



Note

Disseminated aspergillosis in an immunocompetent patient with detectable bis(methylthio)gliotoxin and negative galactomannan



Matxalen Vidal-García^{a,*}, Pilar Sánchez-Chueca^b, María Pilar Domingo^c, Carlos Ballester^d, Lourdes Roc^e, Isabel Ferrer^e, María José Revillo^e, Julián Pardo^f, Eva María Gálvez^c, Antonio Rezusta^{a,e}

^a Universidad de Zaragoza, Microbiology, Preventive Medicine and Public Health, Zaragoza, Spain

^b Unidad de Cuidados Intensivos – Hospital Universitario Miguel Servet, Universidad de Zaragoza, Zaragoza, Spain

^c Instituto de Carboquímica ICB-CSIC, Zaragoza, Spain

^d Servicio de Cirugía Cardiovascular – Hospital Universitario Miguel Servet, Zaragoza, Spain

^e Servicio de Microbiología – Hospital Universitario Miguel Servet, Zaragoza, Spain

^f Fundación Instituto de Investigación Sanitaria Aragón, Centro de Investigación Biomédica de Aragón, Fundación ARAID, Universidad de Zaragoza, Spain

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ABSTRACT

Background: Disseminated invasive aspergillosis is an exceptional finding in immunocompetent hosts. As in immunocompromised patients, it has high mortality rates. Early diagnostic methods are required in order to properly manage the patient. Bis(methylthio)gliotoxin (bmGT) is a novel biomarker, useful in onco-hematological patients.

Case report: A 70-year-old male, with non-insulin dependent type II diabetes mellitus and a past surgery history of aortic valve replacement with coronary by-pass five years ago, was seen in the emergency department with blurred vision. Three days later, endogen endophthalmitis was diagnosed in the ophthalmology clinic. During admission for the vitrectomy, he suffered an ischemia of the right lower limb. A thoracic computed tomography revealed a mycotic aneurysm of the ascending thoracic aorta and parietal thrombus. The ascending aorta was replaced and abundant brittle material of infectious appearance, found between the aortic valve graft and the aneurysm, was removed. *Aspergillus fumigatus* sensu stricto grew in both vitreous and aorta cultures. BmGT was detected in two serum samples obtained prior to intravenous antifungal treatment, which was then reduced after voriconazole treatment was started.

Conclusions: Disseminated invasive aspergillosis is a severe disease regardless of the immune status of the patient. This case report suggests that bmGT could be a suitable early diagnostic biomarker, not only in neutropenic patients, but also in immunocompetent hosts.

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Aspergilosis diseminada en un paciente inmunocompetente con bis(metilthio)gliotoxina detectable y galactomanano negativo

RESUMEN

Antecedentes: La aspergilosis diseminada invasiva es un hallazgo excepcional en pacientes inmunocompetentes, y al igual que en los pacientes inmunodeficientes, alcanza valores de mortalidad elevados. Para el correcto manejo del paciente son necesarios métodos diagnósticos precoces. La bis(metilthio)gliotoxina es un nuevo biomarcador de gran utilidad en pacientes oncohematológicos.

Caso clínico: Varón de 70 años de edad con diabetes mellitus tipo II no dependiente de insulina y antecedente de recambio valvular aórtico con by-pass coronario cinco años antes, que acude al Servicio de Urgencias por visión borrosa. Tres días después se le diagnosticó endoftalmitis endógena en la

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* Corresponding author.

E-mail address: mvidalg@unizar.es (M. Vidal-García).

consulta de Oftalmología. Durante su ingreso para la vitrectomía presentó una isquemia del miembro inferior derecho. La tomografía computarizada de tórax reveló un aneurisma micótico en la aorta torácica ascendente y un trombo parietal. Se reemplazó la aorta ascendente y se eliminó abundante material friable de aspecto infeccioso entre la prótesis valvular aórtica y el aneurisma. En los cultivos de humor vítreo y aorta creció *Aspergillus fumigatus* sensu stricto. Se detectó bis(metilthio)gliotoxina en dos muestras de suero obtenidas antes del tratamiento antifúngico intravenoso, marcador que disminuyó tras comenzar el tratamiento con voriconazol.

Conclusiones: La aspergilosis diseminada invasiva es una enfermedad grave independientemente del estado inmune del paciente. Este caso clínico evidencia que la bis(metilthio)gliotoxina podría ser un marcador diagnóstico precoz no solo en pacientes neutropénicos, sino también en huéspedes inmunocompetentes.

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Invasive aspergillosis (IA) is the most frequent filamentous fungal disease in immunocompromised patients. Immunosuppressed hosts get infected by conidial inhalation, and pulmonary aspergillosis is the most frequent clinical presentation. Dissemination occurs from the lungs by hyphal invasion.³ Although IA generally occurs in immunosuppressed patients, it may also rarely be diagnosed in immunocompetent individuals.² In these cases pathogenesis usually occurs by direct conidial inoculation after trauma. Nosocomial acquisition can also occur due to airborne contamination during operation.¹¹ IA is associated with high mortality rates (around 80%) in immunosuppressed and immunocompetent patients.^{6,11} Diagnosis is difficult in both populations but while serum galactomannan (GM) detection has demonstrated to be a useful tool in neutropenic patients, it seems to be less sensitive in the case of immunocompetent individuals.¹⁰ Our group has previously found that bis(methylthio)gliotoxin (bmGT), the inactive derivative of the virulence factor gliotoxin (GT), can be detected in serum samples from immunosuppressed patients at risk of IA.^{5,13} Here we report the first case of disseminated (aorta and vitreous) invasive aspergillosis in an immunocompetent patient with detectable serum bmGT. Pending larger studies, this case is the first example that reveals the utility of bmGT in the diagnosis of IA regardless of the immune status of the patient.

Case report

A 70-year-old male with non-insulin dependent type II diabetes mellitus and a surgery history of aortic valve replacement with a coronary by-pass five years before and hip replacement three years before, presented to the emergency department with blurred vision. Ophthalmological examination of the left eye showed positive Tyndall effect and turbid vitreous. Uveitis was diagnosed

and topic corticosteroids were prescribed. Three days later he was re-evaluated in ophthalmology consultation where endogenous endophthalmitis was diagnosed and vitrectomy was planned. During the intervention, vitreous was sent for microbiological examination and intravitreal therapy with vancomycin and voriconazole (VOR) was administered. Intravenous vancomycin (1 g/12 h) was also administered. During his admission for the surgery, the patient suffered an ischemia of the right low member. Computed tomography (CT) and an angiography of peripheral arteries and thorax showed a right pedis artery occlusion and a thrombus in aortic arch associated to a small dissection. The patient received intraarterial fibrinolytic treatment, and the aortic lesion study continued. Infectious endocarditis was then ruled out by transesophageal echocardiography. A thoracic CT revealed mycotic aneurysm of the ascending thoracic aorta, including mural thrombus. Antibiotic treatment was empirically initiated with daptomycin (10 mg/kg/d), cloxacillin (4 g/4 h) and gentamicin (240 mg/12 h), and graft replacement of the ascending aorta was carried out. During the surgery abundant brittle material of infectious aspect, found between the aortic valve graft and the aneurysm, was removed (Fig. 1). Samples were sent for histological and microbiological examination. The same day the microbiological report revealed the presence of hyphal elements on the Gram stain, a new treatment with caspofungin (70 mg/d on day 1, followed by 50 mg/d) started. The next day, *Aspergillus fumigatus* was isolated and VOR (6 mg/kg every 12 h on the first day, followed by 4 mg/kg every 12 h) was added to the treatment.

After the surgery, the clinical state of the patient was stable and extubation was possible. He only presented a mild renal impairment. Later on, the patient developed severe respiratory failure and intubation was needed again. He gradually got worse, with severe renal impairment requiring continuous venovenous hemodiafiltration and vasoactive drugs. The patient developed

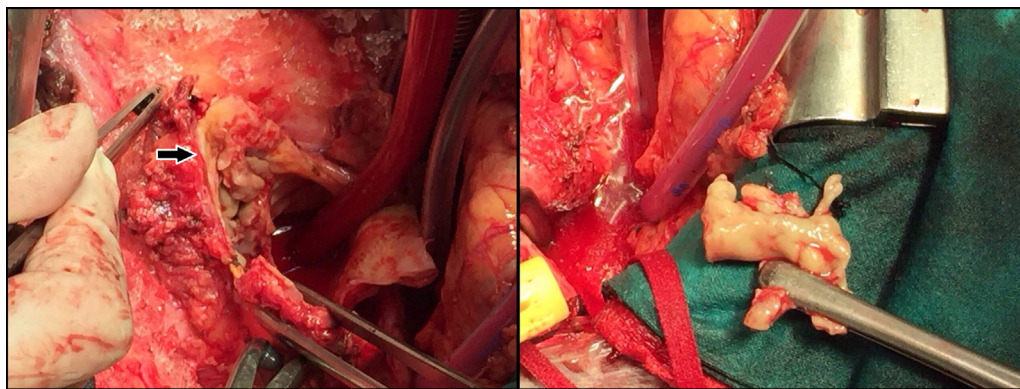


Figure 1. Abundant brittle material of infectious aspect.

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