has been reported that 10% of children are oropharyngeal carriers of this bacteria.[2] In these carrier children, invasion of the respiratory mucosa and access to the skeletal tissue via the circulatory system would appear to be facilitated by the destruction of the epithelial barrier caused by viral infections.[3] El Houmami et al.[4] studied nine outbreaks caused by *K. kingae* in 27 children, 24 of whom suffered osteoarticular infections, with associated viral infections causing mouth ulcers being identified in the majority of patients.

The taking of blood cultures for the diagnosis of bacteraemia without focus in these patients with damage to the oral mucosa would enable us to pre-empt the severe pathologies that result from this microorganism's tropism for osteoarticular and endocardial tissue. In fact, bacteraemia without focus is the second most common presentation of *K. kingae* in paediatric patients.[5] However, suspicion of this pathology on the part of clinicians is complex, as the clinical picture is often mild.[6] Dubnov-Raz et al.[7] studied a total of 322 infections with 140 cases of occult bacteraemia (43.6%) in children under 36 months. The patients studied did not have fever, leukocytosis or elevated acute phase reactants.

The relevance that this microorganism has taken on may be related to a reduction in skeletal infections caused by *Haemophilus influenzae* due to generalised vaccination,[8] improved culture techniques such as inoculation of blood culture vials with samples of synovial fluid,[9] and the development of several commercial methods to identify this microorganism, such as the Vitek2 NH card and mass spectrometry.[6] Moreover, the use of nucleic acid amplification techniques on direct samples of synovial fluid has been a big advance.[10] Nonetheless, these techniques are expensive, often laborious and are not available in all laboratories, and there is very little data on their use on positive blood cultures.

The *Clinical and Laboratory Standards Institute* (CLSI)[11] includes *K. kingae* in the HACEK group and recommends the same cut-off points for sensitivity to antimicrobial agents for difficult-to-grow microorganisms, including *K. kingae*. In 2020, the *European Committee on Antimicrobial Susceptibility Testing* (EUCAST) established specific cut-off points for *K. kingae*,[12] so in the case in question the strain was resistant to penicillin, since it presented an MIC of 0.064 μg/mL.

Our study is focused on the convenience of protocolising the taking of blood cultures in paediatric patients with oral involvement in order to rule out occult bacteraemia due to *K. kingae*, in view of the colonisation rate in children under 2 years of age and the benign clinical picture of this type of infection. The current diagnostic tool in positive blood cultures is still primarily identification of growth in conventional culture. For this, the microbiologist needs to be particularly aware of this type of microorganism to avoid deeming it a contaminant and thus to provide information for decision-making that will avoid complicated infections such as endocarditis and septic arthritis. EUCAST and CLSI differ on their cut-off points for sensitivity to penicillin for this microorganism. Given the relevance that *K. kingae* has acquired as an invasive pathogen in recent years, we consider the use of the European criterion to be justified as it is tailored to this species.

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Voriconazole and tamsulosin: A clinically relevant drug–drug interaction☆

Voriconazol y tamsulosina: interacción farmacológica clínicamente relevante

Drug–drug interactions occur when one drug's activity is modified by the action of another, either increasing or reducing its effect. Certain interactions can lead to therapeutic failure or cause toxicity, so it is necessary to identify them early to optimise treatment, thus guaranteeing its efficacy and safety.[1]

We present a clinical case in which a patient simultaneously received voriconazole and tamsulosin, an α-1A adrenoreceptor antagonist, with a clinically relevant drug-drug interaction being observed.

A 66-year-old male smoker and active drinker was admitted for constitutional syndrome, feelings of dysthermia and productive cough lasting two months. His medical history included hypertension, dyslipidaemia, Leriche syndrome, hyperuricaemia and residual pulmonary lesions due to having suffered from pulmonary

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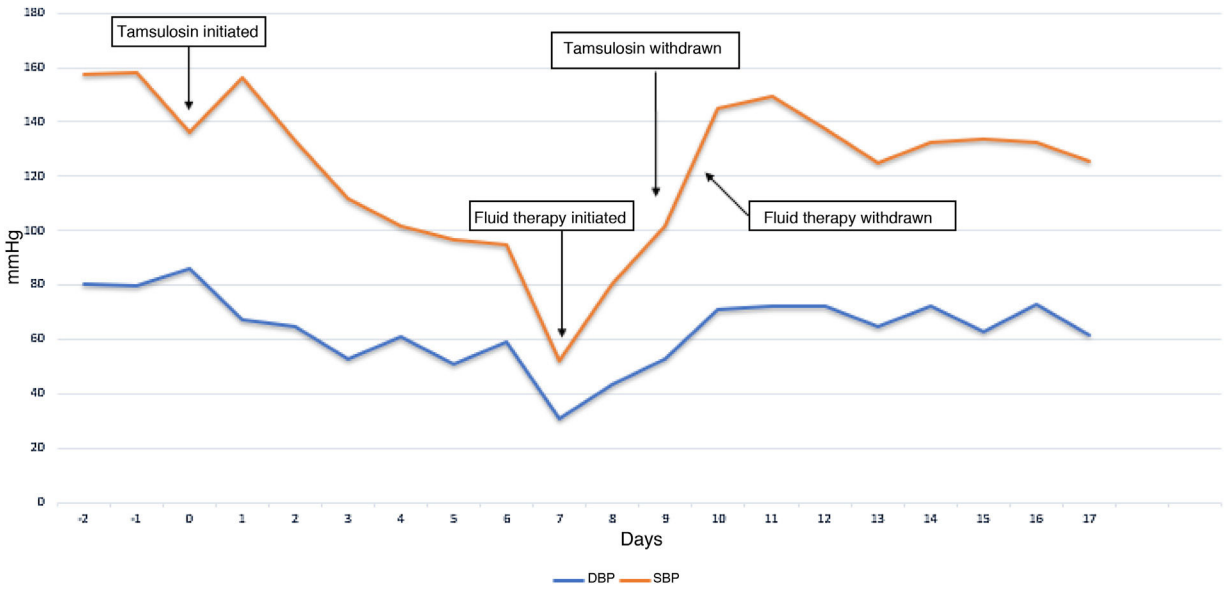

Figure 1. Evolution of the patient's mean systolic blood pressure and diastolic blood pressure over time and changes to the pharmacotherapeutic plan.

tuberculosis at 17 and 25 years of age. In the initial physical examination, the patient was found to be cachexic and febrile, and on pulmonary ausculation presented hypophonesis in the left upper lobe.

The chest X-ray and chest CT revealed multiple pulmonary bullae with invasion of the same and lung opacities predominantly on the left. Multiple sputum cultures were taken and found to be positive for *Aspergillus fumigatus*. Precipitins for *A. fumigatus* were also positive. In view of the clinical picture, together with the radiological and microbiological findings, it was treated as chronic cavitary bronchopulmonary aspergillosis, and treatment was initiated with voriconazole and nebulised amphotericin B. At two weeks from admission, the patient presented an episode of acute urinary retention, for which he required a urinary catheter and was started on tamsulosin, a drug that had never before been prescribed in this patient, to facilitate its management. Seven days after starting tamsulosin, he had an episode of sudden and symptomatic drop in blood pressure (BP), with systolic blood pressure values reaching 52 mmHg and diastolic values of 31 mmHg, with no evidence of hypovolaemia (no bleeding or dehydration) or alterations that would suggest cardiogenic or septic shock (with a review of the negative blood cultures). He was administered 500 ml of physiological serum, which increased his systolic blood pressure to 80 mmHg and diastolic blood pressure to 43 mmHg. He subsequently started fluid therapy with gradual improvement in BP (Fig. 1).

During the daily review of his treatment, after noting that there had been no recent changes in the antihypertensive treatment (he was on chronic treatment with 5 mg amlodipine), the possibility of a drug-drug interaction between voriconazole and tamsulosin was discerned. Simultaneous administration of the two drugs can trigger an increase in plasma concentrations of tamsulosin due to inhibition of its metabolism, accompanied by an increase in its pharmacological effect. In the case described, the pharmacological interaction manifested as a potentiation of tamsulosin's hipotensive effect. Consequently, the risk-benefit ratio of keeping tamsulosin in the pharmacotherapeutic plan was reviewed and it was ultimately decided to withdraw the drug. Over the following days, the patient's BP gradually increased and the supportive measures initiated could be withdrawn while maintaining control of BP within normal limits.

Tamsulosin is a substrate of cytochrome-P450 isoenzymes 2D6 (CYP2D6) and 3A4 (CYP3A4).[2] Voriconazole is metabolised primarily by the isoenzymes CYP2C19 and, to a lesser extent, CYP3A4 and CYP2C9. It also has the potential to be an inhibitor of these three isoenzymes, and is considered a potent CYP3A4 inhibitor.[3,4] It has been demonstrated that combined administration of tamsulosin with potent CYP2D6 inhibitors has only a limited effect on tamsulosin exposure, while with potent CYP3A4 inhibitors the effect is doubled.[3,5,6] In this case, co-administration of tamsulosin and voriconazole was associated with haemodynamic changes (hypotension), deriving from a possible increase in the plasma concentration of tamsulosin. It should be noted that there are no published cases of this interaction in the literature. Nevertheless, without pharmacokinetic studies, the possibility that this was a "first dose phenomenon" associated with starting treatment with tamsulosin cannot be ruled out,[7] even though in this case the clinical effect was observed seven days from initiation.

Taking into account the potential for drug-drug interaction between tamsulosin (substrate) and voriconazole (inhibitor) and the clinical relevance of a possible increase in the hypotensive activity of tamsulosin, the risk-benefit ration of administering the two drugs simultaneously would need to be adequately assessed, considering alternatives wherever possible.

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Catheter-related fungemia caused by *Geotrichum capitatum* in an immunocompetent pediatric patient☆

Fungemia relacionada con catéter por Geotrichum capitatum *en una paciente pediátrica inmunocompetente*

Invasive fungal infections (IFIs) are primarily caused by *Candida* spp. and *Aspergillus* spp. However, there are some emerging fungi such as *Geotrichum capitatum* (now *Saprochaete capitata*) that are characterised by causing IFIs in immunosuppressed patients, primarily those with prolonged neutropenia and oncohaematological disease.[1] Other risk factors, as in other fungal infections, are the presence of a central venous catheter (CVC), receiving parenteral nutrition, use of broad spectrum antibiotics, corticosteroid therapy, chemotherapy and disruption of the skin/mucosal barrier, with nosocomial outbreaks having been described and higher incidence in certain geographic areas such as Italy, France, Turkey and Spain.

There are published cases of IFI caused by *Geotrichum* spp. in oncohaematological paediatric patients,[2–4] but there are few described cases of infection of immunocompetent patients,[5] and none in the paediatric age group.

We present a case of catheter-related fungaemia due to *Geotrichum capitum* in a 4-month-old female infant, who presented a clinical picture compatible with bowel obstruction, and so underwent emergency surgery. In the postoperative period, she was admitted to ICU, a CVC was placed and treatment continued with ceftriaxone and metronidazole. She required parenteral nutrition for 13 days. On the 7th postoperative day, she presented fever, with *Enterococcus faecalis* being isolated in the surgical wound, so the antibiotic treatment was switched to piperacillin-tazobactam. The patient was operated on again for an omental hernia and presented irritability and fever at 48 h. Analytical and new microbiological samples (blood and peritoneal fluid cultures) were taken and linezolid added to her treatment. With the fever persisting, it was decided to withdraw the CVC and it was sent for culture.

A levaduriform fungus was isolated in the culture from the tip of the catheter and in the blood cultures, so empirical treatment with fluconazole was initiated, then replaced with liposomal amphotericin B when the isolation of *Geotrichum capitum* was confirmed (Fig. 1 A, B). The extension study was negative, as was the galactomannan detection. The patient responded favourably with no microbiological isolation in follow-up blood cultures, and treatment was completed in 14 days. A cellular immunodeficiency study was carried out, with normal results, and the absence of neutropenia was confirmed. As a complication, after one week of treatment with amphotericin B, she presented hypokalaemia.

Geotrichum capitatum is an emerging fungus with a mortality rate over 70% in immunosuppressed patients. In this group of patients, the clinical presentation is similar to that of candidaemia, but with a higher frequency of disseminated disease.

An awareness of the fungus's pathogenicity and the host's immune response are essential tools for the management of these infections. Our patient had several predisposing factors, such as use of parenteral nutrition, broad spectrum antibiotics, a history of surgery and being fitted with a CVC. Because this fungus forms a part of the normal microbiota of the skin, digestive tract and respiratory tract, disruption of the mucosal or skin barrier could be considered a route of entry, with colonisation of the CVC and subsequent fungaemia. In spite of the high virulence and poor prognosis described, the good progress of our patient could be explained by her immunocompetent status, as well as the prompt removal of the CVC.

Diagnosis is generally performed through isolation in blood cultures. Fungi in the genus *Geotrichum* grow on Saboureaud agar with white colonies with a creamy appearance that can be confused with the genus *Candida*, but unlike the latter, on microscopic examination of the Gram stain, blastoconidia are observed to emerge from the arthroconidia in a ḧockey stickẗshape. The optimal growth temperature is 30°C. In general, *Geotrichum* spp. is a very asaccharolytic fungus, and *Geotrichum capitatum* in particular only ferments glucose and galactose, lacking even the ability to hydrolyse urea. Cases of cross-reactivity have been described in testing for the galactomannan antigen of *Aspergillus* spp.,[4] something that did not occur with our patient.

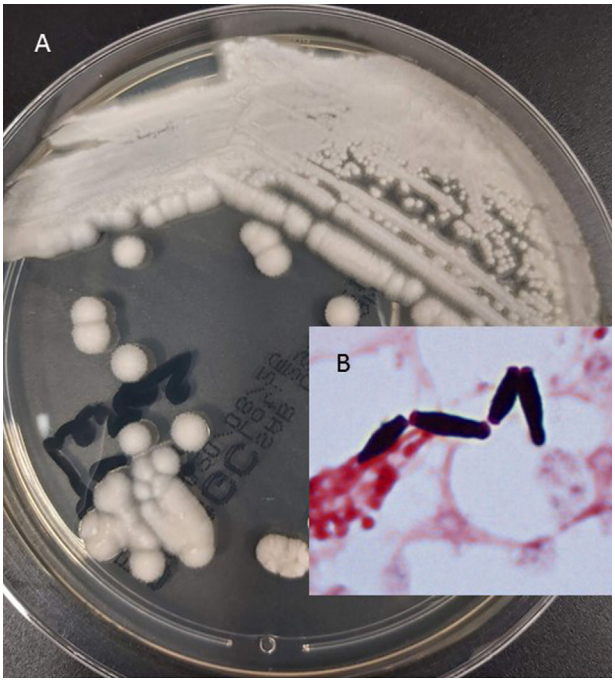

Fig. 1. A. Macroscopic morphology of colonies of *Geotrichum capitatum* after 48 h of incubation on Sabouraud agar. B. Arthroconidia in Gram stain from a blood culture vial (1000×).

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