

criteria, posed concerns for the existence of possible infective endocarditis.

After knowing the blood culture results, the patient was asked about animal contact. He explained he had four dogs, two cats and two domestic rats, but he did not remember being bitten recently. Rats and other rodents are the main reservoir of *S. moniliformis* and its bite is directly related with RBF. Moreover, It can also be transmitted by contact with its saliva, excrements or through other colonized pets.<sup>1,3,4</sup> No history of animal bites, which is the case of our patient, have also been reported by nearly 30% of the patients.<sup>2,5</sup> Although, the incidence of RBF in Spain is unknown, several cases have been reported (three cases of bacteraemia and other cases of arthritis, abscesses and wound infection) after rodents' bite.<sup>2</sup> Overall, this case emphasizes the need for a high clinical suspicion and a well-addressed anamnesis, which was indeed performed inaccurately here, in order to diagnose this infectious disease.

*S. moniliformis* is a fastidious bacillus that requires microaerobic atmosphere (5–10% CO<sub>2</sub>), long incubation period (2–7 days) and culture media with blood for its growth. In blood cultures it is inhibited by the presence of sodium polyanethol sulfonate (used as an anticoagulant in some blood cultures) but it is not affected by the presence of resins in the media.<sup>1–5</sup> The incorporation of MALDI-TOF analysis in clinical Microbiology departments has reduced the time needed for optimal bacterial identification in such a fastidious microorganism.<sup>3</sup> If there is a high clinical suspicion of RBF and difficulties in culturing samples, diagnosis carried out by 16S rRNA PCR analysis can be done.<sup>1,3,5</sup>

In conclusion, infections caused by *S. moniliformis* in Spain are rare; ours is the fourth case of bacteraemia reported. History of rodent contact and high clinical suspicion are essential in order to adapt laboratory protocols and to improve microbiological diagnosis and patient outcome.

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## Traveller's diarrhoea by *Vibrio cholerae* in patients returning from the Dominican Republic



### Diarrea del viajero por *Vibrio cholerae* en pacientes que regresan de República Dominicana

Dear editor,

According to WHO and European Centre for Disease Control, only thirteen imported cases of cholera have been notified by Spain in the last 15 years, the last one in 2013. On August 20, 2015, *Vibrio cholerae* was isolated from two immunocompetent female patients (47 and 62 years-old) returning from Dominican Republic (DR). No patient had previously received the cholera vaccine. Both patients showed acute and watery diarrhoea (12–15 stools/day, no blood and mucus), nausea, abdominal pain, and malaise. They had returned from a tourism trip to Bonao (DR) four days before, where they had stayed for 15 days. Physical examinations were normal, except for lightly dehydrated mucosae and skin. Laboratory analysis revealed hypokalemia and altered C-reactive protein. The patients informed the physician that a cholera outbreak had recently been detected in Bonao. This was related to drinking contaminated water

from Masipédro river. They had not drunk contaminated water (only bottled water) or drinks with ice cubes, but they had swum in the Masipédro river during their stay. This information was notified as suspected cholera cases to the public health authorities. A blood and faecal culture from each patient were sent to the microbiology department. Intravenous fluids, metoclopramide and antibiotic treatment (Doxycycline 100 mg for 3 days) were started. They remained afebrile and this led to quick recovery from their gastroenteritis.

Because of the epidemiological background, testing for *V. cholerae* was included [enriched alkaline peptone water (1% NaCl pH 8.5) and selective thiosulfate citrate bile salts sucrose (TCBS) agar (Becton–Dickinson)]. The TCBS showed yellow colonies (sucrose fermenting) which were identified as *V. cholerae* by API20E® (99.0%, Bionumber: 5346120; bioMérieux) and MALDI-TOF MS (score 1.53; Bruker Daltonics). The isolates reacted with polyvalent anti-O1 antisera (BD Difco™ *V. cholerae* antisera, Becton–Dickinson). They were resistant to the O/129 vibriostatic agent 150 µg (Thermo Scientific Oxoid). The isolates were confirmed as *V. cholerae* O1 biotype El Tor serotype Ogawa in the National Centre for Microbiology. Moreover, the presence of virulence determinants and toxin coding genes were detected by PCR.<sup>1</sup> Pulsed-field gel electrophoresis<sup>2</sup> and

**Table 1**Characteristics of *Vibrio cholerae* O1 El Tor Ogawa strains isolated from two patients returning from Dominican Republic.

| ID number | Species                | Date of the isolation | Country    | Sample type  | PFGE pattern <sup>a</sup> | MLVA pattern <sup>b</sup> | Cholera toxin gene (ctx) | Virulence determinants <sup>c</sup>                                                                                                                                                                                                                                                         | Resistance pattern <sup>d</sup>                                                      |
|-----------|------------------------|-----------------------|------------|--------------|---------------------------|---------------------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| 1 and 2   | <i>Vibrio cholerae</i> | 2015                  | Spain (DR) | Stool sample | A                         | 7-3-6-15-6                | +                        | <i>tcpA</i> <sup>+</sup> , <i>tcpI</i> <sup>+</sup> , <i>hlyA</i> <sup>+</sup> , <i>nanH</i> <sup>+</sup> , <i>hap</i> <sup>+</sup> , <i>rtxA</i> <sup>+</sup> , <i>ace</i> <sup>+</sup> , <i>zot</i> <sup>+</sup> , <i>hepA</i> <sup>+</sup> , <i>gshB</i> <sup>+</sup> , <i>stn-sto</i> - | AMP <sup>S</sup> CIP <sup>S</sup> CHL <sup>I</sup> SXT <sup>R</sup> TET <sup>S</sup> |

<sup>a</sup> Pulsed field gel electrophoresis.<sup>b</sup> Multi-locus variable number tandem repeat analysis types were assigned by combining the number of repeat units of each locus in the order VC0147, VC0436-7, VC1650, VCA0171 and VCA0283.<sup>c</sup> *tcpA*, classical biotype and *tcpI*, the toxin-coregulated-pilus associated genes; *hlyA*, hemolysin gene (classical biotype); *nanH*, neuraminidase gene, *hap*, hemagglutinin protease gene; *rtxA*, cytotoxic actin cross-linking repeats in toxin gene; *ace*, accessory cholera enterotoxin; *zot*, zonula occludens toxin; *hepA*, the transcriptional regulator; *gshB*, glutathione synthetase; *stn-sto*, heat-stable toxin.<sup>d</sup> An antimicrobial susceptibility test was performed for each isolate using the disc diffusion method (Becton–Dickinson) on Mueller–Hinton agar, and interpreted according to Clinical and Laboratory Standards Institute guidelines (M45 3rd edition). AMP (10 µg): Ampicillin, (18 mm); CIP (5 µg): Ciprofloxacin, (25 mm); CHL (30 µg): Chloramphenicol (13 mm); SXT (1.25/23.75 µg): Trimethoprim/sulfamethoxazole (6 mm), TET (30 µg): Tetracycline, (25 mm).

MLVA<sup>3</sup> showed the same pulsotype and pattern in both strains (Table 1).

In locations such as Europe where cholera is a sporadic illness, the clinical microbiology laboratory should be informed of any clinical and epidemiological suspicion of cholera (e.g.: traveller's patient history, risk activities, watery diarrhoea or rice water, current cholera outbreaks). The culture, biochemical identification, commercial identification systems, and immunoassay are time consuming and often lack sensitivity and specificity due to high phenotypic diversity. Furthermore, there have been detected strains resistant to vibriostatic compound O/129.<sup>4</sup> All *Vibrio* species other than *V. cholerae* have been successfully identified by MALDI-TOF MS system, but this tool has failed to identify *V. cholerae* isolates to the species-level, genus-level, or even not to get a reliable identification.<sup>5</sup> However, a newly generated established MALDI-TOF MS database, the VibrioBase, has been very useful for rapid identification of human-pathogenic *Vibrio* spp.<sup>6</sup>

The genes that code for the virulence factors (*ctx* and *tcpA*) traditionally associated with epidemic *V. cholerae* O1 and O139 were detected. Both isolates presented the same pattern of virulence factors, and there were identified genes such as *hlyA* or *rtxA* in agreement with studies from other countries.<sup>4,7</sup> Extensive genetic variation among cholera strains has been observed by MLVA from different regions and times of collection.<sup>8</sup> Based on the history of travel to Bonaio, it is reasonable to assume the patient isolates were related to the outbreak strain. On the other hand, the high negative predictive value of the molecular multiplex gastrointestinal panels has led to the suggestion that they be used as screening tools especially in outbreaks since it would improve diagnosis of infectious gastroenteritis, decisions regarding patient isolation and reduce nosocomial transmission.<sup>9</sup>

There have been reports of increased drug resistance towards antibiotics commonly used among the strains of *V. cholerae*, causing serious problems in management of cholera cases mainly in developing countries. These have appeared in many cholera endemic countries, including ampicillin [resistance (R): 0–100%], tetracycline (0–81.8%), ciprofloxacin (0–9.1%), chloramphenicol (3.2–9.1%), or cotrimoxazole (83.3–100%).<sup>10</sup> Our cases underline the importance of testing for *V. cholerae* in potentially exposed patients with acute diarrhoea who return from epidemic areas. Continuous circulation inside and outside of some American, African or Asian countries increases the likelihood of imported cases. Travellers must be informed about the potential risks of cholera, symptoms, and precautions to prevent disease and secondary transmission. Conventional culture media, MALDI-TOF and multiplex gastrointestinal PCR help us to establish an adequate diagnosis.

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## Conflict of interest

None declared.

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## Tuberculosis of the elbow: A rare form of presentation of extrapulmonary tuberculosis



### Osteoartritis tuberculosa del codo: forma poco frecuente de presentación de tuberculosis extrapulmonar

Osteoarticular tuberculosis (OTB) remains a major diagnostic and management challenge. Globally, OTB accounts for 2.2–4.7% of all tuberculosis cases in Europe and the USA.<sup>1</sup> The most frequent form of OTB is tuberculous spondylitis or Pott's disease, followed by osteomyelitis.<sup>2</sup> Tuberculous (TB) arthritis, less frequent, mainly affects large weight bearing joints, such as the hip and knee, being the elbow exceptionally affected.

We present a case of a 53-year-old Spanish man who was admitted to the emergency department with a 12 years history of pain and swelling of his right elbow which had worsened over the last six months. He denied previous injury and had no underlying disease. He had received corticosteroid infiltrations, last time two months before consulting. Physical examination revealed inflammation of the posterolateral region of the right elbow with associated distal paraesthesia, wrist drop and complete inability to extend the wrist and move the fingers.

On admission, he was afebrile and acute-phase reactants were slightly elevated. The chest X-ray was completely normal. The ultrasound image of the elbow showed discrete articular effusion and thickening of the articular capsule with hairy and nodular projections. Magnetic resonance imaging showed bone destruction with severe subchondral erosions. Under suspicion of pigmented villonodular synovitis, a biopsy was performed for anatomopathological study, which reported chronic synovitis with necrotizing granulomas and no hemosiderin or malignancy features. *Mycobacterium tuberculosis* (MTB) DNA was detected without mutations in the genes associated with resistance to first and second line antituberculous drugs (ANYPLEX<sup>TM</sup> II MTB Detection/MDR/XDR, Seegene). Ziehl–Neelsen stain of the biopsy was positive. Latent tuberculous infection was confirmed with both the tuberculin skin test and the IFN- $\gamma$  release assay (Quantiferon-TB Gold<sup>®</sup>). Treatment with isoniazid (INH), rifampicin (RIF), ethambutol (EMB) and pyrazinamide (PZA) was started for four months and reduced to INH and RIF for 14 months. After 10 days of treatment, the patient reported a transitory increase of the pain and swelling followed by drainage of semi-liquid caseous material, concordant with fistulization, through the puncture site of the elbow. By then, the liquid medium culture (BD MGIT 960) of the biopsy was positive (10 days). Growth on the solid medium (Löwestein–Jensen) was observed after 14 days of incubation. Isolated non-chromogenic mycobacteria were identified as *M. tuberculosis* by PCR and reverse hybridization (GenoType MTBC, HAIN Lifescience). Susceptibility to first line anti-TB drugs was confirmed by culture in Middlebrook (BD MGIT 960). Whole Genome Sequencing (WGS)

of the *M. tuberculosis* strain (Nextera XT protocol and Illumina MiSeq platform) showed no resistance-related mutations and was identified as Lineage 4.10/PGG3, one of the most recently described sublineages within the globally distributed Lineage 4.<sup>3</sup>

The patient progresses favorably a year after treatment completion, with decreased inflammation, resolution of the fistula and recovery of the elbow motility with complete flexion and extension of the right wrist.

OTB follows a progressive course of several months, developing fistulous paths from the cartilage to the skin surface when the infection is advanced. Fever or systemic symptoms are infrequent. Acute-phase reactants are often raised, but levels are lower than those seen in pyogenic vertebral infections.<sup>1</sup> Differential diagnosis includes other subacute or chronic infections such as those caused by *Brucella* spp., *Burkholderia pseudomalle* or *Candida* spp.,<sup>4</sup> together with local or adjacent tissue tumors. Imaging tests are nonspecific but can help to delimit the extent of soft-tissue and bone affection. Anatomopathological examination of the biopsy of the injury might reveal the presence of granulomas. Given the lack of specificity of the manifestations, clinical suspicion is difficult, and the diagnosis is often delayed with subsequent prolonged therapy needed in some cases.<sup>5</sup> After suspicion, MTB growth in conventional culture media takes at least one week in liquid broth and more than two weeks in solid medium.<sup>6</sup> Recently developed molecular techniques might accelerate the detection of MTB, with sensitivity in extrapulmonary samples over 75%.<sup>7</sup>

In summary, we describe a very rare case of TB arthritis in a Spanish patient with no documented previous history of tuberculosis. Since delay in both early diagnosis and adequate treatment of this condition is associated with high morbidity and risk of severe complications, TB must be considered as part of the differential diagnosis of osteoarticular illness in non-endemic regions.

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