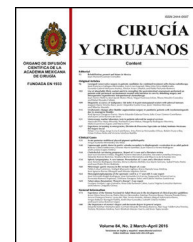




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CLINICAL CASE

Aorto-bifemoral graft infection due to *Candida parapsilosis*. An unusual pathogen[☆]



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KEYWORDS

Graft infection;
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Abstract

Background: Aorto-enteric fistula is a rare and potentially lethal entity. Its presentation may be as an enteric-paraprosthetic fistula, due to injury in the gut caused by direct contact with the vascular prosthesis.

Objective: We report a case of enteric-paraprosthetic fistulae with the unusual finding of *Candida parapsilosis* as the only isolated pathogen.

Clinical case: A 65-year-old male, smoker, with aortobifemoral revascularisation with dacron due to aortoiliac occlusive disease, and re-intervention for thrombosis of left arm at 6 months. Hospitalisation at 22 months was required due to a toxic syndrome, which was diagnosed as enteric-paraprosthetic fistulae after complementary studies. The graft was removed and an extra-anatomic revascularisation was performed. Microbiology specimens taken from the duodenal segment in contact with the prosthesis showed the prosthetic segment and peri-prosthetic fluid were positive to *C. parapsilosis*.

Discussion: The finding of *C. parapsilosis* in all cultures taken during surgery, along with negative blood cultures and no other known sources of infection, is of interest. It is an unusual pathogen with low virulence and limited as regards other *Candida* species. Our patient had no clinical data common to cases of infection with *C. parapsilosis*, and the mechanism of graft infection is unknown.

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PALABRAS CLAVE

Infección protésica;
Candida parapsilosis;
 Gastropatía;
 Fístula
 enteroprotésica

Conclusion: Graft infection by *C. parapsilosis* may be anecdotal. However, its consequences can also be severe. Microbiological tests can be useful to adjust antimicrobial therapy in the post-operative period, but their usefulness for determining the aetiology is doubtful, as it may be just an incidental finding.

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Infección de injerto aortobifemoral por *Candida parapsilosis*. Un germen inhabitual**Resumen**

Antecedentes: La fístula aortoentérica es una entidad rara y potencialmente letal; entre sus presentaciones se encuentra la fístula enteroparaprotésica, producto de una lesión en el intestino como consecuencia del contacto directo con la prótesis vascular.

Objetivo: Este reporte trata de un caso de fístula enteroparaprotésica, donde el único germen aislado fue *Candida parapsilosis*, un germen inhabitual.

Caso clínico: Hombre de 65 años de edad, fumador, con *bypass* aortobifemoral de dacron por enfermedad oclusiva aortoiliaca, que fue reintervenido por trombosis de la rama izquierda a los 6 meses. Fue hospitalizado a los 22 meses por síndrome tóxico que tras exploraciones complementarias fue diagnosticado como fístula enteroparaprotésica. Se le retiró la prótesis y posteriormente se le realizó revascularización extraanatómica. Las muestras microbiológicas extraídas del segmento duodenal, en contacto con la prótesis del segmento protésico y del frotis del líquido periprotésico, fueron positivas para *C. parapsilosis*.

Discusión: Es relevante la presencia de *C. parapsilosis* en los cultivos tomados durante la cirugía, con hemocultivos negativos y sin otros focos infecciosos conocidos. Este es un germen inhabitual, con baja virulencia, limitada con respecto a otras especies de *Cándida*. Nuestro paciente no presentó datos clínicos habituales en casos de infección por *C. parapsilosis* y se desconoce el mecanismo de infección de la prótesis.

Conclusión: La fístula enteroparaprotésica por *C. parapsilosis* puede resultar anecdótica; sin embargo, sus consecuencias pueden ser igual de graves. El estudio microbiológico resulta útil para ajustar una terapia antibiótica posterior a la cirugía. Queda en entredicho su utilidad para la determinación etiológica y puede incluso tratarse de un hallazgo incidental.

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Background

Aorto-enteric fistula is a rare and potentially lethal entity the presentation of which may be due to communication between the aorta, usually aneurysmal, and the enteric tract (primary fistula) or after reconstructive procedures with vascular prosthesis, aorto-renal bypass or endarterectomy (secondary fistula). The latter procedure may present in two ways: by anaestomotic communication between the aortic and intestinal lumen, known as the true enteric-prosthetic fistula and less commonly, due to aorto-enteric erosion, enteroparaprosthesis sinus infection or enteric-prosthetic fistula, where injury is a consequence of direct contact with the vascular graft.¹⁻³

The incidence rate of secondary aorto-enteric fistulae is low, between 0.4% and 1.6%,⁴ which is not insignificant considering the frequency of grafts implanted. The most common aetiological germ is *Staphylococcus spp.* which accounts for 40% of cases, gram-negative bacilli, which

together represent a similar percentage and polymicrobial infections which account for 10–15% of cases.⁵ Fungal infections are rare, and there is no known evidence for *Candida parapsilosis*.

The candida genre is considered as an emerging fungal infection for which many pathogenic mechanisms have been described, such as: the production of prostaglandins, and particularly D2 and E2, which modulate the response of helper lymphocytes, derive their response to Th2 and confer the candida with a resistance mechanism. The creation of biofilms has also been described and high inflammatory responses relating to interleukin 22 and tumour necrosis factor-alpha.^{6,7}

Hospital-acquired infection has been cited as the main mechanism of transmission, with fungemia as the major morbidity factor since in several regions of the world *C. parapsilosis* is considered the most commonly isolated germ in these cases, although in the United States and northern European countries *Candida albicans* and *Candida glabrata*

are the most common germs. Other morbidities have been reported including: endocarditis on the prosthetic valve, arthritis and onychomycosis.^{8,9}

Objective

To present a case of enteric-prosthetic fistula, from which the only isolated germ was *C. parapsilosis*, an unusual pathogen.

Clinical case

A male patient aged 65, a smoker of 68 packs per year and with no other history of note, was referred to our hospital due to critical ischaemia of lower extremities with ankle-arm rates of 0.31 right and 0.19 left. The following was deduced from the digital arteriogram: double bilateral renal artery, with aorta porosity, common right iliac and right hypogastric artery with occlusion of the right external iliac artery and the whole left iliac axis; occlusion of both common femoral arteries, superficial femoral arteries and profound femoral arteries where they begin, with porosity of distal branches of the profound femoral artery through the collateral arteries. The popliteal arteries and the distal trunks were bilaterally porous.

Aortobifemoral bypass was performed with a dacron (16×8 mm, Vaskutek Ltd. Scotland, United Kingdom) prosthesis with proximal side-to-end anastomosis in the aorta and end-to-side in both profound femoral arteries. Antibiotic prophylaxis protocols were correctly followed and were appropriate for this type of surgery. They therefore included: 2 g amoxicillin clavulanic acid+210 mg single dose gentamycin prior to procedure. The only postoperative event of note was paralytic ileus which was resolved with medical treatment. Postoperative angle-arm rates were 0.54 on both sides.

After 6 months the patient was operated on again for acute ischaemia of the left lower limb, occlusion of the left branch of the aorto-bifemoral graft. Thrombectomy and prolongation of left popliteal artery was performed. Antibiotic prophylaxis was again adhered to.

8 months after reintervention, an angiograph was performed due to the suspicion of stenosis of the right branch, detected in ultrasound controls, the severity of which was not confirmed and as a result a wait-and-see approach was adopted.

After 22 months the patient was admitted to hospital again for the study of a toxic syndrome with clinical data of 5–6 months evolution, and which consisted of: a 10 kg weight loss, anorexia, asthenia, sensation of postprandial fullness, odynophagia, dysphagia, nausea, vomiting, abdominal pain with change in intestinal habits and evacuations. No upper or lower digestive haemorrhaging or fever or feeling of dysthermia presented.

A physical examination revealed nothing abnormal, save for the presence of a non-throbbing tumour in the left inguinal region. Femoral pulses were present, with no clinical signs of distal ischaemia or trophic lesions.

The CAT angiograph showed: hypodense halo in the region next to the bypass, with the presence of air in intimate contact with the third duodenal segment and a dotted

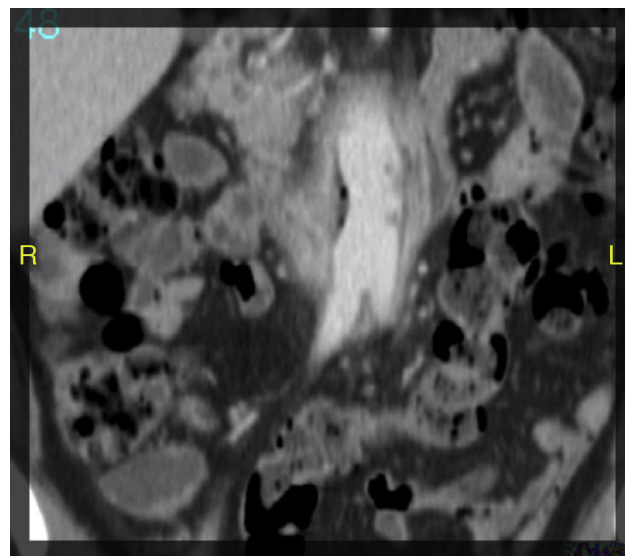


Figure 1 Computed axial tomography, axial slice. Showed hypodense ring in the segment proximal to the bypass, with the presence of air in intimate contact with the third duodenal segment and visualisation of a doubtful contiguous line with intestinal lumen.

line in the proximity of the intestinal lumen. We also observed hypodense protrusion towards the prosthesis lumen, as a continuation of the before-mentioned hypodense halo (Figs. 1 and 2). From a radiological viewpoint, findings were suggestive of graft infection.

An upper endoscopy showed contact with the Dacron prosthesis through the intestinal lumen at the first duodenal segment level (Figs. 3 and 4).

The gamma graph showed a circumscriptive infectious process at the periprosthetic region with extension from the beginning of the upper mesenteric artery to the iliac bifurcation, with no evidence of infection in other sites (fig. 5).

Laboratory tests highlighted: leukocytes 14,600/mm³, with 80% neutrophil; C reactive protein (6.2 mg/dl);



Figure 2 Computed axial tomography, coronal slice. Hypodense protrusions are observed towards the prosthesis lumen, in contiguity with the hypodense ring.

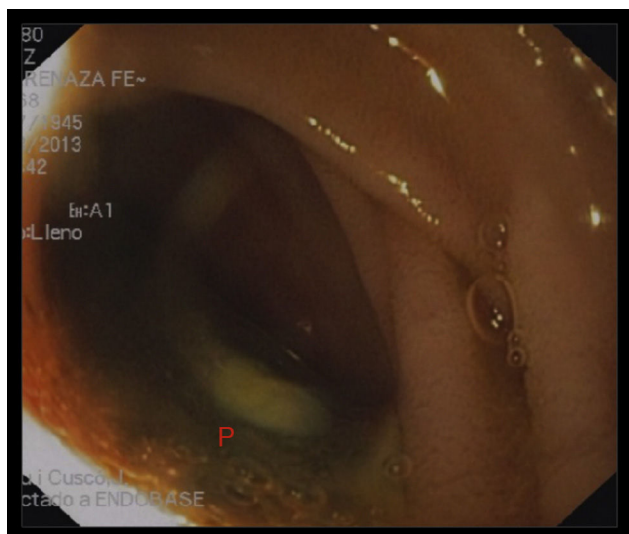


Figure 3 Upper digestive tract endoscopy. P: exposure of Dacron prosthesis through the duodenal lumen.

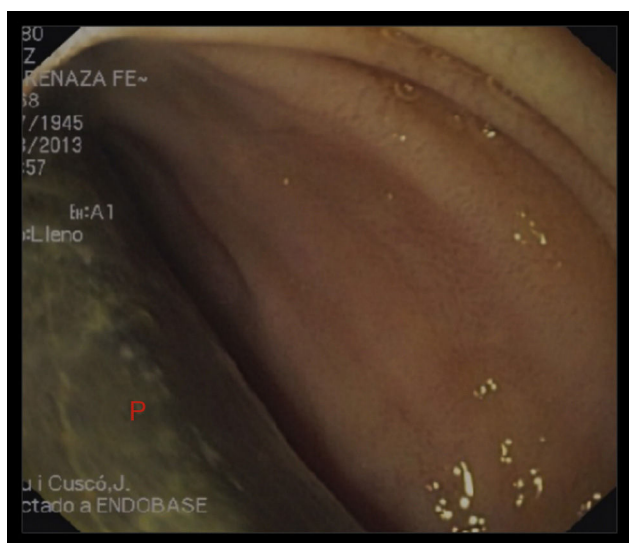


Figure 4 Upper digestive tract endoscopy. P: exposure of Dacron prosthesis through the duodenal lumen.

prothrombin of 62% (INR de 1.41). The other tests performed to locate an alternative focus of infection resulted negative.

Two-stage surgery was scheduled. First-stage surgery was an immediate axillofemoral bypass with expanded polytetrafluoroethylene and disconnection of both femoral branches from the previous bypass. One week later second-stage surgery was performed, which was put forward on observation of lower gastrointestinal bleeding with a laboratory test lowering of 2 g/dl of red blood cells. During surgery we observed that the Treitz angle was intimately attached to a peri-aortic flogotic mass. Once sectioned, we were able to see the absence of the posterior duodenal wall at third segment level, with the prosthesis externalising towards it. The aorto-bifemoral prosthesis was removed and suturing of the infrarenal aortic stump was performed with double rafia 0 prolene sutures. Duodenal excision was performed with

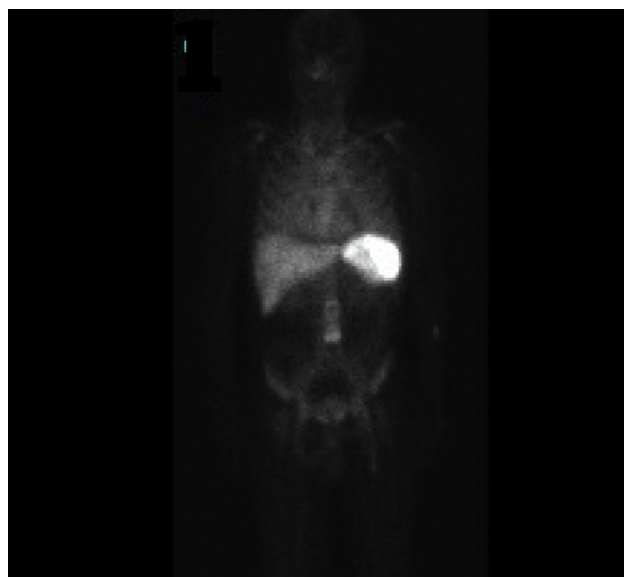


Figure 5 Gammagram marked with leukocytes suggestive of graft infection.

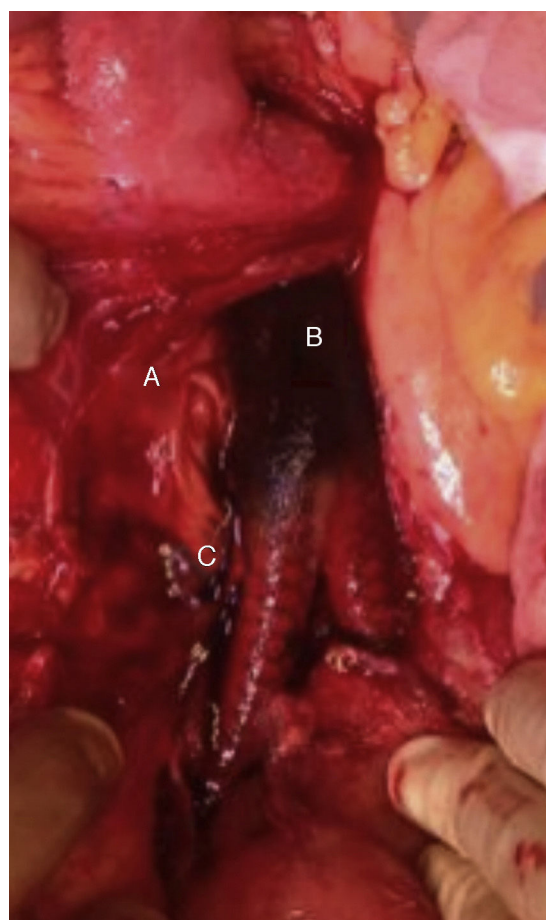


Figure 6 Surgical field, with prosthetic exposure. Letters A, B and C mark the sites where 3 samples were taken during surgery for cultures. These correspond to: (A) the duodenal segment in contact with the prosthesis, (B) the prosthetic segment and (C) the periprosthetic fluid smear.

transmesocolic side-to-side anastomosis at the anterior side of the second duodenal segment.

3 culture samples were taken during surgery which corresponded to the duodenal segment in contact with the prosthesis, the prosthetic segment and a smear of peri-prosthetic fluid, all of which tested positive for *C. parapsilosis* (Fig. 6).

The post-operative period was uneventful except for paralytic ileus, which was resolved with medical treatment. Postoperative treatment was initially with intravenous fluconazol which was continued orally on hospital discharge. After 2 years the patient is within normal limits physically, denies any symptoms and has not had any posterior examinations due to his refusal to go for checkups.

Discussion

Enteric-paraprosthetic fistulae have been reported on occasions as prosthetic erosion or aorto-enteric erosion. The most common location, as occurred in our case, is in the duodenum. In the case referred to the literature, the indication from Leriche's syndrome contrasted with that reported in other publications, which showed almost insignificant incidence when the technique is performed on occlusive arterial disease.^{4,10}

Clinical signs described for entero-paraprosthetic fistulae may vary from gastrointestinal haemorrhaging to non specific clinical symptoms characterised by weight loss, fever which may range from occasional fever to septic shock, abdominal pain or non specific symptoms.

Our patient was admitted to hospital on suspicion of a toxic syndrome and the finding was incidental during a radiological procedure. However, it should be noted that second-stage surgery was put forward on observation of a low gastrointestinal tract haemorrhage.⁴ The CT angiograph showed standard images such as periprosthetic gas, and direct contact of the intestine with inflammatory tissue and the prosthesis.

The following have been described among the risk factors for *C. parapsilosis*: the use of antibiotics such as vancomycin and doripenem and possible connection of a history of alcohol dependence. There was no history of usage of these antimicrobial agents in the case we present nor recent hospital admittances, nor any significant alcohol dependence or consumption.¹¹

Many approaches to the treatment of this entity have been described, from a conservative non surgical approach to the local repair with removal of the graft and in situ replacement, or as in our case, associated with extra anatomical revascularisation. Outcome is varied, depending on the literature consulted.^{2,12}

With regard to antibiotic treatment, the susceptibility of the germ enables its treatment with: amphotericin B, fluconazol, itraconazol, voriconazol and caspofungin. However, resistance to fluconazol has mainly been described related to the post exposure mutation of genes to ERG11, CDR1 and less commonly MDR1 which code drug efflux pumps. Our first line antifungal treatment was fluconazol, with no evidence of germ persistence after treatment.^{13,14}

Notwithstanding, our most relevant finding was the presence of *C. parapsilosis* in all cultures taken during surgery,

with negative blood cultures and no other known foci of infection. Mechanisms of infection have classically been described as direct contamination of the prosthesis when implanted, in which case presentation period is usually the year after implantation, but not in our case. Another possibility is deferred infection via haematogene, but our patients did not present other possible foci of infection. All of the above calls into question the microbiological findings in these cases.

In addition, standard culture techniques and typification using viability in CHROMagar and Sabouraud mediums described typification techniques through genomic analysis. In our case we used Sabouraud agar, since no genomic kits were available in our centre. Even so, in our case, the *C. parapsilosis* findings were only considered to adjust the antifungal therapy. It is unknown whether etiopathogenic mechanisms of the germ, such as haemolytic activity, phospholipase, esterase and phytase played a definitive role in the evolution of our patient, since they were not analysed.¹³

It is known that the low virulence of *C. parapsilosis*, limited with respect to other candida species is mainly related to endocarditis in cases of parenteral drug use, pre-existing valvular diseases, previous heart surgeries, and is more lethal in diabetic patients.^{15,16} None of these conditions was present in our patient. Our study included the performing of a transthoracic and transoesophageal echocardiogram which ruled out the presence of endocarditis. Other diseases related to *C. parapsilosis* are endophthalmitis, arthritis and peritonitis, usually related to previous invasive procedures.

Conclusions

Entero-prosthetic fistulae is particularly complex to diagnose and associated with raised morbidity and mortality. Graft infection by *C. parapsilosis* may be anecdotal but its consequences may also be severe. Microbiological tests can be useful to adjust antimicrobial therapy in the post-operative period, but their usefulness for determining aetiology is doubtful, as it may be just an incidental finding.

Diagnosis of entero-prosthetic fistulae should be considered in patients with a history of aortic graft with clinical signs of febrile syndrome, with or without associated gastrointestinal haemorrhaging. Upper digestive endoscopy used as first line initiative in the case of upper gastrointestinal tract haemorrhage may show direct visualisation of part of the prosthetic wall in the intestinal lumen, although this procedure may concur risks.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflict of interests

The authors have no conflict of interests to declare.

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