Joint Infections Due to *Streptococcus agalactiae* in Non Immunocompromised Adults: Presentation of Two Cases

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Streptococcus agalactiae (S agalactiae) is a germ habitually associated with infections in neonates and women during the pregnancy and the immediate puerperiumum. *S agalactiae* has also been related with bacteriemias, endocarditis and bone, joint, skin and soft tissues infections in adults with concomitant diseases and even in immunocompetent patients. In the last years more than 70 cases of septic arthritis in adults due to this germ have been communicated.
We present 2 cases of axial and peripheral joint infection due to *S agalactiae*, comparing finds, treatment and evolution with the cases published until April 2008.

Key words: Joint Infections. *Streptococcus agalactiae*. Immunocompromised adults.

Infección articular por *Streptococcus agalactiae* en adultos inmunocompetentes: presentación de dos casos

Streptococcus agalactiae (*S. agalactiae*) es un germen habitualmente asociado a infecciones en neonatos y en mujeres durante el embarazo y el puerperio inmediato. *S. agalactiae* también se ha relacionado con bacteriemias, endocarditis e infecciones osteoarticulares, de piel y tejidos blandos en adultos con enfermedades concomitantes e, incluso, en pacientes inmunocompetentes. En los últimos años se han comunicado más de 70 casos de artritis séptica por este germen en adultos.

Se presentan dos casos de infección articular, axial y periférica, por *S. agalactiae*, comparando los hallazgos, el tratamiento y la evolución con los casos publicados hasta abril de 2008.

Palabras clave: Infección articular. S*treptococcus agalactiae* . Adultos inmunocompetentes.

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Introduction

Streptococcus agalactiae is a germ that is commonly associated to infections in newborns and in pregnant and lactating women. *S agalactiae* has also been related to bacteremia, endocarditis, and muscle, bone, soft tissue, and skin infections in adults with concomitant illness and even in immune competent patients. During the past few years more than 70 cases of septic arthritis due to this germ have been reported in adults.
We present 2 cases of peripheral and axial joint infection due to *S agalactiae,* and we compare our findings, treatment and progression with cases published up to April 2008.

Case 1

A 43-year-old woman with a history of being allergic to penicillin and, probable, to quinolones, who smoked 30 cigarettes a day and consumed between 30-50 g/day of alcohol was hospitalized in May 2006 due to pain and swelling of the hands, feet, ankles, and right knee which had appeared 4 days earlier, and were accompanied by low-grade fever. This had been preceded by a self-limited episode of abdominal pain with vomiting of gastric content, diarrhea, and elevated fever (38.5-39ºC), without evident shivering.
Upon hospitalization the body temperature was recorded at 37ºC and the patient had clear livedo reticularis on the legs. Physical examination evidenced pin and swelling with functional limitation of the wrists, ankles, right knee, and

some of the proximal interphalangeal joints of the left hand, accompanied by diffuse edema of the feet and hands; the rest of the examination was normal. Imaging studies showed a slight increase in soft-tissue, visible through x-rays. Echography confirmed the presence of synovitis and effusion of the abovementioned joints, with evidence of signal on the power-Doppler study. Arthrocenthesis of the right knee was performed and 20 mL of synovial fluid of inflammatory characteristics were obtained that, under polarized light microscopy, did not reveal the presence of microcrystals. Because the patient presented fever and diarrhea, blood and synovial fluid samples were sent to the laboratory for microbiology study and fecal cultures were ordered. In addition, serology was ordered for viral causes of arthritis (herpes simplex virus, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, hepatitis B and C viruses, rubella, mumps, and parvovirus) as well as *Salmonella* spp, analytic studies and radiology. Pending the cultures, symptomatic treatment with codeine was begun.

Blood analysis showed an increase in acute phase reactants (erythrocyte sedimentation rate [ESR], 63; C-reactive protein [PCR], 118) with an increase in transaminases of less than 3 times normal values; the rest of the blood chemistry, hemogram, basic urine study, coagulation tests, C3/C4, and blood proteins were normal. Rheumatoid factor, cryoglobulins, AAN, and ENA were negative. After 48 hours both the blood cultures (2/2) as the synovial fluid cultures were positive for *S agalactiae,* sensitive to all of the tested antibiotics, and treatment with intravenous vancomycin was started due to the allergy of the patient to betalactamics and quinolones. Fecal cultures and serology for *Salmonella* were negative and the viral serology did not demonstrate recent viral infection.

A chest x-ray was performed and did not show any significant findings; an abdominal echography only showed simple liver enlargement and a focal lesion that was compatible with hemangioma. A bone scan, which showed increased uptake on the right wrist, right knee, and both ankles, as well as a cold area on the right iliac bone, next to the right sacroiliac joint. Because of this last finding, a magnetic resonance (MR) of the pelvis was performed in which a right sacroilitis was detected with bony erosion and extension to adjacent muscles.

Progression was favorable with iv vancomycin, clinical resolution, laboratory normalization, and negative cultures. Fifty days after being hospitalized the patient was discharged in good health, continuing assisted treatment at home up to a total of 6 weeks. Two months later the patient was still asymptomatic.

Case 2

A 62-year-old male with a history of chronic mechanical lumbar pain came to the emergency department because of an acute increase of the latter after an episode of fever (39.5ºC) and shivering which had lasted a week. Since then, the patient had presented limiting lumbar pain of an inflammatory nature, resistant to common analgesics and with fever under 38ºC, without new episodes of shivering or other clinical signs. His history also included important cigarette smoking and alcohol consumption of approximately 80 g/day.

Upon examination, the patient was feverish and presented pain with great physical limitation to active and passive movements of the lumbar spine, related to important antialgic contracture of the paravertebral musculature. No heart murmurs were detected and the rest of the general and specific examination did not show any significant findings.

Baseline laboratory showed hemoglobin 11.3 g/dL; mean corpuscular volume, 108.5 fl; leucocytosis (15 200/µL) with neutrophilia (11 700/µL); platelets 324 000/µL; fibrinogen, 524 mg/dL; albumin, 3.2 g/dL; ESR, 45; CRP, 276.

The lumbar spine x-ray observed impingement of the disk space on L4-L5 with important sclerosis of the adjacent vertebral surfaces but with relative osteopenia and rarefaction on their anterior and left lateral sides. Chest x-ray showed evidence of emphysema.

Faced with the suspicion of spondylodiskitis, a computerized tomography (CT) was requested urgently upon hospitalization and blood, urine and fecal cultures were taken. CT confirmed the diagnosis of spondylodiskitis of L4-L5, and evidenced irregularity with erosions of the vertebral facets on the anterior surface of the intervertabral disk at the L4-L5 level, with a paravertebral and prevertebral soft-tissue component. Due to technical issues, a CT-guided aspiration was not made. Empiric treatment with ceftriaxone and cloxacillin was begun.

Two days later, blood cultures isolated *S agalactiae* (3/3), resistant to aminoglucosides only. In accordance with the antibiogram and the recommended therapeutic guidelines, antibiotics were substituted for penicillin G.

After the change in treatment, the patient had progressive worsening of the lumbar pain, without fever or other clinical signs. In a parallel manner there was a progressive deterioration of the laboratory findings in which there was thrombocytosis of 1 094 000/µL and hypoalbuminemia of up to 2.10 g/dL. The urine and fecal cultures as well as new blood cultures were all negative.

A lumbar MR was performed in which a stenosis of the spinal canal at the level of L4-L5 was found and was due to disk hernia and epidural inflammation due to spondylodiskitis, with a paraspinal component and involvement of both psoas. An abdominal echography was performed, without any clinical findings and a thoracoabdominal CT only showed emphysema.

Because the patients' poor progression, penicillin was substituted for ceftriaxone after 10 days of use. After the switch, there was clear clinical improvement, with progressive normalization of the platelet recount. Nine days later, ciprofloxacin was added to treatment due to

the slow recovery of the patient. Progression was then clearly favorable due to which this treatment was maintained until 6 weeks of treatment. Nine months later, the patient is completely rehabilitated and only has mechanical back pain that is controlled with analgesics and lumbar back brace. MR of the lumbar spine now shows a resolution of the diskitis image; an impingement of L4-L5 remains with an irregularity of the joint surfaces and degenerative changes with stenosis of the joint foramina bilaterally.

Discussion

S agalactiae is a betahemolytic group B streptococcus frequently implicated in infections related to pregnancy and postpartum infections as well as infections in newborns. However and in spite of the fact that its incidence is still low (2.4-9.2 cases per 100 000 inhabitants/year), in the past few years there has been an increase in the incidence of infections caused by this germ in adults, without a relationship to pregnancy.[1] Therefore, cases of bacteremia, pneumonia, endocarditis, and peritonitis as well as bone, joint and soft-tissues have been communicated.

Of the total of invasive infections, bone and joint represents approximately 4%-14%.[1] The most frequent joint infection is the one related to bones. More than 70 cases of septic arthritis have been reported so far due to this germ in adults. The majority of these patients were adults with concomitant diseases, although cases have also been described in immune competent young patients. Some probable predisposing factors have been described such as a weakening concomitant disease (neoplasia, diabetes mellitus, chronic liver disease, chronic inflammatory joint disease…), the use of steroids or immunosuppressive drugs, advanced age, previous joint disease, instrument manipulation of the joint, and alcohol abuse.[2,3]

In most of the cases, as happens with other pathogens, colonization is produced by blood dissemination of the germ and the presence of *S agalactiae* has been demonstrated in blood cultures of two thirds of the patients published.[1,2] The finding of concomitant infections due to the same germ in other localizations, mainly bone (osteomyelitis) and the urinary tract is frequent.[2] In spite of everything, there may not be fever and leucocyte numbers might remain normal.[4]

In the majority of cases the infection is monoarticular, with a preference for large joints such as the knees, shoulders, and hips. Unlike other germs, poliarticular affection is not infrequent and was the presenting form in a third of the cases communicated, which are related to concomitant systemic illness.[4] As would be expected, progression is worse and complications more frequent in these cases.[5] However, at least 8 cases of septic polyarthritis due to *S agalactiae* have been reported in patients without significant risk factors except alcohol abuse in 2 of them and age over 65 in another 2 patients.[2,6] The lack of shock and systemic affection is noticeable in these cases and differs from what has been described with other germs. Contrary to this, axial skeleton involvement is less frequent. Even so, at least 35 cases of spondylodiskitis and 13 cases of sacroilitis have been described to date.[2,6,7] In addition, one case of vertebral arthritis due to *S agalactiae* has been described in an immunocompetent woman without any risk factors.[3] According to what is reflected in the medical literature, the cases of spondylodiskitis are predominant in 55 to 70 year old males, and the most common localization is the lumbosacral region. Regarding sacroilitis, it must be emphasized that a larger prevalence is present in women between 30 and 40 years.[6,8] Betalactamics, concretely penicillin, are considered as the treatment of choice and are frequently associated to aminoglucosides during the first 2 weeks. In the case of allergy to penicillin, vancomycin has been employed successfully. There is no consensus regarding the duration of treatment, but the guidelines that opt for several months do not seem to offer significantly better results than the 4 to 6 weeks suggested by others. In general, intravenous antibiotics should be maintained for 3 weeks and then oral treatment should be employed for some week's afterwards.[2]

The 2 cases which we presented coincide with what is described in the literature regarding clinical presentation (fever and scarce evidence of systemic disease with a good overall status in spite of confirmed bacteremia and poliarticular affection in one of the patients), diagnostic findings (moderate leucocytosis, positive blood cultures), and treatment (vancomycin in one patients, betalactamics and quinolones in the other; both treated for 6 weeks). In both cases and such as has been previously described, they were immunocompetent patients whose main risk factor for *S agalactiae* infection was excessive alcohol consumption. This risk factor is documented in some patients with poliarthritis in previously published literature. In none of the 2 cases could the primary site of germ dissemination be proven nor infection demonstrated in other localizations in spite of finding *S agalactiae* in the blood.

In the first case and as has been pointed out before, a good general condition, the lack of elevated fever and systemic clinical data in spite of the patients polyarticular affection and positive blood cultures at the moment of diagnosis is of notice. The joint affection had initiated after acute gastroenteritis accompanied by self-limited fever, during which, presumably, blood-borne spreading of the germ took place and led to joint colonization. The literature shows similar descriptions in patients with polyarthritis due to *S agalactiae*.[2,4] On the other hand, it is the first case described of sacroilitis associated to peripheral poliarticular joint disease. To date, simultaneous axial and peripheral affection had been described on only 3 patients, in which the axial affection took the form of an infectious spondylodiskitis associated to acute oligoarthritis.[6,8]

In the case of spondylodiskitis and, like other predisposing factors, the patient had emphysema and the seat of infection was a disk with previous degenerative disease. It must be pointed out that the thrombocytosis in this patient acted as an acute phase reactant and marker of disease evolution, reaching over a million platelets before progressing downward to normality in parallel with the resolution of the infection.

This finding is useful to differentiate infection due to *S agalactiae* from other betahemolytic streptococci.[4] In spite of the fact that penicillin is considered as the antibiotic of first choice and that the antibiogram showed sensibility to this drug, the patient only started improving after switching to a third-generation cephalosporin (ceftriaxone). Although *S agalactiae* arthritis is still infrequent in non-pregnant adults, it must be considered in patients with acute arthritis independent of the joint pattern and the general state of the patient, especially in older patients, with debilitating illnesses (diabetes mellitus, neoplasia, chronic liver disease …) or with alcohol abuse. It is mandatory, therefore, to perform microbiology studies of the synovial fluid in patients with acute joint inflammation when faced with the presence or history of associated fever and even in the absence of fever in the case of immune deficient patients. Progression is usually good with adequate treatment, generally betalactamics, and the functional outcome fundamentally depends on the delay in starting treatment.

References

1. Ramos JM, Blázquez RM, Ramírez C, Moreno S. Varón con fiebre, dolor y limitación funcional del hombro derecho. Enferm Infecc Microbiol Clin. 2001;19:229-30.
2. Nolla JM, Gómez-Vaquero C, Corbella X, Ordóñez S, García-Gómez C, Pérez A, et al. Group B Streptococcus (Streptococcus agalactiae) pyogenic arthritis in non pregnant adults. Medicine (Baltimore). 2003;82:119-28.
3. Dizdar Ö, Alyamaç E, Önal IK, Uzun O. Group B streptococcal facet joint artrhritis. Spine. 2005;30:414-6.
4. Schattner A, Vosti KL. Bacterial arthritis due to beta-hemoytic streptococci of serogroups A, B, C, F and G. Analysis of 23 cases and a review of the literature. Medicine (Baltimore). 1998;77:122-39.
5. Terenzi T, Cunha BA. Consequences of group B streptococcal arthritis in adults. Infect Med. 2005;22:31-3.
6. Díaz-Gonzálvez E, Zarza B, Abreu P, Cobo J, Orte J, Dronda F. Espondilodiscitis y sacroileítis por Streptococcus agalactiae en adultos: caso clínico y revisión de la literatura. Enferm Infecc Microbiol Clin. 2005;23: 71-5.
7. Narváez J, Pérez-Vega C, Castro-Bohórquez FJ, Vilaseca-Momplet J. Group B streptococcal spondylodiscitis in adults: 2 case reports. Joint Bone Spine. 2004;71:338-43.
8. Corominas H, Domingo P, Llobet JM, Caballero F, Díaz C, Vázquez G. Group B streptococcal sacroiliitis: case report and review. Scand J Infect Dis. 2001;33:708-10.