**Vibrio vulnificus** peritonitis after eating raw sea fish in a patient undergoing continuous ambulatory peritoneal dialysis (CAPD)

Sir,

*Vibrio vulnificus* is an opportunistic pathogen that can cause serious, life-threatening infection in susceptible persons. Patients with chronic liver disease, alcoholism, immunodeficiencies, haemochromatosis or other iron overload states have increased susceptibility to infection by *Vibrio species* [1]. End-stage renal disease (ESRD) has been identified as a possible risk factor [2]. Only one case of *V. vulnificus* peritonitis developed after handling (but not ingestion) of sea fish, in a patient receiving continuous ambulatory peritoneal dialysis (CAPD) has been previously reported [3]. Here, we describe an episode of peritonitis in a CAPD patient caused by *V. vulnificus* after eating raw sea fish.

A 63-year-old man receiving CAPD for 5 years was admitted to our hospital with abdominal pain and cloudy peritoneal fluid. The underlying cause of his ESRD was diabetes mellitus and he had no history of peritonitis. He was a non-drinker and had no known history of liver disease. He was treated with erythropoietin, but had no iron therapy. Three days prior to presentation, he ate raw butterfish harvested from the Pacific coast; abdominal pain and vomiting started the next day. There was no history of trauma or exposure to seawater. On admission, the body temperature was 36.4°C, heart rate was 80 bpm, respiration rate was 20/min and blood pressure was 130/80 mmHg. There was tenderness in the lower abdomen, and the exit site of the peritoneal catheter was clean. The peripheral WBC count was 8130/mm³, of which 91% were PMNs (PMN) was 92.8%. The haemoglobin level was 6.2 g/dl, serum iron measurement showed the following values: iron 19 µg/dl, transferrin saturation 6.9%, ferritin 235.54 µg/l. The liver function test results were normal and viral markers for hepatitis B and C were negative. The peritoneal effluent contained >1000 WBCs/mm³, of which 91% were PMNs and 9% were lymphocytes. The patient was treated empirically with intraperitoneal cefazolin 1000 mg and tobramycin 40 mg. Soon after the start of empirical antibiotic therapy, the abdominal pain improved and the peritoneal fluid gradually cleared. Peritoneal effluent culture showed *V. vulnificus* sensitive to ampicillin, ceftriaxone, ciprofloxacin, piperacillin and imipenem, intermediate sensitivity to gentamicin, tobramycin and resistant to amikacin. Blood and stool culture showed no bacterial growth. After receiving the culture result, intraperitoneal cefazolin was discontinued, and oral doxycyclin was added to intraperitoneal tobramycin regimen. Antibiotic therapy was continued for 2 weeks; the patient recovered completely without complication.

*V. vulnificus* infection has been linked to three distinct syndromes: (i) primary sepsicaemia, (ii) wound infection and (iii) gastrointestinal illness [1]. Peritonitis in a patient receiving CAPD was previously reported and suggested that CAPD peritonitis may be another important clinical manifestation of *Vibrio* infection in patients undergoing CAPD [3–5].

In conclusion, patients with ESRD undergoing dialysis have an increased risk of infection with *V. vulnificus*. Furthermore patients receiving CAPD may present with CAPD peritonitis in addition to the previous clinical manifestations. These patients should be counselled to avoid raw seafood.

**Conflict of interest statement.** None declared.


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**Caspofungin in kidney transplant recipients with refractory invasive candidiasis**

Sir,

Fungal infections have been reported frequently in renal transplant recipients [1–3], and they were associated with greatly decreased patient survival [1,3,4].

The treatment of mucosal candidiasis and candidaemia has evolved in previous years: because of its infusion-related toxicity and nephrotoxicity, amphotericin B has been gradually replaced by flucanazole, which has less toxicity and a broader spectrum of activity [5]. However, invasive candidiasis such as oropharyngeal, oesophageal and urogenital candidiasis, are relatively less susceptible to flucanazole [5].

Caspofungin is the first of three new echinocandin antifungal agents to become available for the treatment of invasive mycoses and systemic candidiasis in patients refractory to or intolerant to other antifungal therapy [5,6], and it is more effective than amphotericin B in the treatment of refractory oropharyngeal and oesophageal candidiasis [7].

This study investigates the incidence of invasive candidiasis in a population of 245 kidney transplant recipients, performed in a 3-year period, and evaluates the use of caspofungin for the treatment of azole-refractory oesophageal and urinary candidiasis.

Twenty-two patients (8.9%) presented with an oesophageal candidiasis, while seven (2.8%) presented with a
urogenital candidiasis (two with pyelonephritis, five with bladder infection) (Table 1).

All patients with clinical signs of oesophageal candidiasis underwent an esophagogastroduodenoscopy with biopsy of the lesion. Only histologically proven oesophageal candidiasis were considered in this study. All patients with genital candidiasis underwent a topical treatment with econazole 150 mg for 3 days. None of the patients with urogenital candidiasis had urinary catheter at time of infection.

Fungal infections were more common in tacrolimus-treated patients and in those who experienced an acute rejection or a CMV infection, and the majority of fungal infection developed within 3 months post-transplantation. This could be easily related to the higher level of immunosuppression that could be expected in these patients. Moreover, patients with diabetes as cause of end-stage renal disease and recipients with post-transplant diabetes mellitus are at high risk of fungal infections (Table 2).

Fluconazole was used as a first-line therapy in all patients with a proven fungal infection at a dose of 100–200 mg/day i.v. based on renal functionality; caspofungin was administered i.v. once daily with a loading dose of 70 mg, followed by 50 mg/day.

A refractory fungal infection was defined as an infection which did not improve with a 7–10 day fluconazole therapy with a total received dose of 1–2 g.

Thirteen patients with oro-pharyngeal and oesophageal candidiasis (59%) and four patients (57%) with a urogenital candidiasis did not improve after a treatment with azole. A treatment with caspofungin was started in all patients. A complete relief of symptoms was observed in all patients, after a median time of 12 days (range 3–19 days) of treatment.

The interaction of caspofungin with the immunosuppressive regimen was low, and only three patients in the tacrolimus group required an increase in immunosuppression dosage.

All patients tolerated well the administration of caspofungin; one patient showed a mild cephalgia, while two patients, with a pre-existent hepatitis B and C, showed a mild increase in bilirubin and aminotransferase levels.

One patient with an oesophageal candidiasis recurred and was switched to amphotericin B therapy, and lost his graft because of discontinuation of immunosuppression.

There were no other recurrence of candidiasis in the group of patients treated with caspofungin at a median follow-up of 14 months (range 3–32 months).

The incidence of oesophageal candidiasis in renal transplant recipients is not well documented. Gupta et al. [3] reported a 10.5% incidence among 265 kidney transplant recipients, with 25% of unsuccessful treatment and 10.7% of mortality due to disseminated candidiasis; Abbott et al. [2] in their large series of hospitalizations of kidney transplant recipients for fungal infection, found 21.5% of patients with oesophageal candidiasis and 10.1% of patients with a urogenital candidiasis. Factors significantly associated with hospitalizations for fungal infection were recipient and donor age, cadaveric donation, older recipient age, diabetes as cause of end-stage renal disease, donor CMV seropositivity, per-transplant dialysis, rejection, maintenance tacrolimus and antibody induction therapy [2].

Despite an improvement of antifungal prophylaxis, renal transplant patients remain at high risk for invasive fungal infections, and the correct treatment is often challenging. Our study showed that resistance to azole is now becoming common, and newer antifungals, which have a broader spectrum of activity that includes fluconazole-resistant Candida spp. should be considered for the treatment of refractory oropharyngeal candidiasis.

Although the number of patients was limited, the results of this study indicate that caspofungin is an effective, well-tolerated alternative for difficult-to-treat and azole-refractory candida infections in kidney transplant recipients. The high costs of the drug limit the use of caspofungin as first-line antifungal therapy, restricting its use to those recipients who underwent an unsuccessful therapy with azole.

Conflict of interest statement. None declared.
Gastrointestinal stromal tumours (GIST) in kidney transplant recipients—a report of two cases

Sir,

Gastrointestinal stromal tumours (GIST) represent the most common primary mesenchymal GI neoplasms. GISTs occur in the stomach (60%), small intestine (30%), duodenum (5%), colorectum (<5%) and oesophagus (<1%) [1]. The majority harbour activating mutation in KIT or PDGERFA [1]. No risk factors or predisposing conditions have been identified for GIST. About 10% of GIST occurs in patients with other solid malignancies [2] and rare cases have involved immunocompromised patients [3]. Epstein Barr-virus (EBV) and Kaposi sarcoma-associated Herpes virus (HHV8) were not detected in GISTs [4,5]. GISTs have not been described in renal transplant recipients.

We encountered two female patients aged 59 and 58 years, who presented with non-specific abdominal pain, 40 and 96 months after renal transplantation because of terminal diabetic nephropathy and unspecified glomerulonephritis, respectively. One patient had a low-risk epithelioid gastric GIST (3.5 cm; <5 mitoses/50 HPFs) (Figure 1A–C) and the other had a huge ruptured high-risk spindle GIST of small bowel (23 cm; 14 mitoses/50 HPFs) (Figure 1D–F). The first patient remained disease-free 68 months post-operatively. The second was a recent case. Both tumours stained strongly for c-kit/CD117 (1:50, Dako) and variably for CD34 (1:200, Zymed), but were negative for smooth muscle actin, desmin, S100 and HHV8 (1:25, Novocastra). In situ hybridisation for EBV-encoded nuclear mRNAs (EBER-1 & EBER-2, Zymed), performed in case 2, was negative.

The incidence and types of immune suppression-associated neoplasia in renal transplant recipients varies with extent of follow-up [6]. Kaposi sarcoma, skin cancer and lymphoproliferative disorders are most common and viral agents (HHV8, HPV and EBV, respectively) are detectable in most of these lesions [6,7]. Kaposi sarcoma and smooth muscle neoplasms are the main GIST mimics in transplant recipients [6,7]. Kaposi sarcoma shows a consistent nuclear staining for HHV8, combined with a cytoplasmic staining for endothelial markers (CD31 and factor VIII), but not for c-kit/CD117. Immune suppression-associated smooth muscle neoplasms consistently harbour EBV-infection and they show smooth muscle features, but they have not been evaluated for c-kit/CD117 expression [7].

Imatinib mesylate represents the only therapeutic option for patients with unresectable and metastatic GIST [1]. The use of this drug in organ transplant recipients and the potential interactions with immunosuppressive agents may represent a new challenge for nephrologists and oncologists. Interestingly, it has been demonstrated, in animal experiments, that imatinib prevents chronic allograft nephropathy through inhibition of the platelet-derived growth factor (PDGF) receptor [8].

In summary, we report for the first time the occurrence of GISTs in renal transplant recipients, showing that both spindle and epithelioid GISTs may rarely involve this group of patients. Absence of HHV8 and EBV in the current cases suggests a pathogenesis similar to sporadic GIST. GISTs should be considered in the differential diagnosis of mesenchymal neoplasia involving organ transplant recipients, to enhance their recognition in this unusual clinical setting.

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