7. Gordon R, Brown-Elliott BA, Wallace Jr RJ. *Mycobacterium mageritense* pulmonary disease in patient with compromised immune system. Emerg Infect Dis. 2011;17:556–8.
8. Telenti A, Marchesi F, Balz M, Bally F, Böttger EC, Bodmer T. Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J Clin Microbiol. 1993;31:175–8.
9. Hernández-Lorente E, Lalueza P, Girona L, Simeón CP. Serotonin syndrome associated with linezolid. Med Clin (Barc). 2009;132:157–60 [in Spanish].
10. Ortiz-Pérez A, Martín-de-Hijas N, Alonso-Rodríguez N, Molina-Manso D, Fernández-Roblas R, Esteban J. Importance of antibiotic penetration in the antimicrobial resistance of biofilm formed by non-pigmented rapidly growing mycobacteria against amikacin, ciprofloxacin and claritromycin. Enferm Infecc Microbiol Clin. 2011;29:79–84.
11. Bauer E. Post-dural puncture bacterial meningitis. Anesthesiology. 2006;105:381–93.

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Haemolytic uraemic syndrome associated with bloody diarrhoea caused by *Streptococcus dysgalactiae*

Síndrome hemolítico-urémico asociado a diarrea invasiva por Streptococcus dysgalactiae

Dear Sir,

The haemolytic uraemic syndrome (HUS) includes the triad of haemolytic anaemia, thrombocytopenia, and acute renal failure. HUS can be distinguished in typical HUS and atypical HUS (aHUS). Enterohaemorrhagic *Escherichia coli* (STEC), which produces Shiga toxin, and *Shigella dysenteriae* are frequently the cause of bloody diarrhoea, which characterized typical HUS. Atypical HUS defines non-Shiga-toxin HUS and even if some authors include secondary aHUS due to infectious agents (mostly *Streptococcus pneumoniae*), or other causes (malignancy, cancer chemotherapy, transplantation), aHUS designated a primary disease due to a disorder in complement alternative pathway regulation that shows a poorer outcome.[1] Although extremely rare, infections due to *Streptococcus pyogenes* (GAS) with and without diarrhoea have been associated with HUS.[2,3] *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) causes invasive streptococcal infections, including streptococcal toxic shock syndrome, as does Lancefield group A *S. pyogenes*. Similarly to group A streptococci, SDSE possesses virulence factors including M protein, streptolysins and others.[4] We report the first case of bloody diarrhoea and HUS probably due to SDSE in a three-year-old girl.

The 3-year-old girl was transferred to Puerta del Mar University Hospital with a history of crampy abdominal pain associated with bloody diarrhoea and oliguria. No previous intake of antibiotics was referred. On admission, BUN and serum creatinine were 167 and 3.1 mg/dl, respectively, haemoglobin was 11.3 g/dl and platelet count was 100,000 μl^{-1}. C-reactive protein was 18.18 mg/dl (normal 0–0.5 mg/dl). Serum fibrinogen levels, prothrombin time and partial thromboplastin time were normal. Blood smear showed polychromasia with the presence of schistocytes. She was admitted to the intensive care unit, and antibiotic despite hydratation, her renal function continued to deteriorated and continuous veno-venous hemodiafiltration was started. By the fourth hospital day, C3 levels were 79 mg/dl (normal 90–180 mg/dl), returning to normal levels at the time of discharge, and C4 was 21.6 (normal 10–40 mg/dl). Renal function was not re-established, and at discharge she was treated with continuous ambulatory peritoneal dialysis. There was no familial history for HUS.

In two stools samples cultured on admission and one day after were isolated with pure growth of *S. dysgalactiae* subsp. *equisimilis*. Identification was made in accordance with the differentiating characteristics described by Ruoff et al.,[5] including agglutination positivity for Lancefield group C (DiaMondial Strept kit, France), strong beta-haemolysis, formation of large, glossy colonies and bacitracin resistance. Susceptibility to antibiotics was determined by disk diffusion test according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2011). The isolate was susceptible to penicillin, vancomycin and levofloxacin, and resistant to erythromicin and clyndamicin. No *Salmonella* sp, *Shigella* sp, *Campylobacter* sp, *Vibrio* sp, *Aeromonas* sp or *Yersinia* sp were isolated by culture. Shiga toxins genes, intimin *eae* gene, and virulence factor *ipah* gene, to detect enterohaemorrhagic *E. coli*, enteroinvasive *E. coli* enteropathogen *E. coli* and *Shigella* was performed by PCR (GenoType EHEC, Hain LifeScience, Germany) on stools, with negative results. Blood cultures submitted at the time of admission were also negative. No throat culture was processed.

In 1996, Vandamme et al.,[6] proposed that a novel subspecies, *S. dysgalactiae* subsp. *equisimilis*, was a clinical pathogen. In the present century, the prevalence of invasive and non-invasive SDSE infections has increased gradually year by year.[4,7] The spectrum and clinical courses of SDSE infection show substantial overlap with those of GAS. Haemorrhagic enteritis caused by GAS has been described[2,8] but, at our knowledge, this could be the first case of bloody diarrhoea caused by SDSE, as no other enteropathogenic bacteria were detected by culture or molecular methods. Recently, it has been determined the complete genomic sequence of SDSE strain GGS_124 isolated from a patient with streptococcal toxic shock syndrome (STSS). SDSE shares most of the virulence factor genes of GAS, including streptolysin O, streptokinase, fibronectin-binding, collagen-binding T antigen (FCT-like regions), and NADase and distantly related to streptococcal inhibitor of complement (DRS), although lacks several virulence factors, such as superantigens, cysteine protease SPE-B and the ABC operon.[9]

An important mechanism underlying aHUS involves the complement system, but endothelial cell activation may play an important role too. The association of GAS with HUS is not well known, however, it has several virulence factors that may predispose to microangiopathy. Activation of endothelial cell matrix metalloprotease by GAS extracellular cysteine protease resulted in endothelial cell damage,[10] but SDSE lacks this enzyme. The release of inflammatory mediators in the presence of SDSE infection may play a role in the pathogenesis of HUS.

Although there more studies are necessary to conclude that SDSE can cause bloody diarrhoea and HUS, we consider that it is important to underline the increased clinical importance of this microorganism.

References

1. Loirat C, Fremeaux-Bacchi V. Atypical hemolytic uremic syndrome. Orphanet J Rare Dis. 2011;6:60.
2. Shepherd AB, Palmer AL, Bigler SA, Baliga R. Hemolytic uremic syndrome associated with group A beta-hemolytic streptococcus. Pediatr Nephrol. 2003;18:949–51.
3. Yildiz B, Kural N, Yara C. Atypical hemolytic uremic syndrome associated with group A beta hemolytic streptococcus. Pediatr Nephrol. 2004;19:943–4.
4. Takahashi T, Ubukata K, Watanabe H. Invasive infection caused by *Streptococcus dysgalactiae* subsp. equisimilis: characteristics of strains and clinical features. J Infect Chemother. 2011;17:1–10.
5. Ruoff KL, Whiley RA, Beighton D. Streptococcus. In: Murray PR, Baron EJ, Jorgensen JH, Pfaller MA, Yolken RH, editors. Manual of clinical microbiology. Washington, DC: American Society for Microbiology; 2003. p. 405–21.
6. Vandamme P, Pot B, Falsen E, Kersters K, Devriese LA. Taxonomic study of Lancefield streptococcal groups C, G and L (*Streptococcus dysgalactiae*) and proposal of *S. dysgalactiae* subsp. *equisimilis* subsp. nov. Int J Syst Bacteriol. 1996;46:774–81.
7. Broyles LN, Van Beneden C, Beall B, Facklam R, Shewmaker PL, Malpiedi P, et al. Population-based study of invasive disease due to ß-hemolytic streptococci of groups other than A and B. Clin Infect Dis. 2009;48:706–12.
8. Isozaki A, Matsubara K, Yui T, Kobayashi K, Kawano Y. Group A beta-hemolytic streptococcal hemorrhagic colitis complicated with pharyngitis and impetigo. J Infect Chemother. 2007;13:411–3.
9. Shimomura Y, Okumura K, Muruyama SY, Yagi J, Ubukata K, Kirikae T, et al. Complete genome sequencing and analysis of a Lancefield group G *Streptococcus dysgalactiae* subsp. equisimilis strain causing streptococcal toxic shock syndrome (STSS). BMC Genomics. 2011;12:17.
10. Burns EH, Marciel AM, Musser JM. Activation of a 66-kilodalton human endothelial cell matrix metalloprotease by *Streptococcus pyogenes* extracelullar cysteine protease. Infect Immun. 1996;64:4744–50.

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