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Scientific letter

Capnocytophaga canis as an uncommon cause of cat related infection

Capnocytophaga canis, *una causa poco común de infección causada por gatos*

Capnocytophaga canis is a capnophilic facultative anaerobic gram-negative bacillus. It belongs to the *Flavobacteriaceae* family and is part of the commensal oropharyngeal microbiota of dogs and cats mainly, together with *Capnocytophaga canimorsus* and *Capnocytophaga cynodegmi.*

We present the case of a 72-year-old male patient who presented symptoms of asthaenia and a loss of 10 kg in recent months without fever or other accompanying symptoms. For three months, he had also presented persistent vomiting together with alternating episodes of watery diarrhoea and normal stools. His medical history included type 2 diabetes mellitus, as well as stage IV follicle centre lymphoma in 2007 with a complete response after six cycles of R-CHOP and two years of maintenance treatment. This was followed by progression several years later by R-CHOP and R-Bendamustine, which were interrupted due to the onset of atrial *flutter*.

In the blood tests, mention should be made of CRP of 159.64 mg/l [0–5] with 5.15×10^3 µl leukocytes [4.5–11], with normal chest and abdominal X-rays. Twenty-four hours after admission, he presented a fever spike of 38.6 °C and blood and stool culture samples were taken. The anaerobic bottles were positive at 52 h and 107 h, with gram-negative spindle-shaped bacilli (Fig. 1A). Re-inoculations were carried out on MacConkey, Brucella, chocolate and TSA + 5% sheep blood agars (BD™) and incubated under microaerophilic (5% CO_2) anaerobiosis conditions. After 10 days no growth was observed. After 48 h, *Campylobacter jejuni* was detected in the BD MAX™ Ënteric Bacterial Panelšystem, which was subsequently grown on Campy BAP (BD™)agar and presented susceptibility to macrolides. The patient was treated with oral azithromycin (500 mg/24 h for three days). In addition, a full-body computed tomography was performed in which only inguinal and external iliac chain swollen lymph nodes of up to 16 mm were observed. in view of the symptoms and the result of the stool culture, this episode was considered gastroenteritis and transient bacteraemia due to *C. jejuni*, the patient was discharged and he completed a further three days of treatment with oral azithromycin.

A blood culture sample was extracted to sequence the 16S rRNA gene (Appendix B additional material), following the protocol proposed by Oldham and Duncan, and a 463 bp sequence was obtained, which was analysed by BLAST® (version 2.13.0, available at: https://blast.ncbi.nlm.nih.gov/Blast.cgi)[1]. *Capnocytophaga canis* was identified with an identification coincidence of 99.57% with strains previously isolated from infections, and 99% with the reference strain (highlighted in green in Fig. 1B).[2,3]. Since the patient had already been discharged, no other complementary examinations were performed.

One year later he was re-admitted for septic shock and empyema due to *Pasteurella multocida*, which causes infection after bites, scratches or contact with cat saliva. After the patient had been questionned again, he reported having taken in a stray cat two years earlier, which frequently bit and scratched him. The finding of *C. canis* from the previous year was then taken into consideration. The sequence obtained previously after 16S sequencing of the rRNA was registered in GenBank (accession number: SUB11305064 HUBCCS1) of the NIH/NCBI. A phylogenetic tree was constructed using BLAST® (NCBI *tree view*) with the *neighbour-joining* method, using alignments by pairs of sequences and based on partial sequences of the 16S gene of between 853 and 1440 bp or complete genome according to the strains (Fig. 1B).

C. canis grows with concentrations of 5%–10% CO_2 or in anaerobiosis. It presents fastidious and slow growth (from 48 h to six days) and does not grow on media such as McConkey agar. *C. canis*, *C. canimorsus* and *C. cynodegmi* are capable of causing infection in humans[4–6].

One of the virulence factors recently described in*C. canimorsus* is the capsular polysaccharide (CPS), which seems to protect it against

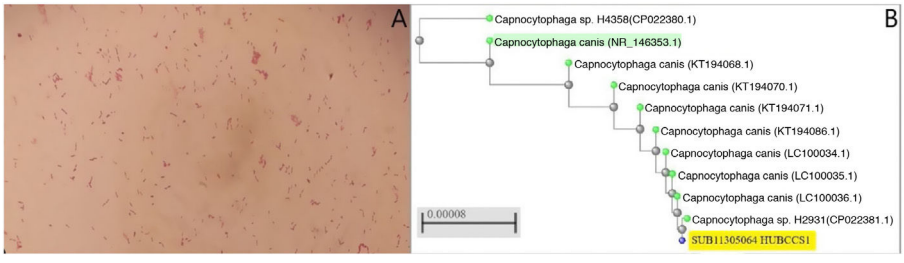

Fig. 1. A) Gram-negative rod-shaped bacteria are observed after three days of incubation in the two anaerobic blood culture bottles. B) Phylogenetic tree obtained following comparison of the sequences of several strains of *C. canis*with the sequence of the strain of the present case (accession number: SUB11305064 HUBCCS1) with the *neighbour-joining*method. Our strain had a 99.57% identification match to neighbouring strains (CP022381.1, LC100034.1, LC100035.1 or LC100036.1, pertaining to the articles by Oldham and Duncan[1] and Suzuki et al.[2]) and 99% with the reference strain (*C. canis* type strain LMG29146, highlighted in green in Fig. 1B) demonstrating the similarity between them.

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the bactericidal action of human serum and allows it to cause invasive disease[7]. Renzi et al. characterised several isolates from human clinical samples and healthy dogs, finding that some strains of *C. canis* and *C. cynodegmi* also presented CPS[8].

Suzuki et al. characterised three cases of *C. canis* in 2016 from septic patients, and a case of septic shock caused by this microorganism was also described in 2020[2,9–11]. In three of the cases the patients were heavy drinkers, and in addition one of them was asplenic, risk factors previously related to *C. canimorsus*[7] infections. This is the second time that our institution has reported a case of *C. canis*infection.

To conclude, *C. canis* has demonstrated its capability to cause infections in humans. An infection by this species must be ruled out, especially in immunosuppressed patients if there is contact with animals (bites, scratches or contact with their saliva) and antibiotic treatment should be initiated quickly to avoid fatal consequences.

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Author contributions

Domingo Fernández Vecilla: drafted the scientific text and reviewed the literature.

Estíbaliz Ugalde Zárraga: assisted with the molecular diagnosis (sequence in GenBank) and reviewed the case and the literature.

Mikel Joseba Urrutikoetxea Gutiérrez: reviewed the case, helped to modify it and reviewed the literature.

Felicitas Elena Calvo Muro: helped with the diagnosis, reviewed and suggested changes for the case.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eimce.2022.10.001.

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Influence on sputum microbiology with CFTR modulator (tezacaftor-ivacaftor) in adult patients with cystic fibrosis: Multicenter study

Influencia en la microbiología del esputo del modulador CFTR (tezacaftor-ivacaftor) en pacientes adultos con fibrosis quística: estudio multicéntrico

Symkevi®(tezacaftor-ivacaftor) is indicated in a combination regimen of 150 mg ivacaftor and 100 mg tezacaftor pills for the treatment of patients with cystic fibrosis (CF) 6 years of age or older who are homozygous for the F508del mutation or heterozygous for the F508del mutation with residual function.[1] Tezacaftor is a selective corrector of the altered or deficient CF protein, cystic fibrosis transmembrane conductance regulator (CFTR), which facilitates cellular processing and transport of CFTR to the cell surface. Ivacaftor is a CFTR protein enhancer that increases the opening of the CFTR channel at the cell surface. The combination works against the abnormal CFTR protein, increasing the amount and function of CFTR at the cell surface, resulting in an increase in airway surface fluid volume and ciliary beating frequency *in vitro* in human bronchial epithelial cells.[2] This drug is available in Spain from 1st October 2019.[3] The various clinical trials conducted with this drug demonstrate its clinical efficacy on lung function, reduction of chloride concentration in sweat, improvement of body mass index, quality of life, as well as a 35% reduction in the number of pulmonary exacerbations compared to the placebo group.[4,5] To date, there are no published data on the tezacaftor-ivacaftor effect on microbiological cultures.

The aim of this study is to assess, in real life, the effects on sputum microbiological cultures in adult CF patients from different units in Spain who received the combination tezacaftor-ivacaftor for 1 year.