hospital A), where they stayed in a surgical and then orthopaedic wards; the clinical records of these patients are not available.

The other two seriously injured Polish patients were operated on in the same surgical unit of a hospital in Tunis and stayed in there until 28 March (10 days), at which point they were transported by air to a surgical ward in Hospital B in Warsaw. The patients were microbiologically screened on admission and later monitored at least once a week during their hospitalisation. The specimens and body sites examined included blood, wounds and rectum, to test for the presence of CPE.

Case description

Patient A, in their late 50s, was shot in the sacrum during the attack. A rectal swab taken on admission yielded a *Klebsiella pneumoniae* isolate, identified by VITEK 2 (bioMérieux, Marcy l'Etoile, France) as carbapenem resistant. The isolate was subsequently tested for metallo-beta-lactamase (MBL)-, carbapenem-hydrolysing oxacillinase OXA-48- and *K. pneumoniae* carbapenemase (KPC)-like carbapenemases using CARBA NP and phenotypic tests [2-5]. The isolate was positive in Carba NP and the MBL EDTA double-disk test, and was resistant to temocillin, suggestive of OXA-48 [5]. Polymerase chain reaction (PCR) analysis for several carbapenemase genes [6] showed that the isolate was positive for bla_{NDM} only and sequencing identified bla_{NDM-1}. The gene resided in a remnant of the Tn*125* transposon, shown by PCR mapping to include the 3' part of the upstream IS*Aba125* element, the bla_{NDM-1}-ble_{MBL} operon, genes *iso*, *tat*, *dct*, *groES* and *groEL*, and to be truncated downstream of *groEL* [7,8]. By multilocus sequence typing (MLST) [9], the isolate was classified as sequence type (ST) 147. No CPE isolates were recovered from other sites of the patient either on admission or during hospitalisation.

Patient B, in their early 20s, had severe damage of subcutaneous tissue near the trochanter of the femur as a result of being shot. A rectal swab on admission yielded a carbapenem-resistant *K. pneumoniae* isolate that was Carba NP-positive, negative in MBL and KPC tests, but resistant to temocillin. PCR and sequencing

Table

Antimicrobial minimum inhibitory concentrations for the carbapenemase-producing *Enterobacteriacae* isolates from two Polish patients wounded in a terrorist attack in Tunisia, March 2015

Species, sequence type, carbapenemase	Minimum inhibitory concentration (µg/mL)															
	AMX	AMC	PIP	TZP	CTX	CAZ	FEP	ATM	IPM	MEM	ERT	CIP	GEN	AMK	SXT	TET	TGC	CML	CST
Patient A																			
Klebsiella pneumoniae ST147 NDM-1	>256	>256	>256	>256	>256	>256	128	>256	12	>32	>32	>32	64	12	>32	>256	2	8	1
Patient B																			
K. pneumoniae ST101 OXA-48	>256	>256	>256	>256	>256	128	>256	>256	>32	32	>32	>32	64	6	>32	>256	0.75	8	1.5
K. pneumoniae ST147 NDM-1	>256	>256	>256	>256	>256	>256	96	128	32	>32	>32	>32	128	8	>32	128	3	8	1
Escherichia coli ST410 NDM-1	>256	>256	>256	>256	>256	>256	>256	48	32	>32	>32	>32	128	12	>32	128	0.38	>256	1.5

AMC: amoxicillin-clavulanic acid; AMK: amikacin; AMX: amoxicillin; ATM: aztreonam; CAZ: ceftazidime; CIP: ciprofloxacin; CML: chloramphenicol; CST: colistin; CTX: cefotaxime; ERT: ertapenem; FEP: cefepime; GEN: gentamicin; IPM: imipenem; MEM: meropenem; NDM: New Delhi metallo-beta-lactamase; PIP: piperacillin; ST: sequence type; SXT: trimethoprim-sulfamethoxazole; TET: tetracycline; TGC: tigecycline; TZP: piperacillin-tazobactam.

showed bla_{OXA-48} to be the only carbapenemase gene found. PCR mapping revealed that the gene was located in the Tn*1999.2* transposon, with the upstream IS*1999* element disrupted by IS*1R* [10]. The isolate was found to be ST101.

Ten days after admission, MBL-positive *K. pneumoniae* and *Escherichia coli* isolates were cultured from wound and rectal swabs. Isolates from the wound were analysed by molecular methods: both the *K. pneumoniae* and *E. coli* isolates were identified as New Delhi metallo-beta-lactamase-1 (NDM-1) producers; no other carbapenemases were found. The Tn*125*-like elements with their bla_{NDM-1} genes produced the same PCR mapping pattern as that of the *K. pneumoniae* isolate from Patient A. The *K. pneumoniae* isolate belonged to ST147, whereas *E. coli* was classified by MLST [11] as ST410.

Antimicrobial susceptibility testing

Antimicrobial susceptibility of the CPE isolates from both patients was tested by MIC Test Strips (Liofilchem, Roseto degli Abruzzi, Italy) and interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [12]. The isolates showed extensive resistance patterns, all being susceptible only to colistin, and all *K. pneumoniae* isolates to chloramphenicol (Table). Amikacin minimum inhibitory concentrations (MICs) of the four isolates indicated either susceptibility or intermediate resistance (EUCAST breakpoints: S ≤ 8 µg/mL, R › 16 µg/mL).

Discussion

The global spread of CPE is a public health problem of great concern. MBLs of the NDM type and OXA-48-like oxacillinases are among the most frequently reported carbapenemases in CPE, mainly *K. pneumoniae* and *E. coli*. Their multiple emergence in many European countries has been often attributed to imported cases from the Indian subcontinent [13,14] or the eastern and southern parts of the Mediterranean basin. These parts of the Mediterranean basin have been mostly associated with transmission of OXA-48-positive CPE. The second CPE transmitted from these areas was NDM-producing *Acinetobacter* species [13-15].

Partial molecular analysis revealed that the NDM-1-producing isolates from both Polish patients probably had the same genetic context of the bla_{NDM-1} gene, and both NDM-1-producing *K. pneumoniae* isolates were ST147. According to National Reference Centre for Susceptibility Testing records, the four isolates differed genetically from all NDM-1 or OXA-48 producers identified in Poland to date (data not shown). Therefore, the patients were most probably colonised in Tunisia, either during hospitalisation or, less likely, before the attack, outside the hospital setting.

It is unclear why NDM-1 producers from Patient B were recovered only 10 days after admission to a Warsaw hospital. Both patients had shared common care

exposure in the Tunis hospital and it is possible that the fact that the cultures were NDM negative on admission to the hospital in Warsaw was due to limited sensitivity of the screening.

In the Warsaw hospital, a set of enhanced infection control measures were used, including separate rooms with dedicated sanitary facilities, strict contact isolation and dedicated equipment. Nevertheless, transmission from Patient A to Patient B in Warsaw cannot be entirely excluded, especially as both patients were treated by the same personnel. To date, no secondary transmission of the CPE to other patients in the hospital has been observed. To date, Patient A is still hospitalised whereas Patient B was discharged on 22 April 2015. Control measures are in place: all patients admitted to high-risk wards, such as intensive-care units, surgery, haematology and oncology, are screened on admission.

Although a number of reports have indicated North Africa as a reservoir of OXA-48- and NDM-producing organisms, lack of local surveillance data impedes full assessment of the situation there. Some reviews articles have shown these organisms as being of 'sporadic occurrence' in that region [13-17], especially NDM-positive *Enterobacteriaceae*, which have been reported in North African countries only a few times [15], including one NDM-1- and OXA-48-producing *K. pneumoniae* ST11 isolate recovered in Tunisia from a Libyan patient in 2012 [18].

ST101 and ST147 are emerging clones of *K. pneumoniae*, found worldwide with various beta-lactamases, including carbapenemases [19]. *K. pneumoniae* ST101 with OXA-48 encoded by Tn*1999.2* was described in Tunisia and other North African countries [16,20,21]. *K. pneumoniae* ST147 with NDM-1, as well as NDM-1-producing pandemic *E. coli* ST410, have been reported in many regions, but to the best of our knowledge not in North Africa [22-26]. Our report once again reinforces the need for microbiological screening of patients returning from travel, especially following hospitalisation in countries where CPE are endemic, as specified, for example, in Polish infection control guidelines [27].

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Conflict of interest

None declared.

Authors' contributions

RI performed the molecular analysis, collected the data and drafted the manuscript; KB performed the microbiological analysis; AB performed the molecular analysis and collected the data; EL performed the microbiological analysis; MH performed the microbiological analysis; DŻ coordinated the microbiological analysis; AG performed the hospital laboratory analysis and collected the isolates with clinical data; MP coordinated the hospital infection control measures and collected the clinical data; WH consulted the cases and edited the manuscript; MG supervised the research and analysis, coordinated and edited the manuscript.

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Community-acquired infections due to Staphylococcus argenteus lineage isolates harbouring the Panton-Valentine leucocidin, France, 2014

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We describe two cases of human infections caused by *Staphylococcus aureus* clonal complex (CC) 75, also called *Staphylococcus argenteus*, harbouring the Panton-Valentine leucocidin (PVL). These two sporadic cases were community-acquired, and identified in France in 2014. Both had an epidemiological link with Mayotte, an overseas department of France located in the Indian Ocean off the south-eastern African coast. This report illustrates that, contrary to previous descriptions, *S. argenteus* can acquire important virulence factors and be responsible for severe infections.

In 2014, two cases of human infections caused by *Staphylococcus aureus* isolates belonging to clonal complex (CC) 75 lineage, also called *Staphylococcus argenteus*, harbouring the Panton-Valentine leucocidin (PVL) occurred in France. The two cases were sporadic and community-acquired, and had an epidemiological link with Mayotte, a French archipelago in the Indian Ocean. The two strains affecting the respective cases were both isolated from blood culture.

Description

Case 1

In January 2014, a French woman of Comorian origin in her mid-twenties presented to the Emergency Department of a hospital in Lyon, with an eight-day history of deterioration of the general condition, chills and cough complicated by haemoptysis starting the day before. The symptoms had appeared three weeks after the excision of a recurrent abscess in the left thigh for which the patient had initially received oral treatment with amoxicillin-clavulanic acid during five days, then roxithromycin during the following eight days. Interview of the patient revealed a travel to Mayotte six months earlier. The patient was immediately admitted to hospital. At that time, she presented with cough, haemoptysis and chest pain. Body temperature was high at 39.1°C and heart rate was 119/min. Laboratory findings showed a white blood cell count of 17.4 x 10^9/L (norm: 4–10.5 x 10^9/L), a C-reactive protein (CRP) of 251 mg/L (norm: <3 mg/L), and abnormal liver function tests (alanine and aspartate transaminases, alkaline phosphatase and gammaglutamyl transpeptidase were all elevated). A chest radiography revealed a bilateral abscessed pneumonia with right pleural effusion. Blood cultures were immediately initiated but no pulmonary sample was taken prior to antibiotherapy at the hospital. Treatment was started with ceftriaxone-spiramycin on the same day. The next day, blood culture was positive with *S. aureus*. As the strain was susceptible to meticillin and positive for Panton-Valentine leucocidin (PVL) by polymerase chain reaction (PCR), treatment was changed to intravenous oxacillin and clindamycin per os. After initiation of this treatment, fever disappeared in only one day while haemoptysis persisted for seven days. No other pathogen was identified. After 21 days, treatment was stopped due to a drug rash with eosinophilia and systemic symptoms (DRESS) syndrome and replaced by linezolid up to a total duration of five weeks. *S. aureus* decolonisation was performed during hospitalisation to eradicate nasal carriage and to prevent recurrences.

Case 2

In November 2014, an 18-month-old child living in Mayotte presented at a dispensary with a three-day history of fever and right lower limb pain. They were referred to the hospital Emergency Department of Mamoudzou. At the time of admission, the clinical examination led to suspect arthritis of the right knee with a skin lesion in front and inflammatory extension to the rest of the leg. Body temperature was 39.8°C

and heart rate 193/min. Laboratory findings showed a white blood cell count of 13.4 x 10^9/L and a CRP of 229 mg/L. Ultrasound revealed joint effusion which could not be punctured. Blood cultures were immediately collected and treatment started with amoxicillin-clavulanic acid and gentamicin intravenously. The next day, the child was transferred to the intensive care unit due to worsening tachycardia and cold extremities despite the infusion of a volume expander. Blood culture was positive with *S. aureus* susceptible to meticillin. Based on suspicion of a toxin-mediated infection, treatment was changed to clindamycin, gentamicin, linezolid and polyvalent immunoglobulins intravenously. Blood culture became negative 48 hours after the initiation of antibiotherapy. Three days after admission, ultrasound showed joint effusion of the right knee associated with a collection at the quadriceps bursa. Culture from pus aspiration yielded an *S. aureus* isolate susceptible to meticillin. The *S. aureus* isolate was positive for PVL by PCR. Treatment was continued intravenously with oxacillin and clindamycin. Multiple pulmonary abscesses appeared on the tenth day, which led to change treatment for clindamycin-rifampicin and finally for amoxicillin-clavulanic acid-rifampicin orally for a total of six weeks, allowing the patient's recovery.

Analysis of strains

Blood cultures from the two patients yielded *S. aureus* isolates, which were sent to the French national reference centre for staphylococci in Lyon for characterisation.

The two strains were identified by matrix-assisted laser desorption/ionization time-of-flight (Maldi-Tof) mass spectrometry as *S. aureus*. Antimicrobial susceptibility testing was performed by disk diffusion assay or on automated Vitek2 system and interpreted according to the 2013 guidelines of the Antibiogram Committee of the French Society for Microbiology (CA-SFM). The following panel of antibiotics was tested: penicillin, oxacillin or cefoxitin, kanamycin, tobramycin, gentamicin, erythromycin, clindamycin or lincomycin, pristinamycin, levofloxacin or ofloxacin, tetracycline, rifampicin, trimethoprim-sulfamethoxazole, fusidic acid, fosfomycin, linezolid, teicoplanin, and vancomycin. The two isolates were susceptible to meticillin and to all the antibiotics tested except penicillin.

Further characterisation of the strains with the DNA microarray Identibac *S. aureus* Genotyping (Alere Technologies, Jena, Germany) for staphylococcal cassette chromosome (SCC) *mec* typing and toxin profiling [1] revealed that the two strains harboured the PVL genes and belonged to the *S. argenteus* lineage sequence type (ST) 2250/2277. This was confirmed by PVL PCR and by assignment by multilocus sequence typing (MLST) to ST2250 using specific primers for *aro*E [2]. Alignment of the seven MLST gene sequences from the patients' respective strains to those of *S. argenteus*, and neighbour-joining phylogenetic analysis showed that the two strains belonged to the *S. argenteus* lineage. Moreover, after 48 hours of growth, the two strains presented a lack of pigmentation typical of *S. argenteus* [3].

Discussion

This is, to the best of our knowledge, the first observation of *S. argenteus* lineage isolates harbouring the PVL genes. *S. argenteus* has recently been described as a novel species in the genus *Staphylococcus*, and is - as *S. schweitzeri* is – part of an *S. aureus* species complex [1]. Several studies previously described the CC75 lineage as grouping clones of *S. aureus* belonging to STs that are very distant from all other clones and characterised by the lack of staphyloxanthin (e.g. ST75, ST850, ST883, ST1223, ST1304, ST1850) [2-5]. Such strains were isolated mainly from indigenous populations in Australia and French Guyana [2,4,6], but also in Cambodia, Fiji, Trinidad and Tobago, Thailand [7-10] and from animals in Africa [11,12]. No strain harbouring the PVL was described among these isolates, which were considered as having an attenuated virulence compared with other *S. aureus* strains [5,13,14].

By confering cytotoxicity on neutrophils and monocytes-macrophages, PVL leads to a high degree of virulence [15]. PVL-positive strains are most frequently responsible for skin and soft-tissue infections, but can also cause severe necrotising pneumonia or aggressive bone and joint infections [16]. The present results indicate that some strains belonging to the *S. argenteus* lineage are able to acquire the PVL phage. Moreover, the severity of the clinical presentation of the two cases described in this report strongly suggests an important role of PVL in their infections.

Both cases described had a link to Mayotte which indicates the potential geographical origin of these isolates there. Enhanced surveillance is therefore necessary to determine whether PVL-positive *S. argenteus* lineage might emerge as a cause of infections in Mayotte and might disseminate further in France and in other countries.

Conflict of interest

None declared.

Authors' contributions

C. Dupieux was involved in clinical data collection with R. Blondé and S. Laurent, and in writing. C. Bouchiat, M. Bes, H. Meugnier and A. Tristan carried out the analysis of strains and revision of the drafts. F. Vandenesch, F. Laurent and A. Tristan critically revised the manuscript and carried out the final corrections. All authors read and approved the final manuscript.

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Application in Europe of a urine-based rapid diagnostic test for confirmation of Schistosoma mansoni infection in migrants from endemic areas

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In February 2015, a male patient from Eritrea with persistent abdominal pain and rectal bleeding was diagnosed with *Schistosoma mansoni* infection upon examination of a rectal biopsy. In May 2015, repeated stool microscopy identified *S. mansoni* infection in another Eritrean patient with abdominal pain and considerable eosinophilia (34%). Use of point-of-care circulating cathodic antigen (POC-CCA) tests on urine confirmed *S. mansoni* infection in both patients. Wider application of non-invasive POC-CCA urine tests will improve schistosomiasis diagnosis and clinical management in migrants.

We report the application of a urine-based antigen detection test for rapid, non-invasive diagnosis of intestinal schistosomiasis in two migrants from Eritrea. The potential implications of this rapid and highly sensitive diagnostic test with a short turn-around time for improved migrant health in European hospital settings and travel clinics are discussed.

Descriptions

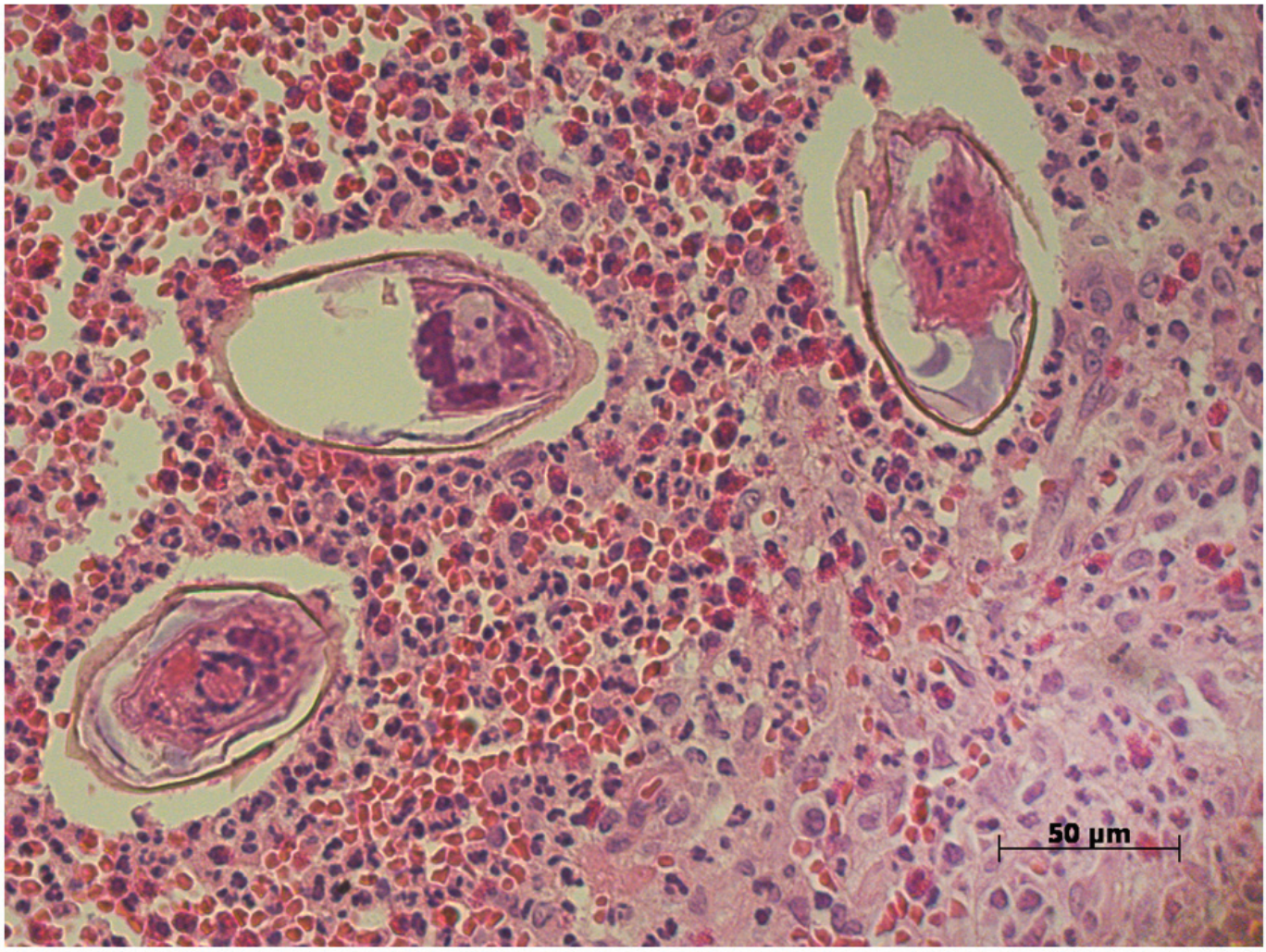
Patient 1

At the beginning of February 2015, a previously healthy male patient from Eritrea in his late teens presented to a German hospital with a history of rectal bleeding during the preceding days and persistent abdominal pain that had lasted for several weeks. No diarrhoea and no further digestive symptoms were reported at the time of presentation. The patient did not take any medication and past medical history was unremarkable. He was of Eritrean origin and had migrated to Germany approximately one year before presenting at the hospital. On physical examination, the patient was afebrile, vital signs were normal and no abdominal abnormalities were noted. However, rectal examination revealed a small, palpable mass, located approximately 7 cm from the anal verge. Blood tests showed a normal white blood cell count (5,800 cells/mL) with 6% eosinophils. Liver function tests and C-reactive protein were normal. Flexible colonoscopy identified two polyp-like lesions in the rectum, measuring up to 20 mm and 3 mm, respectively, while the rectal mucosa appeared macroscopically normal. Polypectomy was performed and biopsies were taken for histological workup, which showed erosive lesions and chronic intestinal inflammation. Upon microscopic examination of both polyps, typical pathognomonic features of eggs of the blood fluke *Schistosoma mansoni* were observed (Figure 1). Distinct histopathological features were the unique shape and size of parasite eggs (measuring 130–140 x 50–60 µm and lateral spine) and the eosinophil infiltration around the granulomas.

A stool sample could not be obtained from the patient. However, a urine sample was subjected to a rapid point-of-care (POC) antigen test. This test detects a schistosome-excreted circulating cathodic antigen (CCA). This POC-CCA test is commercially available (Rapid Medical Diagnostics; Pretoria, South Africa) and has been validated in various schistosomiasis-endemic settings of sub-Saharan Africa, where it proved more sensitive for *S. mansoni* than stool microscopy using the Kato-Katz technique [1]. Indeed, the reported sensitivity and specificity of the POC-CCA urine test for *S. mansoni* diagnosis during a multi-centre evaluation in five African countries were in the range of 78–92% and 56–94%, respectively, whereas the estimated sensitivity of the Kato-Katz technique was 44–77%. The POC-CCA in our patient with histologically proven schistosomiasis gave a faintly positive test line (termed ‘trace’ and

Figure 1

Biopsy of a rectal polyp, with typical granulomatous lesions with eosinophil infiltration, in a patient with intestinal schistosomiasis, Germany, February 2015



Haematoxylin and eosin, original magnification x40.

considered to be positive by the manufacturer) (Figure 2), thereby confirming the suitability of this non-invasive test to be employed in the diagnostic workup of patients with suspected schistosomiasis.

Abdominal ultrasound examination was performed to exclude hepatic fibrosis and other indicators of *Schistosoma*-induced chronic morbidity. The patient was treated with praziquantel, 40 mg/kg for three consecutive days [2], which led to complete resolution of clinical symptoms.

Patient 2

While preparing this report, we observed in May 2015 another young male patient from Eritrea with long-lasting abdominal pain and considerable peripheral blood eosinophilia (34%; norm: ≤5%).

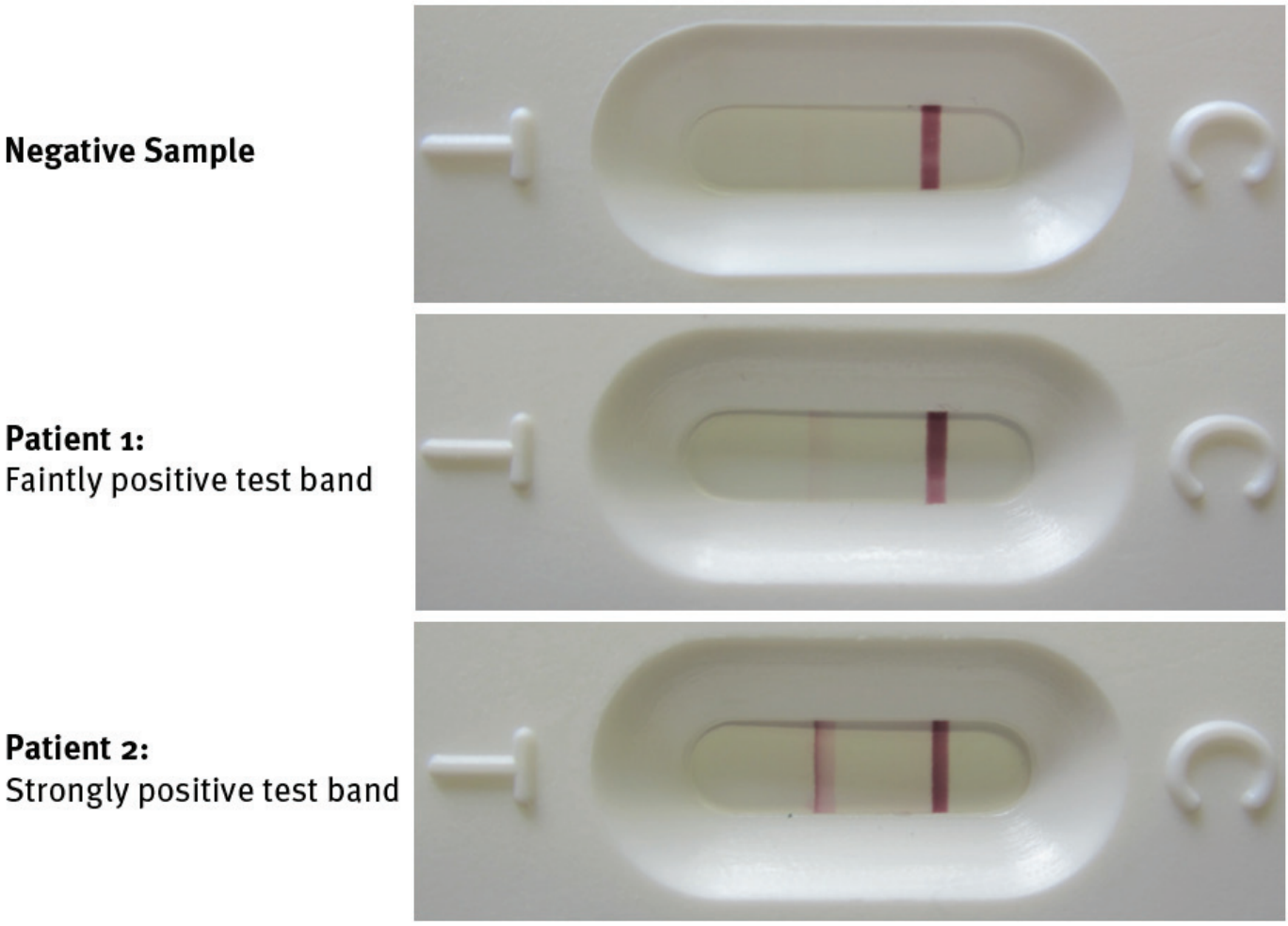
The patient, who was in his early twenties, had migrated to Germany 10 months before presentation and did not report any diarrhoea or rectal bleeding. Upon clinical examination and abdominal ultrasound, no abnormalities were noted. A POC-CCA test was applied on urine on the day of presentation and gave a strongly positive test result (Figure 2), while the initial stool microscopy was negative and only few eggs of *S. mansoni* were detected upon repeated stool examination. No additional parasitic or bacterial intestinal infections were found during the further diagnostic workup. Based on the positive test result in the POC-CCA urine test, intestinal schistosomiasis was diagnosed and treatment with praziquantel promptly initiated. A follow-up visit for this patient is scheduled in June 2015.

Discussion

Schistosomiasis is a parasitic disease that is endemic in large parts of sub-Saharan Africa, including Eritrea. The two main schistosome species in Africa are *S. mansoni* (causing intestinal schistosomiasis) and *S. haematobium* (causing urogenital schistosomiasis)

Figure 2

Results obtained by application of the point-of-care circulating cathodic antigen (POC-CCA) test for rapid diagnosis of *Schistosoma mansoni* infection on two patients' urine samples, Germany, February–May 2015



The control band (C) is present in all three specimens, while a test band (T) is only present in positive samples and its strength may depend on the infection intensity.

[3-5]. Infection is acquired through contact with cercariae-infested freshwater bodies. More than 250 million people are infected with schistosomes [6,7]. While long-term morbidity from chronic *S. mansoni* infection can result in hepatic fibrosis, portal hypertension and hypersplenism [8], many infections may be missed due to the unspecific clinical presentation and the low sensitivity of the most widely used diagnostic assays (i.e. stool microscopy) [3].

Persistent abdominal pain and occasional blood in stool were the only symptoms reported by our patient 1, despite the significant inflammation observed in the intestinal mucosa. Inflammatory rectal polyps have been described as a feature of chronic *S. mansoni* infection [9-11], but schistosomiasis is rarely considered in the differential diagnosis of intestinal polyposis outside endemic areas [12]. In patient 2, the incidental finding of considerable peripheral blood eosinophilia was the main reason to perform diagnostic tests pertaining to parasitic infections.

POC rapid diagnostic tests (RDTs) have the potential to improve the diagnosis and management of schistosomiasis patients. Thus far, repeated stool microscopy on several faecal specimens is the recommended diagnostic 'gold' standard, but light-intensity infections (i.e. ≤100 eggs per gram of stool) are often missed [3] and technical expertise in microscopic recognition of intestinal parasites is waning in many laboratories worldwide [13]. The urine-based POC-CCA is increasingly used in risk mapping and epidemiological surveys in schistosomiasis-endemic countries [1,14-16]. Previous studies have shown the positive and negative predictive values of a single POC-CCA to be 77% and 72–89%, respectively, if compared to multiple Kato-Katz thick smears as diagnostic reference standard [17,18]. The test has, however, not yet entered clinical practice in European hospitals and laboratories [7].

In our patient 1, the POC-CCA reliably detected the *S. mansoni* infection and confirmed the previously established histopathological diagnosis. Although polypectomy needed to be performed, an earlier use of a non-invasive urinary RDT may have provided evidence of active schistosomiasis more promptly. Indeed, in patient 2, the POC-CCA gave a positive test result on the first day of presentation, while helminth eggs of *S. mansoni* could only be detected upon repeated stool microscopy some days later. The clinical presentation of persistent abdominal pain and rectal bleeding is indicative of schistosomiasis in patients from endemic areas. A rapid diagnosis of this infection may allow faster adequate treatment, which in turn may lead to a resolution of the symptoms and avoid the need for further invasive diagnostic workup. While the POC-CCA is a highly sensitive and rapid tool to complement parasitological diagnostics, it cannot however replace a thorough microscopic examination of stool and urine, as the sensitivity for detection of *S. haematobium* is not sufficiently high [1], and no other parasites (e.g. soil-transmitted helminths) can be detected by POC-CCA.

Over the past decade, there has been a significant increase in migration from Africa and the Arabian Peninsula into Europe, with new arising challenges for the healthcare systems in various European countries [19]. Previous research has shown that inadequate communication and cultural barriers negatively affect the health-seeking behaviour of newly arrived Eritrean asylum seekers in Europe [20]. These immigrants may frequently present with imported infectious diseases that are not typically considered by European physicians in the differential diagnosis. A report from Sweden in 2014, for instance, has highlighted a dramatic increase of imported *Plasmodium vivax* malaria that was closely linked to newly arrived refugees from Eritrea [21]. While unexplained fever in African migrants usually prompts diagnostic testing for malaria, it is conceivable that rather unspecific gastrointestinal complaints, which are a key feature of many infections with helminths, including schistosomiasis, will not always lead to repeated stool sampling and in-depth diagnostic workup. Hence, we speculate that wider use of POC-CCA urine tests could improve the *S. mansoni* detection rate and, in turn, may reduce the number and costs of invasive diagnostic procedures.

Conclusions

Imported infections with *Schistosoma* spp. might increase in Europe due to a rise in migration from endemic settings, particularly from Africa. Due to the frequently unspecific clinical presentation of intestinal schistosomiasis and the insufficient sensitivity of stool microscopy, infections may easily be missed. We describe the successful use of POC-CCA urine tests for diagnosis of schistosomiasis and encourage physicians caring for migrants from endemic areas to consider implementing this rapid, relatively inexpensive (single test costs approximately EUR 1.50), and highly sensitive test as part of the diagnostic workup for gastrointestinal disorders.

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Conflict of interest

None declared.

Authors' contributions

Patient examination, history taking and endoscopy: SZ, DV. Histopathological analysis: PAS, RMB. Microbiological diagnostics: SLB, HM, MH. Wrote the manuscript: SLB, MH, JU. All authors have read and approved the final version of the manuscript.

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Zika virus infection in a traveller returning to Europe from Brazil, March 2015

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We report a case of laboratory-confirmed Zika virus infection imported into Europe from the Americas. The patient developed fever, rash, and oedema of hands and feet after returning to Italy from Brazil in late March 2015. The case highlights that, together with chikungunya virus and dengue virus, three major arboviruses are now co-circulating in Brazil. These arboviruses represent a burden for the healthcare systems in Brazil and other countries where competent mosquito vectors are present.

Case presentation

A male Italian traveller in his early 60s presented to the Infectious and Tropical Diseases Unit, Azienda Ospedaliero Universitaria Careggi, Florence (Italy), four days after his return from a 12-day holiday in Salvador de Bahia, Brazil at the end of March 2015. The patient had a four-day history of confluent slightly-pruritic erythematous rash, diffused on the face, trunk, arms, and legs, accompanied by fever (maximum temperature 38 °C), conjunctivitis, general weakness, and painful oedema of both hands and feet. Blood tests revealed a normal white blood cell count (6,180 cells/µL; reference: 4,000–10,000/µL) with normal differential count, but some activated lymphocytes, thrombocytopenia (112,000/µL; reference: 140,000–440,000/µL) and slightly elevated C-reactive protein (10 mg/L, reference: <9 mg/L). Serum transaminases and creatinine were normal. Because of the clinical presentation and the travel history, a viral infection was suspected, and patient serum was tested for antibodies against chikungunya virus (CHIKV), dengue virus (DENV), Zika virus (ZIKV), Yellow fever virus, West Nile virus, Japanese encephalitis virus, Parvovirus B19, human herpes virus 6 (HHV6), and HIV [1]. The serum sample taken four days after symptom onset showed a positive result for anti-ZIKV-IgM and -IgG antibodies, suggesting an acute or recent ZIKV-infection. Results of the serological tests for the other viruses tested were negative (Table). A follow up sample, taken 26 days after symptoms onset, showed a threefold increase of the anti-ZIKV-IgM and -IgG antibody titres (Table). In addition, a low-titre DENV IgG was now observed (Table), most likely representing a serological cross-reaction of the anti-ZIKV-IgG antibodies (Table). ZIKV-specific real-time reverse transcription-PCR [1] was negative from both samples. Generic flavivirus and alphavirus RT-PCR [1] were also negative. The presence of ZIKV-specific neutralising antibodies in the second serum sample was confirmed by a virus neutralisation assay (Table). The patient was discharged, managed and followed-up in the outpatient department. The patient was recommended symptomatic treatment with paracetamol. The symptoms rapidly resolved in the following week (fever and rash lasted for only four days).

Background

ZIKV is an arbovirus belonging to the flavivirus genus that was first isolated from a rhesus monkey in the Zika forest in Uganda [2]. It is transmitted by different species of *Aedes* mosquitoes. Clinical manifestations of ZIKV infection are very similar to those of DENV and CHIKV infections, but usually milder [3]. Human infections have been documented in several African and south-eastern Asian countries [4]. ZIKV was responsible for several outbreaks on islands in the Pacific Ocean, such as Yap Island (Federated States of Micronesia in 2007 [4]) and more recently in French Polynesia, New Caledonia, Easter Island and the Cook Islands in 2013 [5,6]. In several non-endemic countries including Japan, Germany, Italy, Canada, Australia and the United States (US), the infection has been diagnosed in returning travellers [1,7-11].

ZIKV infections have recently been reported in Brazil, where the virus has probably been circulating since 2014 [12]. So far, 16 cases have been confirmed in accordance to the Ministry of Health of Brazil [13].The emergence of ZIKV in Brazil is of concern since Brazil is the country with the highest number of DENV infections

Table

Serological test results and virological data of a case of Zika virus infection imported from Brazil into Italy, March 2015

Antibody or antigen tested	Serum samples taken after symptom onset (days)	
	4	26
Anti-ZIKV-IgG[a]	1:160	1:1,280
Anti-ZIKV-IgM[a]	1:160	1:1,280
ZIKV NAb[b]	ND	1:640
Anti-DENV-IgG[a]	<1:20	1:20
Anti-DENV-IgM[a]	<1:20	<1:20
DENV-2 NAb[b]	ND	<1:20
DENV-4 NAb[b]	ND	<1:20
DENV NS1[c]	Negative (0.1 arbitrary units)	Negative (0.1 arbitrary units)
Anti-JEV-IgG[a]	<1:20	<1:20
Anti-JEV-IgM[a]	<1:20	<1:20
Anti-WNV-IgG[a]	<1:20	<1:20
Anti-WNV-IgM[a]	<1:20	<1:20
Anti-YFV-IgG[a]	<1:20	<1:20
Anti-YFV-IgM[a]	<1:20	<1:20
Anti-CHIKV-IgG[a]	<1:20	<1:20
Anti-CHIKV-IgM[a]	<1:20	<1:20

CHIKV: chikungunya virus; DENV: dengue virus; DENV-2: dengue virus serotype 2; DENV-4: dengue virus serotype 4; JEV: Japanese encephalitis virus; NAb: neutralising antibodies; ND: not done; NS1: nonstructural protein-1; WNV: West Nile virus; YFV: yellow fever virus; ZIKV: Zika virus.

[a] Indirect immunofluorescence assay (IIFA) titres <1:20 for serum were considered negative [1].

[b] Virus neutralisation test (VNT) titres <1:20 for serum were considered negative [1].

[c] SD BIOLINE Dengue Duo NS1 Ag + Ab Combo and Bio-Rad Platelia Dengue NS1 Ag.

world-wide [14]. Moreover, CHIKV has been introduced to South America as well with more than one million of cases diagnosed since 2013 to date [15].

Discussion and conclusions

The ongoing outbreak of now two major mosquito-borne infections in addition to endemic DENV infections has the potential of posing a serious threat to local and supra-national South American healthcare systems, as observed in the Pacific region in recent years [16].

In endemic areas, but also in the setting of travel medicine, ZIKV infection represents both a clinical and diagnostic challenge since the symptoms are very similar to other arboviral diseases, no specific commercial serological tests are available, and cross-reactive DENV serology (IgG or IgM) during ZIKV infection has been described in previously reported cases [11] which may lead to incorrect diagnoses. Recently, neurological complications possibly related to coinfections or sequential infections with dengue virus have been reported in French Polynesia [17].The European Centre for Disease Prevention and Control (ECDC) published a Rapid Risk Assessment on ZIKV in the Americas on 25 May 2015, with the aim of increasing awareness and enhancing vigilance towards the detection of imported cases of ZIKV infection in Europe [18]. This case is, to the best of our knowledge, the first laboratory-confirmed case of a ZIKV infection acquired in the Americas and imported into Europe. The patient had returned to Italy, his home country, where *Aedes albopictus*, a potential competent vector, is widely distributed. Considering the extensive airline travel between Latin America and other parts of the world where the viruses have not yet been established, but competent vectors are present, such as southern Europe and the southern part of the US, the surveillance systems have to be aware of the appearance of ZIKV in Brazil to avoid further dissemination of the disease. In order to prevent seeding of ZIKV into local mosquito populations, as it happened for CHIKV in Italy in 2007 and in France in 2010 and 2014 [19, 20, 21], screening of febrile returning travellers for arboviral infections, especially in the summer months, is highly advised.

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Conflict of interest

None declared.

Authors' contributions

Wrote the manuscript: LZ, DT, JSC, GV; performed laboratory investigations: DT, CF, MER, JSC, GV, SG; revised the manuscript: AB, JSC; managed the patient: LZ.

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EU publishes call for proposals for projects under third health programme 2015 work plan

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Following the publication on 2 June by the European Union (EU) Consumers, Health and Food Executive Agency of the 2015 work plan of the third health programme [1], a call for proposals for projects under the work plan was published on 5 June [2]. The deadline for submitting proposals is 15 September 2015.

The call for proposals covers five topics: alcohol, hepatitis, tuberculosis, active and healthy ageing and transplantation therapies. The submission of proposals is now open, and further details about the projects and about how to submit a proposal are available here.

The third health programme [3] is the main instrument used by the Commission to implement the EU Health Strategy. Read more about the programme here.

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