

# Endocarditis of the Native Tricuspid Valve caused by Extended-Spectrum Beta-Lactamase-Producing *Escherichia Coli*

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## Abstract:

*E.coli* endocarditis is rare condition with high risk of complications and mortality. We present the case of a 60 year-old patient with infective endocarditis of the native tricuspid valve due to *E.coli* ESBL. Infective endocarditis (IE) with this strain is even rarer, and very few cases have been described [1-3]. Treatment is based on a multidisciplinary approach and includes early surgical management combined with antibiotic therapy; carbapenem/aminoglycoside combination seems to be first choice.

## Background

Infective endocarditis with tricuspid or pulmonary valve involvement accounts for 5-10% of all presentations. Commonly, the affected population is drug-using patients, patients with healthcare-associated infections, hemodialysis patients, and wearers of intra-cardiac devices or central venous catheters [4]. The most frequently encountered micro-organisms found in IE are gram-positive cocci (staphylococci, streptococci), gram-negative bacilli (5%), and yeasts (3%). Gram-negative bacilli found in IE are generally subdivided into two groups: bacteria of the HACEK group (*Haemophilus spp*, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*) and those of the non-HACEK group, including *Escherichia coli* and *Pseudomonas aeruginosa* [5].

*Escherichia coli* infection accounts for 0.5% of all IEs, with a higher mortality rate than other gram-negative bacilli (20% vs. 4%) [6]. The infectious source is mainly genitourinary. The main risk factors are female gender, advanced age, diabetes, immunosuppression, and intra-cardiac or intra-vascular devices [7]. Excessive alcohol consumption also appears to be a risk factor [1]. In Switzerland, around 11% of *E.coli* strains produce an extended-spectrum beta-lactamase among clinical isolates [8]. The aim of this review is to highlight *E.coli* endocarditis, a rare pathology that can lead to serious complications, and to review its therapeutic management.

**Key words:** endocarditis; tricuspid valve; ESBL *Escherichia coli*; antibiotic treatment

## Case presentation

We report the case of a 60-year-old Caucasian patient with untreated indolent IgG lambda multiple myeloma and pyoderma gangrenosum treated three months previously with prednisone and infliximab. He presented two weeks earlier a fever of 41°C (105.8° F) associated with low urinary tract symptoms. A urine dipstick performed by the physician

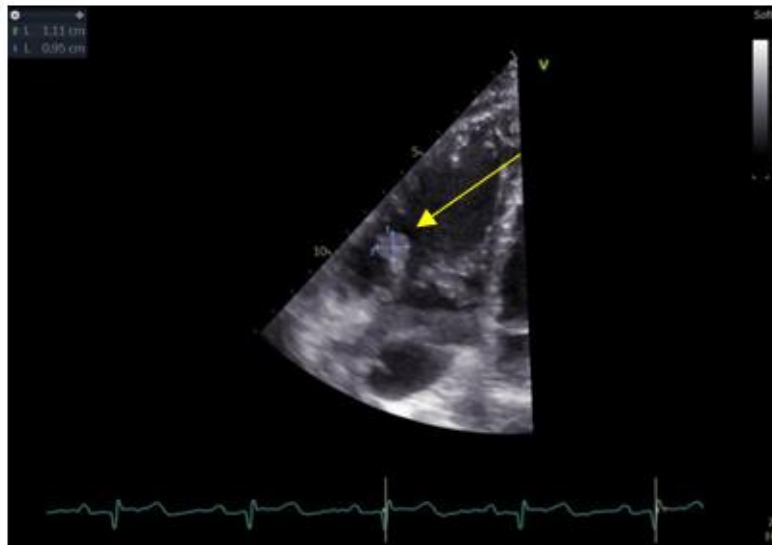
revealed positive leukocyturia and nitrites, prompting empirical treatment with 3rd-generation cephalosporin. Due to lack of improvement after seven days, antibiotic therapy was relayed with fluoroquinolone, and a new urine culture was taken (the first one apparently being sterile). The

evolution remained unfavorable, and he noted the appearance of painful non-erythematous swelling of the right elbow.

He therefore consulted the emergency department and arrived in septic shock, requiring aminergic support (SOFA score 5). Clinical examination showed painful right elbow bursitis, a painless percussion of the renal areas and normal prostate examination. The ECG showed left anterior fascicular block with inversion of T waves from V4-6, the patient was asymptomatic. Troponins were elevated to 200 ng/l, with no kinetic, and pro-BNP increased to 3000 ng/l. Transthoracic echocardiography (TTE) revealed no impairment of overall cardiac function. Microbiological samples (urine culture, blood cultures, puncture of the elbow swelling) were taken, and antibiotic therapy was continued with

piperacillin/tazobactam due to lack of improvement under 3rd generation cephalosporin and fluroquinolone.

Urine and blood cultures then revealed an *E.coli* BLSE infection, allowing for the adjustment of antibiotic therapy to ertapenem after 48 hours. After an initial clinical improvement, the patient subsequently developed solemn chills associated with episodes of hypotension. Despite of negative blood cultures under ertapenem, an aminoglycoside (amikacin) was added to enhance bactericidal effect. Meanwhile, PCR (Polymerase Chain Reaction) analysis of the elbow puncture also came positive for *E.coli*, while the culture remained negative. Given this clinical picture, a new TTE was repeated at day 5, demonstrating a 1.1 x 1.6 cm mobile element on the tricuspid valve associated with mild valve insufficiency (figure 1).



**Figure 1:** Apical view centered on the right cavities. The arrow indicates vegetation.

The diagnosis of *E.coli* ESBL infective endocarditis was retained. The delay in the introduction of targeted antimicrobial therapy undoubtedly contributed to this infectious complication. Because of the causative germ (non-HACEK gram-negative bacillus) and the persistence of a septic state despite adequate antibiotic therapy with ertapenem and amikacin, the patient was referred for surgical management in a university setting. Antibiotic treatment was relayed with meropenem/gentamycin and the patient underwent tricuspid valve replacement with a biological valve on day 9. Treatment with meropenem/gentamycin was maintained for two weeks post-operatively, then relayed with meropenem monotherapy for another four weeks. Post-operative TTE revealed preserved biventricular function and the absence of significant valvular disease, including a biological tricuspid prosthesis with no detectable insufficiency.

Post-operative follow-up was complicated on day 4 by the occurrence of a segmental pulmonary embolism in the right inferior medio-basal lobar associated with a pulmonary infarction, with no repercussions on the right heart chambers. It has been treated with therapeutic oral anticoagulation. On postoperative day 8, the patient had a degree II Wenckebach-type atrioventricular block (AVB), which was transient and had no hemodynamic repercussions. The additional work-up (coronary angiography, TEE) did not reveal any significant coronary lesions or signs of wall abscesses. No treatment was recommended given the patient's asymptomatic condition and rhythmic stability. The clinical course was subsequently favorable, and the patient was transferred to rehabilitation.

## Discussion

The prevalence of non-HACEK gram-negative IE, particularly *Escherichia coli*, is rare but has been increasing in recent years. In most described cases in the literature, *E. coli* IE is the consequence of a urinary

tract infection in the presence of the above-mentioned risk factors [1,9,10]. As observed in our patient, a long duration of symptoms, with sustained bacteremia before initiating targeted antibiotic therapy, is also a risk factor [1,]. This underlines the importance of performing microbiological examinations in the presence of a complicated UTI. On the other hand, in the described case, microbiological cultures on the explanted valve and PCR for bacterial DNA were negative, as were tests for other pathogens such as *Bartonella henselae*, *Coxiella burnetii*, and *Brucella* sp. However, these tests were carried out after nine days of targeted antibiotic treatment, which may have contributed to the negative results.

A possible link between the virulence factors produced by specific *E. coli* serotypes, which could facilitate adhesion to heart valves, has been suggested as an additional factor predisposing to IE [11]. In this respect, studies have shown that most of the *E. coli* found in patients with IE belong to the same phylogenetic group as the "ExPEC" (extra-intestinal pathogenic *E. coli*), described for their virulence [12,13]. In addition, Gram negative bacteria release toxin lipopolysaccharides (LPS) which induces cardiac disturbances including endocarditis [14].

The most frequent complications of *Escherichia coli* infective endocarditis are peripheral embolization (24%), heart failure (22%), intracardiac abscess (18%), left ventricular aneurysm (6%), and atrioventricular block (AVB) (6%) [15]. Our patient presented several of these complications, including multiple peripheral embolizations (elbow, pulmonary) and AVB. Nevertheless, etiology cannot be established, as pulmonary embolism and AVB could also have been secondary to surgery. It should be noted that atrioventricular blocks have already been described post-interventionally in patients with tricuspid valve endocarditis [16].

The recommendations of the European Society of Cardiology (2023) [16] call for early surgical management of non-HACEK gram-negative IE, combined with antibiotic therapy for at least 6 weeks. Antibiotherapy includes a beta-lactam combination (penicillins, cephalosporins or carbapenems) with an aminoglycoside for at least 14 days, or with a fluoroquinolone for 6 weeks, due to the often poorly controlled nature of infections and the high risk of complications [18]. For ESBL-producing Enterobacteriaceae, the choice is limited to a carbapenem/aminoglycoside combination [3]. There is very little data on the best combination for this type of infection.

Around thirty described cases of *E.Coli* IE were reported in 2018 [11]. Of these, six involved *E.Coli* ESBL IEs and were treated as follows: imipenem alone (2 cases), imipenem/gentamycin (1 case), imipenem/amikacin (1 case); meropenem/gentamycin (1 case). No data are available for the sixth case. More recently, one patient has been reported to have been treated with a 6-week course of imipenem-cilastatin monotherapy [2]. In this case, valve replacement was unnecessary, the outcome being favorable with antibiotic treatment alone. There are no data on the use of ertapenem in non-HACEK gram-negative IE.

## Conclusion

This case highlights the importance of taking microbiological samples before starting antibiotic therapy, targeting treatment as quickly as possible in order to avoid severe complications such as endocarditis. From a therapeutic point of view management remains multidisciplinary. It must consider the risk of complications associated with uncontrolled infection, as well as the patient's clinical condition, comorbidities, and operative risk. For non-HACEK gram-negative IE, surgical treatment is often necessary in association with antibiotic therapy, combining beta-lactams with an aminoglycoside or fluoroquinolone.

## Conflicts of Interest

This article is written in the absence of conflicts of interest.

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