

INFECTIVE ENDOCARDITIS DUE TO *STREPTOCOCCUS GALLOLYTICUS* Associated with Colonic Displasia

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SUMMARY

Streptococcus gallolyticus is a microorganism belonging to the *Streptococcus bovis* I group isolated in humans, bovines and equines pigeons, among other animals. *Streptococcus bovis* is a *Streptococcus* strain found in the rumen, and has been isolated in the milk of animals with mastitis. The authors describe a case of an adult immunocompetent patient with underlying valvular heart disease, with bacteraemia and infective endocarditis by *Streptococcus gallolyticus*, in whom adenomatous colonic polyps with dysplasia were identified.

RESUMO

ENDOCARDITE INFECCIOSA POR *STREPTOCOCCUS GALLOLYTICUS* Associada a Displasia do Cólon

O *Streptococcus gallolyticus* é um microrganismo pertencente ao grupo *Streptococcus bovis* I, isolado tanto no homem como em outros animais, entre eles, bovinos equinos. O *Streptococcus bovis* é a espécie de *Streptococcus* predominante no rúmen, tendo sido isolado no leite de bovinos com mastite.

Os autores descrevem um caso clínico de um adulto imunocompetente com patologia valvular prévia, com bacteriemia e endocardite infecciosa por *Streptococcus gallolyticus*, no qual foram identificados pólipos adenomatosos com displasia no colon.

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INTRODUCTION

More than 50% of cases of native valve infective endocarditis in patients without previous history of injected drug use are caused by *Streptococcus spp.* Mitral valve is the most frequently affected valve alone, or in association with aortic valve infection¹.

Streptococcus gallolyticus is a microorganism belonging to the *Streptococcus bovis* group D, type 1 of the subspecies *gallolyticus*^{2,3}. In the last two decades there have been changes in the nomenclature of this group of microorganisms as a result of the use of molecular techniques, which facilitate the process of differentiation of bacterial genus and species^{4,5}. It is a non- β -haemolytic strain, belonging to Lancefield group D, whose name derives from its ability to decarboxylate gallic acid⁵.

The *Streptococcus* genus includes at least 50 species, many of which are pathogenic both for humans and domestic animals. *Streptococcus gallolyticus* is the *Streptococcus* species which is predominant in the rumen⁶ and has been related with cases of bovine mastitis^{7,8} from which milk is isolated⁹. It is also found in humans and in a number of domestic animals including pigs, pigeons, equinos and also in wild animals^{6,10}.

Many studies suggest a possible association between infective streptococcal endocarditis, in particular *S. bovis*, and colorectal neoplasia¹¹.

The authors describe the clinical case of an immunocompetent adult with bacteraemia and infective endocarditis by *S. gallolyticus* in whom adenomatous colon polyps were identified.

CLINICAL CASE

JCN, a 76-year-old male patient, a farmer who had bred pigeons for more than 30 years, born and living in the Porto area, came into the Emergency Department at Hospital São João, Portugal on 15th January 2009 complaining of high temperature (39-39.9°C) that had started insidiously in the previous week, accompanied by shivering, a general feeling of malaise and night sweats.

A partial improvement of symptoms occurred with self-medication with paracetamol. He denied dyspnoea, chest pain or other respiratory, gastrointestinal or urinary symptoms.

The patient had a previous history of arterial hypertension and dyslipidaemia. Six months previously echocardiographic examination revealed a mitral valve insufficiency and, since then he has been observed regularly as an outpatient by his cardiologist and has been medicated with rosuvastatin 10 mg/day, acetylsalicylic acid 100 mg/day, amlodipine 5mg/day and candesartan 16 mg +hydrochlorothiazide 12.5 mg once a day.

He had also undergone dental treatment in November 2008 without antibiotic prophylaxis.

The patient denied any alcoholic intake, smoking, or injecting illicit drugs and he had not travelled outside his area of residence. He lives in an urban environment with a pigeon coop next to his house, with no other domestic animals.

There was no other relevant personal or family history, namely of colon neoplasia.

On physical examination the patient was conscious, cooperative and lucid, febrile, (axillary temperature: 39°C), blood pressure was 104/59 mmHg, heart rate was 81 beats/min, regular and rhythmic, and respiratory rate was 16 cycles/min. Lung auscultation was normal; cardiac auscultation revealed a grade III/VI holosystolic murmur on the aortic area, with no radiation. There were no signs of peripheral embolism, nor enlargement of the liver or spleen. Neurological examination and fundoscopy were normal. There were no other relevant abnormalities on physical examination.

Blood tests revealed Hemoglobin: 15.5g/dL leucocytes: $20.31 \times 10^9/L$, with $16.43 \times 10^9/L$ neutrophils; urea: 87 mg/L, creatinine: 15.7 mg/L, C reactive protein: 229.4mg/L, erythrocyte sedimentation rate: 67mm/1st hour. Urinalysis revealed proteins: 1.00g/L, leucocytes: 31.2/uL, erythrocytes: 2882.4/uL, with dysmorphic erythrocytes.

Coagulation study revealed APTT: 35.8 sec, prothrombin time of 12.9 sec and fibrinogen of 563 mg/dl. Blood serology for *Rickettsia conorii*, *Coxiella burnetti*, *Chlamydia psittaci*, *Brucella*, *Salmonella*, *Treponema pallidum*, HIV, HCV and HBV were negative.

The chest X-ray revealed no significant alterations, with a normal cardiopulmonary rate.

Renovesical ultrasound showed normal sized kidneys with bilateral lithogenic foci, the largest measuring 7mm and simple bilateral cysts. No other alterations.

The patient was admitted and, after blood and urine culture, empirical antibiotherapy with ampicillin 2.000 mg 4/4 hours was started.

Blood culture identified *S. gallolyticus* sensitive to penicillin, (Figure 1). Urinalysis was found to be sterile.

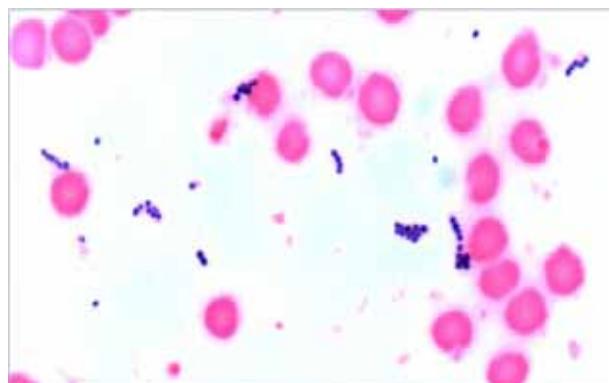


Fig. 1 – Gram Stain of Scrape. Chain coccus can be seen.

The electrocardiogram (ECG) revealed sinus rhythm, right bundle branch blockage, left ventricular hypertrophy with widening of the QRS and repolarization abnormalities.

A transthoracic echocardiography revealed slight dilation of the left auricle, and the slight hypertrophy of left ventricle, particularly in the region of the basal septum.

Slight hypertrophy of left ventricle, particularly in the region of the basal septum. Ascending aorta of normal dimensions, with wall calcification. Slight thickening of aortic valve with calcification of leaflets conditioning slight aortic stenosis with maximum left ventricle/aortic pressure gradient 38 mmHg. Slight aortic, mitral and tricuspid insufficiency. Estimated systolic pressure of pulmonary artery 36 mmHg. No signs of vegetation was observed. Left ventricular systolic function was preserved. No pericardial bleeding or thrombus were detected.

In spite of the result of transthoracic echocardiogram the probability of endocarditis remained high so a transesophageal echocardiogram was performed. A small, 6 mm-vegetation attached to the posterior mitral valve leaflet, on the auricular side, in an area of sclerosis and calcification, was identified, as well as a small abscess on the base of the anterior leaflet in the *inter-valve fibrosa* region (Figures 2, 3).

Colonoscopy revealed the presence of seven sessile polyps located in the ascending, proximal and distal transverse colon, and several diverticuli in the sigmoid colon. (Figure 4)

Polypectomy with diathermic loop was carried out and subsequent histological examination revealed tubular and tubulovillous adenomatous polyps with slight dysplasia; severe dysplasia was found in one polyp. (Figures 5, 6).

The immunological study revealed immunoglobulin A 470mg/dL, (90-410 mg/dL) suggesting IgA nephropathy with clearance of creatinine of 50 ml/min; IgG, IgM and IgE were normal. The total complement and C3c fractions were 129mg/dL (83-177 mg/dL) and C4 fractions were 44 mg/dL (12-36 mg/dL). Crioglobulin, circulating immune complexes and rheumatoid factor were negative.

The patient was given parenteral antibiotic treatment through peripheral catheter for 6 weeks with clinical improvement. He became afebrile at 2nd day of therapy. The transthoracic and transesophageal echocardiogram repeated after 15 days of antibiotic treatment showed no signs of the vegetation and the abscess in the fibrous/intervalve fibrosis was less evident, the other alterations remained stable. (Figure 3)

Successive blood cultures were negative and no other abnormalities were detected.

After completing the 6 weeks of treatment with intravenous ampicillin, the patient had one acute episode of fever (38° C) with intense shivering. Clinical examination did not reveal alterations in either cardiac or pulmonary auscultation or the presence of systemic embolism. There



Fig. 2 – Transesophageal Echocardiogram (A): 6 mm Vegetation adherent to the base of the posterior leaflet of the mitral valve and small abscess at the base of the anterior leaflet.

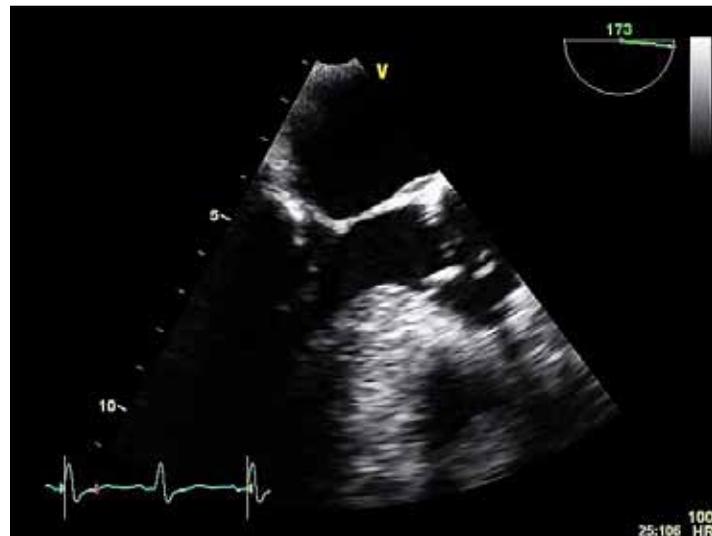


Fig. 3 – Transesophageal Echocardiogram (B): After 15 days of antibiotic therapy, reveals absence of vegetation and the site of the abscess in the intervalve fibrosis is less obvious.



Fig. 4 – Low Digestive Endoscopy: sessile polyp.

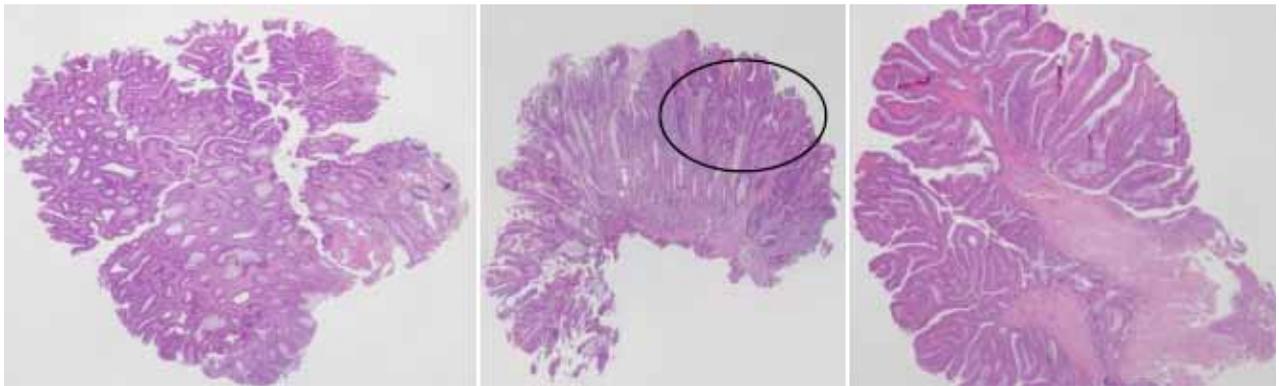


Figure A
The figure on circle shows the high-grade dysplastic.

Figure C

Figure E



Figure B

Figure D

Figure F

Fig. 5 e 6 - Biopsy of the polyp: tubular and tubulovillous adenomatous polyps with lowgrade

was no sign of phlebitis at the site of the intravenous infusion or venous thrombosis in the lower limbs. Arterial pressure was 90/50 mmHg, pulse 76 beats /min.

Emergency blood tests revealed: increase of leucocytes to 20.58×10^9 /L and C reactive protein to 165.8mg/L, D dimers: 1.53 mcg/mL. Brain Natriuretic Peptide (BNP) test: 138.1pg/mL; arterial blood gases pH 7.51 and PO₂: 62.8 mmHg and PCO₂: 31.6 mmHg; O₂ saturation of 94.3% (FiO₂: 21%) and lactates 1.69 mmol/L.

Chest x-ray, abdominal echography and electrocardiogram revealed no further alterations; urinalysis was normal. Transthoracic and transesophageal echocardiogram were repeated and no signs of vegetations or abscess were seen. New blood cultures were taken and empirical treatment with vancomycin and ceftriaxone was started. The patient's temperature returned to normal on the second day of this treatment. No microorganism was isolated and the patient underwent a further 8 days of treatment. Scintigraphy with anti-granulocytic antibodies -99m Tc (Leucoscan®), revealed hyper fixation in D8/9. Radiological examination of this area showed moderate spondilosis as a result of an earlier fracture of D9.

The patient was discharged asymptomatic. Three weeks later he reobserved as an outpatient and he remained well and afebrile.

DISCUSSION

Streptococcus gallolyticus is a gram-positive coccus a sub-species of *Streptococcus bovis*, which is easily identifiable using automatic techniques. It is found in the natural world in ruminants and causes infections in pigeons. It can be found in the faeces of 2-10% of healthy humans¹². Correct identification of the *Streptococcus* is important because of its known sensitivity to antibiotics and its association with colorectal neoplasia.

In humans it can cause bacteraemia with or without endocarditis and, in rare cases, meningitis or osteomyelitis. Patients with endocarditis caused by *Streptococcus* spp. are usually over 50 and, the left cardiac valve are mainly affect, sometimes more than one valve and larger vegetations, than in endocarditis from other aetiologies are observed¹³. The association between streptococcal endocarditis and colorectal cancer was first described by McCoy and Mason in 1951¹⁶, and, since, it has been well is documented¹³⁻¹⁵. The prevalence of this association reported to be between 25-80%^{16,17} which justifies systematic colonoscopy for screening colon neoplasia of patients with previous bacteraemia caused by *S. bovis*¹⁸. It is not clear whether this association reflects any influence of *S. bovis* in the development of the neoplasia, but it is known that there is increased colonization by *Streptococcus* in patients with

colorectal cancer^{19,20}.

There is no clear predominance of sex, although various studies report a higher incidence among males^{15,21,22} in comparison to females²³.

The mortality rate associated to *S. bovis* endocarditis is estimated to be 2-4%.

In the case described, the patient presented some predisposing factors to endocarditis described in the literature¹²⁻¹⁵: male, over 50 years old, suffering from aortic valve insufficiency with mitral ring calcification and he was a pigeon breeder. He had undergone tooth extraction 3 months previously with no antibiotic prophylaxis.

There is no clear relationship between these two factors considering the length of time between tooth extraction and the beginning of symptoms. His clinical presentation was subacute and the diagnosis was suspected from the outset based on the detection of a cardiac murmur with fever. It is noteworthy that the transthoracic echocardiogram did not reveal vegetations which were only visible on the transesophageal echography.

Blood culture was positive, and a *Streptococcus gallolyticus* was isolated which was sensitive to all beta-lactam antibiotics tested. Treatment was instituted with intravenous ampicillin, and an aminoglycoside was not instituted due to low creatinine clearance. After the identification of *Streptococcus gallolyticus*, therapy was maintained and was well tolerated. A clinical and analytical response was rapidly obtained. Periodical echographic control, including transesophageal echography, demonstrated the disappearance of the vegetation and of the abscess. There was no worsening of the valvular insufficiency.

Once the causal agent was identified, the patient was submitted to colonoscopy for colorectal neoplasia screening and seven polyps were found and removed. Severe dysplasia was observed in one presenting polyp. A preventive action was taken in this patient who had no family history of dysplasia, and who had not been previously examined for it.

The febrile acute episode that was observed at the end of the treatment, accompanied by hypotension and strong shivering had analytical evidence of an acute infectious process. No evidence of recurrent endocarditis, embolism, or other extra-cardiac focus of infection was identified. The patient was nonetheless treated empirically for an infection associated to health care without any apparent focus and it was rapidly resolved with no after-effects.

The patient was discharged asymptomatic and with no signs of cardiac dysfunction.

In conclusion we emphasize the adequate diagnosis and treatment of infective endocarditis and the timely screening of a neoplasia based on the knowledge of the infectious agent.

Conflito de interesses:

Os autores declaram não ter nenhum conflito de interesses relativamente ao presente artigo.

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