

Invasive infections due to *Streptococcus pyogenes*: a report of 2 cases

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None

Since the 1980s there has been increasing interest in invasive infections due to *Streptococcus pyogenes* (the Lancefield Group A streptococci [GAS]). A number of reports have warned of a possible resurgence of severe clinical forms of GAS infections, which can range from uncomplicated superficial forms to severe invasive disease. Invasive GAS infection is associated with high mortality despite early antimicrobial therapy. We present 2 such cases, one involving pneumonia and the other bacteraemia with no detected primary focus. Our aim is to draw attention to the continuing importance of GAS infections and the use of population-based surveillance to provide data for monitoring trends in incidence and identifying the relevance of particularly virulent strains. This provides a rational basis for disease control measures and future vaccine development. [Emergencias 2008;20:435-438]

Key words: Group A *Streptococcus*. Invasive infections. *Streptococcus pyogenes*. Mortality.

Introduction

Group A *Streptococcus* (GAS) continues to be one of the major causes of infectious disease related to morbimortality throughout the world¹. Although the clinical course of GAS infections is mild, in a notable percentage of patients (15%) the infection progresses as a severe invasive disease². One of the important features of invasive GAS infections is their epidemiology. After more than one century in which both the mortality and the morbidity have diminished, since the middle of the 80s a re-emergence and persistence in invasive GAS infections have been observed²⁻⁵. The cause of this re-emergence is enigmatic and, in fact, numerous hypotheses have been considered focused not only on possible alterations in the immune systems but also on the increase in the infective capacity of the bacteria itself^{6,7}.

The incidence of this infection in Europe varies from 0.06 to 4.8 per 100,000 inhabitants/year⁸. Some of these studies have reported both clinical and microbiological findings in an attempt to catalogue invasive GAS disease⁹⁻¹¹. In agreement with the Working Group on Severe Streptococcal Infec-

tions (1993), invasive disease by GAS may be classified as "confirmed" and "probable" cases¹². Thus, confirmed invasive GAS disease is defined as the isolation of GAS in a normal sterile medium, together with clinical symptoms or invasive bacterial disease. On the other hand, isolation of GAS in a normal non-sterile medium associated with invasive bacterial disease defines a probable invasive GAS disease. This study presents two clinical cases of invasive GAS infection, one of pneumonia and another of bacteraemia with no infectious foci in which the importance of this entity in our setting is demonstrated.

Clinical cases

A 49-year-old male with no medical history of interest except for lumbar-sciatica in the previous days for which the patient was receiving anti-inflammatory and muscle relaxant treatment attended the Emergency Department (ED) for chest pain of sudden onset, dyspnoea and dry cough of 4 days of evolution. The initial physical examination showed arterial hypotension (80/40 mm Hg),

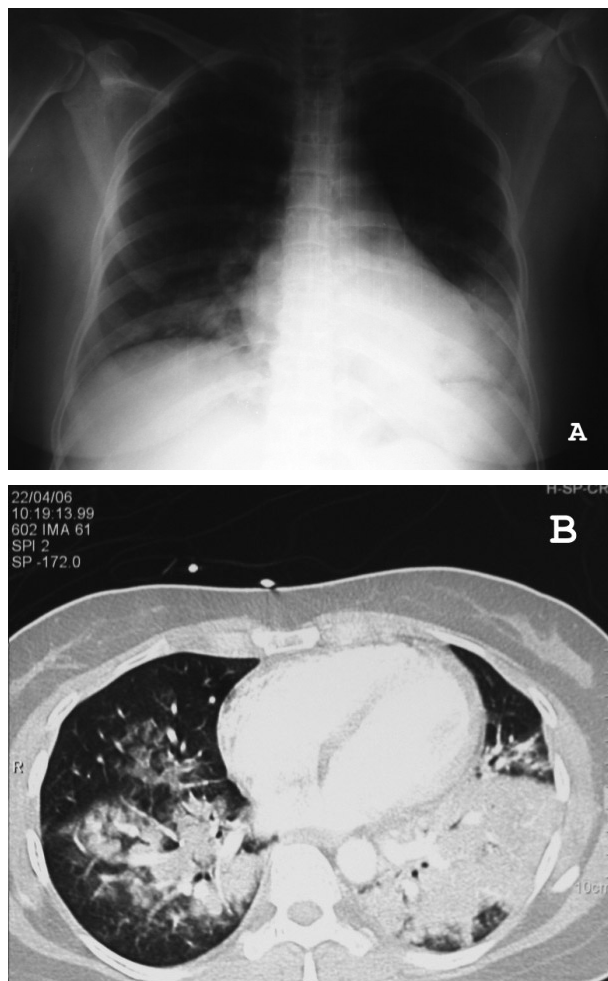


Figure 1. Radiography (A) on admission and CT (B) on admission of the first case.

tachypnoea (25 rpm) and respiratory insufficiency with oxygen saturation with room air of 81%. Auscultation showed crackling rales and bibasal bronchial breathing in posterolateral regions. Chest x-ray showed a bilateral alveolar pattern in the middle and inferior thirds (Figure 1A). Laboratory analysis presented severe respiratory insufficiency with PO₂ of 44 mm Hg, mild renal insufficiency (creatinine: 1.2 mg/dL), liver involvement (GPT: 133 U/L and total bilirubin: 1.8 mg/dL), leucopenia of 2,300/ μ l with (13% of bands and 38% segmented) and coagulopathy (prothrombin index: 37.9%). Computerised tomography (CT) demonstrated bilateral pulmonary parenchymatous condensation with aerial bronchogram in the lower lobes and ground glass areas in the upper right lobe (figure 1B). Bronchial brush specimens taken 36 hours after admission to the intensive care unit (ICU) and in the pharyngeal exudates showed growth of *Streptococcus pyogenes*. The clinical evolution was unfavourable despite wide

spectrum antibiotic treatment, corticotherapy and inotropics and the patient died 13 days after admission. *S. pyogenes* was isolated in the pulmonary secretion culture obtained during the autopsy in which the appearance of multifocal pneumonia of necrotic-haemorrhagic character with zones of abscessification was of note.

A 19-year-old male with no medical history of interest was seen in the ED for a picture of odynophagia of 3 days of evolution which had been treated by his primary care physician with anti-inflammatory drugs but had worsened in the previous 24 hours, with asthenia, diarrhoea and fever of up to 40°C. Physical examination showed the patient to be obtunded (Glasgow scale of 11), temperature of admission of 40°C, arterial hypotension of 75/40 mm Hg, generalised cyanosis and intense respiratory insufficiency with oxygen saturation with room air of 74%. Analytical results showed metabolic acidosis with a pH of 7.00, acute renal failure with creatinine of 7.3 mg/dL, liver involvement (GPT: 189 U/L and total bilirubin 1.4 mg/dl), leucocytosis of 41,000/ μ l with 40% bands, platelet count of 90,000/ml and severe coagulopathy (prothrombin index: 34.9%). Blood culture isolated *Streptococcus pyogenes*. Chest x-ray on admission was normal. The patient was admitted to the ICU and despite established support measures (treatment with vasoactive substances, volume overload and mechanical ventilation) and antibiotic treatment with ceftriaxone and vancomycin he died 4 hours after admission.

Discussion

An estimate of a minimum of 500,000 deaths annually place the GAS as one of the greatest pathogens of man, only being surpassed by the human immunodeficiency virus, *Mycobacterium tuberculosis*, *Plasmodium falciparum* and *Streptococcus pneumoniae*¹³. The GAS cause major long term morbidity compared with these pathogens and its global importance has been underevaluated¹³. Thus, some studies have reported mortality rates between 14% and 18%¹⁴ and even up to 34% in patients with necrotising fasciitis¹⁵. On the other hand, different studies have determined why patients with bacteraemia by GAS, such as the cases presented here, have a worse prognosis. The prevalence of cases with bacteraemia reaches rates of between 56% and 85%. Nonetheless, despite the evident greater fatality of the cases with bacteraemia, in different studies this difference does not seem to be statistically significant¹⁴. In a

recent study¹⁴, hepatic dysfunction and coagulopathy were identified as factors significantly related to mortality similar to what was observed in the cases presented here. On the other hand, in a cohort studied in Ontario, Canada, age, arterial hypotension and bacteraemia were identified as determinant factors¹⁶.

As occurred in our patients, most of the cases of infection by GAS are community-acquired and only 4% to 13% of the cases are intrahospital^{17,18}. European studies⁸ have identified a greater incidence of cases of infection by GAS in specific ethnic groups. One study carried out in London¹⁹ found a greater number of cases of streptococcal pharyngitis in orthodox Jewish children and adults. On the other hand, infections by GAS mainly occur at the end of the winter and the beginning of spring. Similar patterns have been observed with scarlet fever and streptococcal pharyngitis. The reason for these seasonal patterns in relation to the manifestations by GAS, which are vulnerable to the climatic effect, is not clear⁸. However, it was observed that the two cases presented here were in agreement with this climatic pattern since both were attended at the beginning of spring.

Few countries have undertaken continuous surveillance measures sufficiently in depth to monitor the cases according to specific risk factors or modes of acquisition. Improvement in the data obtained by surveillance techniques during the 90s in European countries confirms the following risk factors related to the infectious disease by GAS: alcoholism, malignant process, diabetes, cutaneous lesions, recent delivery, the use of steroid and varicella^{17,18}. Nonetheless, in an important proportion of the cases of between 17% and 31%^{17,18}, there is no evidence of risk factors or predisposing factors such as in the case of our two patients.

The impetus generated in the middle of the 90s led to the formation of an *ad hoc* work group for *S. pyogenes* in the World Health Organisation. The main recommendation of this group was to help the member states to establish health programmes for the control of infections by GAS⁸. The implementation of surveillance programmes of GAS infections in Europe in the last 15 years has led to the identification of a notable increase in these infections. However, the variability among the surveillance programmes of the different countries impedes solid comparisons and demonstrates the need to unify surveillance strategies throughout Europe. The Strip-EURO programme was created with this aim in 2002²⁰.

Sepsis continues to have a high mortality of up to more than 40% in severe sepsis or septic shock²¹. Thus, management in the ED is of transcendental importance. Despite early diagnosis, the adequate choice of antibiotic treatment and intensive support measures are of critical importance. These patients should be placed in areas which facilitate correct diagnostic management and complex monitoring (ICU). However, this final setting should not be a conditioner to not initiate support measures in the ED²¹.

The use of explicit diagnostic scales for the management of streptococcal infections is a valid approach for the ED and may improve the patterns of antibiotic prescription. At present, rapid antigenic detection tests for streptococci infection are available which may reduce the sensitivity of detection. A combined approach with clinical scales and cultures in patients with negative results with the rapid antigenic test would reduce antibiotic prescription and the necessary follow up without affecting the sensitivity of the detection of streptococcal disease^{22,23}.

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Enfermedad invasiva por *Streptococcus pyogenes*

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La enfermedad invasiva producida por el *Streptococcus* del grupo A (SGA), el *Streptococcus pyogenes*, ha motivado un interés creciente desde los años 80. Diversos informes alertan sobre el posible resurgimiento de las manifestaciones clínicas severas del *Streptococcus pyogenes*. Los SGA causan infecciones de diversa magnitud, lo que abarca desde procesos sin complicación a enfermedad grave invasiva. Esta última está asociada a una elevada mortalidad, incluso tras instaurar terapia antibiótica temprana. Presentamos dos casos de enfermedad grave invasiva producida por SGA, una neumonía y una bacteriemia sin foco infeccioso. Pretendemos resaltar la importancia que hoy en día siguen teniendo estas infecciones y cómo los programas de vigilancia poblacionales, aportan datos para monitorizar las tendencias de la incidencia y su particular virulencia, así como proporcionar bases razonables para tomar medidas de control de la enfermedad y el desarrollo de futuras vacunas. [Emergencias 2008;20:435-438]

Palabras clave: *Streptococcus* del Grupo A. Enfermedad invasiva. *Streptococcus pyogenes*. Mortalidad.