

## SEVERE EVOLUTION WITH MULTIPLE SEPTIC DETERMINATIONS IN A PATIENT DIAGNOSED WITH STREPTOCOCCUS GALLOCYTICUS INFECTION

Constantin Marilena<sup>1</sup>, Neața Mădălina<sup>1</sup>, Ștefan Liliana<sup>1</sup>, Acatrinei Eliza<sup>1</sup>, Bumbu Aurelia<sup>2</sup>, Enyedi Mihai<sup>1</sup>, Nica Maria<sup>1</sup>, Voinea Cristina<sup>1</sup>, Calistru Petre<sup>1</sup>

<sup>1</sup>“Dr. Victor Babes” Foundation

<sup>2</sup>“Dr. Victor Babes” Hospital

### ABSTRACT

*Streptococcus gallolyticus*, member of *Streptococcus bovis* group colonizes digestive tubes of birds, cows and human (2.5-15%). Literature describes the association between bacteriemia with *Streptococcus gallolyticus* and colon tumours but also extracolonic lesions (bacterial endocarditis, vertebral osteomyelitis, dyscitis, colangitis, lung tumors, ovarian tumors).

We report the case of a 60 years old male caucasian patient who was diagnosed with vertebral osteomyelitis as the first lesion of *Streptococcus gallolyticus* infection identified by blood culture. Other lesions were diagnosed on aortic valve (bacterial endocarditis), right popliteal artery (popliteal artery thrombosis), right knee (arthritis). Even if there was a clinical and biological improvement during the treatment, the imaging tests done after 30 and 45 days from the diagnosis showed severe aortic insufficiency so surgical intervention for aortic valvuloplasty was done in a short time. Vertebral and popliteal artery lesions have improved within two months of antibiotic treatment. Colonoscopy, which was done 6 weeks from the diagnosis showed colonic polyps – risk factors of *Streptococcus gallolyticus* bacteriemia.

This case proves that *Streptococcus gallolyticus* infection has a silent period followed by severe evolution by multiple septic lesions inspite of the precocious treatment and warn of the necessity of digestive investigations at these patients.

**Keywords:** *Streptococcus Gallolyticus* infection, vertebral osteomyelitis, endocarditis, thromboses

### INTRODUCTION

*Streptococcus Gallolyticus*, a member of *Streptococcus Bovis* group is an opportunistic microorganism that colonizes digestive tube of birds, cows and human, but in the presence of predisposing factors (incipient colonic lesions) may induce bacteriemia with multiple septic determinations. *Streptococcus Gallolitycus* infection is associated with gastrointestinal neoplasia (polyps and colon carcinoma) usually diagnosed after an episode of endocarditis and responds to Penicillin treatment (5).

Data from literature shows that 25-80% of patients with *S.Bovis* have colorectal tumours, 18-62% of the patients have bacterial endocarditis and colon neoplasia, 94% of *S.Bovis* bacteriemia are due to type 1 (*Streptococcus Gallolyticus*) and are associated with colorectal tumors (1).

In 1951 Mc Coy and Mason suggested the relationship between colon carcinoma and bacterial endocarditis but in 1974 the association between *S.Bovis* and colorectal cancer was recognized (1).

Corresponding author:

Constantin Marilena, “ Dr. Victor Babes Foundation ”, 281 Mihai Bravu Avenue, District 3, Bucharest

E-mail: marilena.constantin@cdt-babes.ro

The most frequent extracolonic manifestations are: osteomyelitis, diskitis, neck abscess (1).

Possible mechanisms for *Streptococcus Gallolyticus* to induce colon cancer and bacterial endocarditis are described in literature: chronic inflammation, promotion of angiogenesis, increasing vascular permeability, uncontrolled cellular proliferation (1). *Streptococcus Gallolyticus* has two essential factors of virulence represented by polysaccharides capsules and pili structures which are implicated in paracellular translocations, capacity to escape innate immune system, resistance to complement system. *Streptococcus Gallolyticus* remains in circulation and adheres to endocardium with bio-film formation (2).

### CASE PRESENTATION

A 60 years old, male, caucasian patient presented to my office with very intense right back pain in July 2015. He accused fatigue and had lost about 6 kg in the last 3-4 months. In June 2015 he had anitis and urinary infection with *E. Coli* treated with Cefuroxime, but also an episode of diplopia. Twenty years ago he was operated for left knee menisc fracture. The patient is a smoker (10-15 cigarettes per day) and drinks alcohol occasionally. His medical family history is relevant for: colon cancer (mother), pulmonary tumor (father), leukemia (sister).

Clinical exam showed an overweight patient (BMI= 28.7 kg/m<sup>2</sup>) with medium physical condition, normal pulmonary exam, HR=64/min, BP=100/70 mmHg, right flank pain and right lumbar pain.

Blood tests described WBC = 9170/mm<sup>3</sup>, neutrophilia (87.7%), inflammatory syndrome (ESR = 51 mm/h, Fib = 552 mg/dl, CRP = 8.3 mg/dl, total protein = 7.2 g/dl, albumine = 55.9%, alfa1globuline = 4.3%, iron = 65 mcg/dl, serum ferritine = 903 mcg/dl), positive rheumatic factor, enlarged spleen (abdominal ultrasound).t

Lumbar MRI showed disk hernia with anterolistesis L5-S1. Cerebral MRI described un-specific demyelinating lesions.

Clinical exam and investigations guided us to the diagnosis of: disk hernia; inflammatory syndrome. We excluded other causes for inflammatory syndrome (rheumatic, hematological, pulmonary, prostate causes).

Under the treatment with NSAID drugs, dexametasone and tramadolum the patient continued to have right lumbar pain and he began to present fever. He was hospitalized on 10<sup>th</sup> of August.

Blood tests showed leucocytosis (16200/mm<sup>3</sup>), neutrophilia (86%), lymphopenia (7.4%), thrombocytopenia (141000/mm<sup>3</sup>), inflammatory syndrome (ESR = 37 mm/h, fibrinogen = 488 mg/dl, CRP = 3.3 mg/dl). Urine exam was normal.

Ecocardiography done in the first day of admission and repeated two days later described mild aortic insufficiency but no vegetations.

Blood culture was done.

We initiated intravenous treatment with Amoxipenicillin 2.4 g/day and Gentamicine 160 mg/day.

**Table 1.** Blood culture was positive for *Streptococcus gallolyticus* in the fourth day of hospitalization. Susceptibility test to antibiotic was done (VITEK system)

|                | CMI   | interpretation |
|----------------|-------|----------------|
| Benzylpenicili | ≤0.6  | S              |
| Ampicillin     | ≤0.25 | S              |
| Cefotaxim      | ≤0.12 | S              |
| Ceftriaxon     | ≤0.12 | S              |
| Levofloxacin   | 4     | I              |
| Erithromycin   | ≤0.12 | S              |
| Clindamycin    | ≤0.25 | S              |
| Linezolid      | ≤2    | S              |
| Vancomycin     | 0.25  | S              |
| Tetracycline   | ≥0.16 | R              |

Persistence of right lumbar pain and fever imposed repeating lumbar MRI which described inflamatory lesion in vertebra L1 (Fig. 1)

Two days after hospitalizing patient described pain in the left lower limb in standing position with decreasing intensity in sitting position. Ddimeri test was positive (3589 ng/ml), Doppler ultrasound for veins and arteries and lower limb angio-CT established the diagnosis of left popliteal artery thrombosis (Fig. 2).



Figure 1. Lumbar RMI describes inflamatory lesions in L1

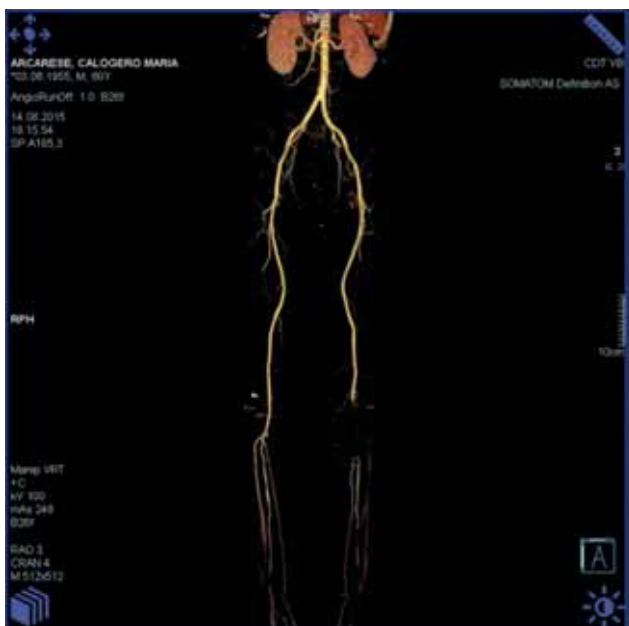


Figure 2. Angio CT for lower limb describes the absence of blood stream in the terminal level of left popliteal artery, the emergencies and proximal levels of anterior and posterior tibial arterieris and fibular artery up to the linkage between the upper third with the lower two thirds of gluteal region

We initiated anticoagulant therapy with enoxaparine in therapeutical dose. Vascular surgery consultation recommended anticoagulant therapy with heparin, and arteriography. It was not recommended emergency surgical intervention for artery thrombosis.

Pulmonary embolism was excluded by chest tomography with contrast substance.

In the sixth day of hospitalization we repeated transthoracic ecocardiogram which described possible vegetations of 9 and 4 mm on the aortic valve. We started the bacterial endocarditis protocol with Penicillin G 18 millions/day (in six doses) and Gentamicine 240 mg/day (in three doses).

Two days later transesophageal echocardiogram confirmed the diagnosis of endocarditis, but it was a lot of uncertainty about the sterility of vegetations. Taking in consideration clinical context we decided to continue the protocol for infectious endocarditis described above. There was no indications for surgery intervention at that moment.

After ten days of treatment we tried to decrease Penicillin dose to 12 millions/day but fever reappeared with an episode of left knee arthritis.

Table 2. Positive diagnosis

|   |  |
|---|--|
| Sepsis  | 4 criteria<br>fever > 38 grd. C; tachycardia > 90/min;<br>leucocytosis > 12000/mm <sup>3</sup> ; positive blood culture  |
| Infectious endocarditis with Streptococcus Gallolyticus | Duke criteria:<br>one major criteria: ecocardiography<br>4 minor criteria: fever ≥ 38 grd.C, vascular phenomena (major arterial embolism), immunological phenomena (positive rheumatoid factor), microbiological criteria (positive blood culture) without meet a major criteria |
| Vertebral osteomyelitis                                 | fever; lumbar pain; inflamatory syndrome; positive blood culture; lumbar RMI; predisposing factors (degenerative lesions of lumbar column)   |
| Popliteal artery thrombosis                             | Positive D-dimeri; Doppler ultrasound of lower limb artery; angio-CT   |
| Left knee arthritis                                     | Clinical exam: tumefaction, inflammation, pain   |
| Disk hernia L5-S1                                       | Lumbar MRI   |

Patient was followed up during hospitalization by monitoring temperature every four hours, blood pressure and heart rate. We did periodic evaluation by ECG, transthoracic ecocardiography, Doppler ultrasound for lower limb arteries. We used CRP to monitor inflammatory syndrome. We made the patient recommendations of minimal mobilization, wearing thoraco-lumbar corset, passive mobilization of lower limbs, hydration.





Lumbar MRI done after thirty-two days of hospitalization showed vertebral lesions in progression comparative the last exam (Fig. 4).

Doppler Ultrasound for left popliteal artery was repeated on day forty-five of hospitalization with no changes of thrombus image.

On October 2015 patient was admitted to Niguarda Hospital – Milano where surgical intervention for aortic valve replacement with biological valve was done (vegetations were sterile at the moment of surgical intervention) with favorable evolution after surgery.

Colonoscopy performed at Niguarda Hospital on October identified two colonic polyps and polypectomy was done (histopatological exam on working).

Doppler ultrasound for the left popliteal artery repeated at Niguarda Hospital showed partial repermeabilisation of left popliteal artery.

The last lumbar MRI which was done three months and two weeks after beginning antibiotic treatment (on november 2015) described an improvement of lesions (Fig. 5).

## DISCUSSION

This case represented a diagnosis and treatment challenge. We could explain lumbar pain



**Figure 5.** LT12-L2 lesions compatible with osteodiscitis in mild improvement; unchanged T11 lesions

by MRI changes but the presence of inflammatory syndrome, fatigue, weight loss imposed other investigations that showed positive rheumatoid factor and splenomegaly. Fever was a key element for diagnosis, the association fever- lumbar pain – inflammatory syndrome imposed repeating lumbar MRI and established the diagnosis of vertebral osteomyelitis. Literature describes the association between osteomyelitis and bacterial endocarditis. The second key element in this case was identification of *Streptococcus Gallolyticus* in blood culture. Its association with bacterial endocarditis is well known. Studying literature data induced the initiation of treatment protocol of infectious endocarditis before the confirmation of diagnosis by transesofageal ecocardiography. Popliteal artery thrombosis and left knee arthritis were septic determinations of bacterial endocarditis. Antibiotic therapy was chosen taking in consideration the antibiotic susceptibility of *Streptococcus Gallolyticus* to antibiotics, treatment protocols for bacterial endocarditis and the penetrance of antibiotic into the bone.

Another question in this case was how *Streptococcus Gallolyticus* induced bacteriemia. Literature data (1,2) (describe the association between *Streptococcus Gallolyticus* bacteriemia and colon tumours. Even if colonoscopy was postponed because of the clinical condition of the patient, it was done two months later from the diagnosis and confirmed the presence of colonic polyps- possible entrance gate for *Streptococcus Gallolyticus*. It is worth to be mentioned that septic determinations appeared in damaged zones (lumbar column with osteophytosis, left knee affected by surgical intervention for broken meniscus).

Studying literature data shows that relationship *Streptococcus Gallolyticus*-colorectal tumours-bacterial endocarditis has a central element - collagen type IV- which is presented at the level of basal membrane of colonic mucosa and endocard ( *Streptococcus Gallolyticus* colonized 10% of normal population, but 55% of

patients with colonic lesions). Bacteria adhere by pili structures and form biofilm (2).

The particularity of the case results from difficulty to establish diagnosis but also to elaborate therapeutic management in the context of multiple septic determinations (endocarditis, osteomyelitis, arthritis, arterial thrombosis) that followed a silent evolution (fatigue, low

grade fever, weight loss). Extracolonic manifestations preceded the identification of colonic lesions (colonoscopy which was done later identified colonic polyps-possible entrance gate for etiological agent).

This case shows the gravity of *Streptococcus Gallolyticus* infection and draws attention to investigate digestive system in these patients.

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