

**Table 1**

Prevalence of IgG anti-HEV among different groups of population in Spain according to Refs. 3–6.

|                                            | Number of samples | Prevalence |
|--------------------------------------------|-------------------|------------|
| Blood donors                               | 863               | 2.9%       |
| Haemodialysis patients                     | 63                | 6.3%       |
| HCV post transfusionally infected children | 42                | 0%         |
| Sub Saharan immigrants                     | 90                | 5.5%       |
| Pregnant women                             | 1040              | 3.6%       |
| Pig handlers                               | 113               | 18.6%      |
| HIV-infected patients                      | 178               | 10.11%     |

antibodies in all the population tested, with the exception of pig handlers<sup>5</sup> (18.6%) and HIV-infected patients (10.11%). In blood donors and pregnant women, the prevalence is 2.8% and 3.6%, respectively,<sup>6,7</sup> significantly lower than in the HIV infected population, 10.11% ( $p < .01$ ).

Our data are similar to those reported by Jordi et al. in Catalonia,<sup>8</sup> Spain. They found a prevalence of 9% among 238 HIV-infected patients. However, it is interesting that in healthy adults the prevalence is much higher in Catalonia<sup>9</sup> than in Madrid,<sup>4</sup> 7% and 2.8%, respectively. This difference may be due to epidemiological characteristics of the patients studied (rural or urban areas, gender, age, profession), or methodology. The geographical situation of Madrid inside the country may also have a role, since a very high prevalence has been reported in southwest France.<sup>10</sup>

In summary, our results show a high seroprevalence of HEV infection in HIV positive patients different to that observed in blood donors, pregnant women, and other considered high risk groups (except pig handlers, as hepatitis E is a zoonosis and its reservoir is swine). The normal values of ALT and absence of clinical symptoms recorded in all the patients suggests that asymptomatic infection could have taken place frequently in the past in these patients, and they can be considered as a risk group for HEV infection.

## Bibliografía

- Rodriguez-Frías F, Jordi R, Buti M. Hepatitis E: virología molecular, epidemiología y patogénesis. *Enferm Infecc Microbiol Clin*. 2012; doi:10.1016/j.eimc.2012.01.014.

- Keane FE, Gompels M, Bendall RP, Drayton R, Jennings L, Black J, et al. Hepatitis E virus coinfection in patients with HIV infection. *HIV Med*. 2012;13:83–8.
- Fernandez Barredo S, Galiana C, Garcia A, Vega S, Gomez MT, Pérez-Gracia MT. Detection of hepatitis E virus shedding in feces of pigs at different stages of production using reverse transcription polymerase chain reaction. *J Vet Diag Invest*. 2006;18:462–5.
- López-Velez R, Turrientes C, Gutierrez C, Mateos M. Prevalence of Hepatitis B, C and D markers in Sub-Saharan African immigrants. *J Clin Gastroenterol*. 1997;25:650–2.
- Mateos ML, Camarero C, Lasa E, Teruel JL, Mir N, Baquero F. Hepatitis E virus: relevance in blood donors and risk groups. *Vox Sang*. 1999;76:78–80.
- Galiana C, Fernández-Barredo S, Pérez-Gracia MT. Prevalencia del virus de la hepatitis E (VHE) y factores de riesgo en trabajadores de explotaciones porcinas y donantes voluntarios. *Enferm Infecc Microbiol Clin*. 2010;28:602–7.
- Mateos Lindemann ML, Gabilondo G, Beatriz Romero J, Martín S, de la Maza O, Pérez-Gracia MT. Low prevalence of Hepatitis E Infection among pregnant women in Madrid, Spain. *J Med Virol*. 2010;82:1666–8.
- Jardi R, Crespo M, Homs M, Van den Eyden E, Girones R, Rodríguez-Manzano J, et al. HIV, HEV and cirrhosis: evidence of a possible link from eastern Spain. *HIV Med*. 2012; doi:10.1111/j.1468-1293.2011.00985.
- Buti M, Dominguez A, Plans P, Jordi R, Schaper M, Espuñes J, et al. Community based seroepidemiological survey of hepatitis E virus infection in Catalonia, Spain. *Clin Vaccine Immunol*. 2006;13:1382–432.
- Mansuy JM, Legrand-Abravanel F, Calot JP, Peron JM, Alric L, Agudo S, et al. High prevalence of anti-hepatitis E virus antibodies in flood donors from southwest France. *J Med Virol*. 2008;80:289–93.

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## Influenza A (H1N1) complicated by invasive aspergillosis in non-severely immunocompromised patients

### Influenza A (H1N1) complicada en pacientes sin inmunocompromiso severo: coinfección con *Aspergillus* pulmonar

## Introduction

Pulmonary aspergillosis (PA) is a disease which usually occurs in immunocompromised hosts with an overall mortality around 60%.<sup>1</sup> There have been some reports in the literature of invasive PA after pandemic influenza A (H1N1) infection.<sup>2,3</sup> We present two cases of invasive aspergillosis after influenza A (H1N1) infection in patients without classical predisposing factors.

## Case report

The first patient is a 43-year old diabetic male, who was admitted to the intensive care unit (ICU) due to diabetic ketoacidosis, pneumococcal pneumonia and influenza A (H1N1). He received levofloxacin, ceftriaxone, oseltamivir and methylprednisolone (80 mg/day/1 wk). On day 12, fever and respiratory failure

reappeared, invasive mechanical ventilation was required. The chest computed tomography (CT) scan showed a cavity of 6 cm × 5 cm. *Aspergillus fumigatus* grew in a sputum sample and the galactomannan antigen (AGA) tested positive in BAL fluid. Intravenous voriconazole was started as well as corticosteroids due to respiratory distress syndrome. He was discharged after three months of hospitalization. The second case is a 56-year old diabetic man with alcoholic liver cirrhosis admitted to ICU due to alcoholic hepatitis, a methicillin sensitive *Staphylococcus aureus* bacteraemic pneumonia and influenza A (H1N1). He was started with oseltamivir, cloxacillin, meropenem and methylprednisolone (60 mg/day/1 wk). On day 14, the patient developed right hemiparesis. Magnetic resonance imaging showed various parenchymatous lesions suggestive of brain abscesses. A chest CT had bilateral cavitated nodules. *A. fumigatus* grew in BAL fluid. Treatment was switched to voriconazole, anidulafungin and cloxacillin. The patient died on hospitalization day 21.

## Discussion

We present two cases of influenza A (H1N1) complicated by invasive aspergillosis. These patients had none of the risk factors

traditionally related to IA but they fulfilled the criteria for proven Aspergillosis according to the EORT/MSG consensus group.<sup>4</sup> The second patient developed a neurological deficit and it is difficult to determine if the cause was *Aspergillus* or *S. aureus*. However neurological impairment appeared when the bacteraemia had already cleared and the CT scan showed images suggestive of aspergillosis.

Influenza A (H1N1) virus infection may cause various immunological or respiratory tract disorders. Defects in cellular immunity, mucociliary transport as well as leukocyte dysfunction are among the described mechanisms.<sup>3</sup> On the other hand, Influenza pneumonia may result in acute respiratory distress syndrome that requires high doses of corticosteroids.<sup>5</sup> All of these can predispose to pulmonary aspergillosis.

Sporadic cases of invasive aspergillosis complicating influenza A have been reported since the 1990s.<sup>6</sup> The question is whether infection by the current pandemic A (H1A1) virus is a stronger predisposing factor than infection by other strains. An affirmative answer is plausible based on the increased clinical and pathological morbidity associated with pandemic A (H1A1) virus infection, probably due to a broader range of susceptible respiratory cells.<sup>7</sup> Invasive pulmonary aspergillosis should be considered as a possible complication in patients presenting with severe influenza A (H1A1) and who have received corticosteroids, even if they do not have classical immunocompromising conditions. Taking this into consideration may be helpful for an early diagnosis and treatment which could be valuable for a favourable outcome.

## Bibliografía

1. Nivoix Y, Velten M, Letscher-Bru V. Factors associated with overall and attributable mortality in invasive aspergillosis. Clin Infect Dis. 2008;47:1176-84.
2. García-Vidal C, Barba P, Arnan M. Invasive aspergillosis complicating pandemic influenza A (H1N1) infection in severely immunocompromised patients. Clin Infect Dis. 2011;53:e16-9.
3. Lat A, Bhadelia N, Miko B, Furuya EY, Thompson 3rd GR. Invasive aspergillosis after pandemic (H1N1) 2009. Emerg Infect Dis. 2010;16:971-3.
4. De Pauw B, Walsh TJ, Donnelly JP. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008;46:1813-21.
5. Poulakou G, Souto J, Balcells J. First influenza season after the 2009 pandemic influenza: characteristics of intensive care unit admissions in adults and children in Vall d'Hebron Hospital. Clin Microbiol Infect. 2012;18:374-80.
6. Lewis M, Kallenbach J, Ruff P, Zaltman M, Abramowitz J, Zwi S. Invasive pulmonary aspergillosis complicating influenza A pneumonia in a previously healthy patient. Chest. 1985;87:691-3.
7. Guarner J, Falcón-Escobedo R. Comparison of the pathology caused by H1N1, H5N1, and H3N2 influenza viruses. Arch Med Res. 2009;40:655-61.

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## Caracterización de blaOXA-48 detectada en cepas clínicas de *Enterobacter cloacae* aisladas en el sur de España

### Characterization of blaOXA-48 in *Enterobacter cloacae* clinical strains in southern Spain

Sr. Editor,

La oxacilinas OXA-48 es una beta-lactamasa de clase D que fue identificada por primera vez en una cepa de *Klebsiella pneumoniae* en 2004<sup>1</sup>, y desde 2008 se han aislado cepas portadoras de esta enzima que han sido responsables de brotes hospitalarios o casos aislados en diversos países mediterráneos. Desde el primer brote detectado en Turquía<sup>2</sup>, se han producido otros aislamientos de cepas OXA-48 en el entorno mediterráneo, como Israel, países del norte de África, España y Francia<sup>3,4</sup>, demostrando una capacidad de diseminación muy alta y extendiéndose a otros países europeos.

Los brotes suelen ser producidos por *K. pneumoniae*, pero también se han detectado esporádicamente en cepas de *Enterobacter cloacae* y *Escherichia coli*.

Comunicamos el aislamiento y la caracterización molecular de dos cepas de *E. cloacae* que se aislaron de 2 pacientes hospitalizados en enero y septiembre del año 2010, respectivamente, en los que se ha identificado OXA-48. El primer caso corresponde a una mujer de 41 años, diagnosticada en diciembre de 2009 de leucemia mieloide aguda en tratamiento quimioterápico en la Unidad de Hematología del hospital. Tras el tratamiento de su proceso basal desarrolla un cuadro de aplasia y fiebre, siendo tratada con vancomicina, meropenem y caspofungina. La cepa de *E. cloacae* (Ecl536) resistente a carbapenem es aislada un mes después de sangre y lavado broncoalveolar y se añade ciprofloxacino al tratamiento. La paciente fallece por fallo renal en febrero de 2010. El segundo caso corresponde a

un hombre de 77 años de edad, hospitalizado el 31 de agosto de 2010 en la Unidad de Neumología (situada en una planta inmediatamente superior a la del caso anterior), por exacerbación de un proceso de enfermedad pulmonar obstructiva crónica y tratado con ciprofloxacino. El 21 de septiembre se aísla en esputo una cepa de *E. cloacae* (Ecl537) con susceptibilidad intermedia a meropenem y resistente a imipenem y quinolonas, falleciendo de insuficiencia respiratoria al día siguiente.

La identificación y el antibiograma se realizaron mediante métodos comerciales (Wider, Soria Melguizo). Las concentraciones mínimas inhibitorias (CMI) fueron confirmadas por E-test (Biomerieux). La detección fenotípica de carbapenemasas fue demostrada por el test modificado de Hodge (THM). El análisis molecular de beta-lactamasas plasmídicas fue realizado con Check Carba ESBL (Check-Points). El gen blaOXA-48 fue detectado por PCR<sup>5</sup> y confirmado por secuenciación. Se realizaron análisis de porinas mediante SDS-PAGE<sup>6</sup>, y la relación clonal fue estudiada por Rep-PCR. Los plásmidos fueron caracterizados por tipificación de los replicones mediante PCR<sup>7</sup> y fueron extraídos por el método de Kado y Liu<sup>8</sup>. El tamaño aproximado de cada uno de los plásmidos detectados fue calculado usando como referencia diferentes cepas de *E. coli* con un contenido en plásmidos de tamaños conocidos (fig. 1). El entorno genético del gen blaOXA-48 fue determinado por PCR y secuenciación con primers de blaOXA-48 y del transposón Tn1999<sup>1</sup>.

Los 2 aislamientos fueron resistentes a todos los beta-lactámicos ensayados: amoxicilina, amoxicilina/clavulánico y cefalosporinas, incluyendo cefotaxima, ceftazidima y cefepima. Además, ambos aislamientos fueron resistentes a cotrimoxazol, tobramicina, gentamicina, amikacina y minociclina, pero susceptibles a colistina y fosfomicina. El primer aislamiento fue susceptible a ácido nalidixico y ciprofloxacino, con CMI de  $\leq 16$  y 1 µg/ml, respectivamente, mientras que el segundo fue resistente a ácido nalidixico