INFECTIONOUS ENDOCARDITIS SECONDARY TO NEISSERIA SPP IN PATIENTS WITH CARDIAC PROSTHESES: RARE ENTITY AND DIFFICULT DIAGNOSIS

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Abstract
Infectious endocarditis is an infrequent pathology but with a very significant morbidity and mortality context. The most common responsible germs are streptococci and staphylococci. Neisseria is a strain of bacteria characterized by several subgroups such as gram-negative diplococci which are present in the respiratory tract and which are generally harmless and other gram-negative bacteria such as Neisseria gonorrhoeae which are known to be pathogens involved in several pathologies. We report a case of infectious endocarditis in a 37-year-old patient with mitral valve replacement who presented a prolonged febrile syndrome with discovery on transesophageal echocardiography of vegetation and blood cultures of an SP Neisseria.

INTRODUCTION
Infectious endocarditis is an infrequent pathology but with a very significant morbidity and mortality context. Within our Maghreb context, the prevalence of rheumatic valve disease remains high, which favors the increase in the prevalence of this pathology. The emergence of new risk factors contributes to the increasing appearance of this pathology in our society. The most common responsible germs are streptococci and staphylococci.

Neisseria is a strain of bacteria characterized by several subgroups such as gram-negative diplococci which are present in the respiratory tract and which are generally harmless and other gram-negative bacteria such as Neisseria gonorrhoeae which are known to be pathogens involved in several pathologies. The presence of infective endocarditis secondary to Neisseria infection remains rare with fatal consequences in most cases.

During this paper we tried, through a case report and review of the literature, to objectify the singularity and the danger presented by this type of infection, particularly in patients with intracardiac prosthesis.

CASE REPORT
We report the case of Mrs. OF, 37 years old, treated for an acute rheumatoid arthritis for 17 years treated with Penicillin M until the age of thirty, with a mitral valve replacement at the age of 13 years by a mechanical valve currently under VKA.

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In 2015, the patient presented an acute ischemia of the lower limbs related to emboli of the primary iliac arteries treated by embolectomy. Etiological investigation at the time did not show an obvious cause.

The patient had no known cardiovascular risk factors, admitted for the management of long-term fever with deterioration of general condition.

The history of the symptoms dates back to one month before her admission, with the onset of an unstated fever associated with a dry cough symptomatically treated by her attending physician with antibiotic therapy based on amoxicillin and clavulanic acid without improvement. The patient was admitted at the emergency room due to the persistence of fever and the worsening of her general condition.

The emergency room admission examination found a conscious patient eupneic, with normal temperature at 37.6°C, normally stained conjunctiva. Cardiovascular examination revealed a sternotomy scar with heart sounds perceived at a regular rate and an audible protosystolic click from a mechanical prosthesis without associated signs of heart failure.

Pleuropulmonary exam showed right basithoracic crackles. Neurological, mucocutaneous and osteoarticular examination were normal with good oral hygiene.

The EKG showed a steady sinus rhythm with a heart rate of 69bpm, with no repolarization or rhythm abnormalities. The chest x-ray showed cardiomegaly with a cardiothoracic index of 0.53 and the presence of a right basithoracic density.

The biological assessment showed an HB at 11.6g/dl, a CRP at 183mg/l, leukocytes at 6800/µl, with normal renal function and a normal hemostasis checkup.

The patient was initially admitted to the virology and infectious diseases department and was put on Bi antibiotic therapy based on ceftriaxone and ciprofloxacin. Given the clinical and biological non-improvement, a transthoracic and transesophagealechocardiography were requested as part of the etiological assessment.

Transthoracic echocardiography showed a functioning mitral prosthesis with an average gradient at 4mmhg with an undilated, non-hypertrophied left ventricular of good overall and segmental contractility.

The transesophageal echocardiography objectified a filiform moving image measuring 6 * 2 mm on the atrial and septal side of the prosthesis, suggesting vegetation on a mitral prosthesis.

**Figure 1:** Image of vegetation at the level of the mitral prosthesis on transesophageal echocardiography.
The patient was transferred to the cardiology department for further care. 03 series of blood cultures including one carried out at the time of a fever peak were carried out and which came back negative. Considering the high clinical probability, the patient was put on amoxicillin 12g / 24h and gentamycin 5mg / 24.

![Image](image.jpg)

**Figure 2:** Image showing the mean gradient measured on transesophageal echocardiography.

The extension workup showed a right basithoracic density of infectious appearance with the presence of a lacunar cerebral lesion of the frontal horn of the left lateral ventricle probably of old occurrence.

Nine days after the start of antibiotic therapy, the patient presented a constricting chest pain at rest. The EKG was normal, but echocardiography control showed an increase in the transprosthetic gradient from 4 to 16mmhg with increasing vegetation volume. The decision to have a mitral valve replacement was made. The bacteriological study of the removed prosthesis showed the presence of Neisseria SPP and given the occurrence of a technical problem; the identification of the precise strain was not retained.

The patient stayed for 5 days in the intensive care unit with good clinical and biological improvement.

**Discussion:**
Infectious endocarditis presents as ulcerative lesions associated with grafting on the endocardium, valve (IE on native valve), much more rarely parietal, or on an intracardiac prosthesis (IE on prosthesis) of a microorganism, the more often bacterial.

In France, the crude annual incidence of AE in adults was three cases per 100,000 inhabitants (1)

The incidence is twice as high in men as in women and increases dramatically with age (1)

Three stages are involved in the development of IE. During the first stage, there is a deposition of fibrin and platelets on the valve endothelium facilitated by pre-existing mechanical or inflammatory endothelial damage. The second stage involves bacterial adhesion to the valves during transient bacteremia. The third stage corresponds to the multiplication of bacteria at the level of the valves with extension and local destruction followed by distant dissemination (1).

An infectious endocarditis should be suspected in front of any long-term fever without obvious cause, particularly if there is an appearance or modification of a pre-existing heart murmur or the appearance of recent vascular or immunological signs. The physical examination must also focus on the search for a source (urinary or dental ...) or the search for extension (splenic, renal, cerebral ...) and complications such as signs of heart failure or stroke Confirmation of infective endocarditis is based on modified DUKE criteria (major and minor citers).
Definite infective endocarditis
Pathologic criteria
(1) Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
(2) Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis
Clinical criteria
(1) 2 major criteria; or
(2) 1 major criterion and 3 minor criteria; or
(3) 5 minor criteria
Possible infective endocarditis
(1) 1 major criterion and 1 minor criterion; or
(2) 3 minor criteria
Rejected
(1) Firm alternate diagnosis explaining evidence of infective endocarditis; or
(2) Resolution of infective endocarditis syndrome with antibiotic therapy for ≤4 days; or
(3) No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for ≤4 days; or
(4) Does not meet criteria for possible infective endocarditis, as above

Figure 1: Definition of infective endocarditis according to the proposed modified Duke criteria (2).

As part of the diagnosis of an IE, it is essential to perform three pairs of blood cultures over 24 hours spaced at least one hour apart before taking any antibiotic. If no positive results, we need to repeat the blood cultures three days later and check for negative blood culture endocarditis.

Cardiac ultrasound is the gold standard that documents valve infection and assesses the associated valve damage and its course. Transthoracic ultrasound (TTE) is the first-line examination for rapid, non-invasive assessment of valve damage and associated systolic dysfunction. Because of its better sensitivities and specificities, transesophageal ultrasound (TEE) is recommended in cases of strong suspicion of AEs with negative or poor quality TTE, in case of prosthetic valve material or implanted material, and to confirm the anomalies identified in ETT.(1)

A full extension workup should be requested, especially in the event of infectious endocarditis of the left heart. It is necessary to eliminate the presence of distant septic foci, in particular at the level of the liver and the spleen by an appropriate imaging (CT scan). If there is a clinical suspicion of a vascular accident or mycotic aneurysm, a brain scan should be performed. In case of suggestive symptomatology, spondylodiscitis should be ruled out by standard x-rays or, better, MRI. On the biological level, it is necessary to look for glomerulonephritis by quantifying proteinuria as well as the presence of vasculitis by looking for circulating immune complexes and rheumatoid factors and other immunological markers (antinuclear factors, etc.). (3)

Neisseria spp. include a group of closely related gram-negative bacteria that are primarily commensal inhabitants of the mucus membrane of mammals. Within the Neisseria spp., Neisseria gonorrhoeae and Neisseria meningitides are considered important pathogens [4]. However, several Neisseria species other than these two species are also reported to act as human pathogens, with some acting as opportunistic pathogens sporadically involved in infections(4). Infectious endocarditis caused by Neisseria spp. has been reported for N. gonorrhoeae, N. meningitidis, N. elontgata, N. mucosa, N. sicca, and N. bacilliformis(4)

Endocarditis due to Neisseria gonorrhoeae, observed in young adults without pre-existing valve involvement, is the most serious complication of disseminated gonorrhea. This localization was described by Thayer in 1896. It was frequent before the use of antibiotics, 11 to 26% of endocarditis, and its outcome was almost always fatal within 11 days to 14 weeks.

Currently 25 known Neisseria species have been isolated in humans and animals. Neisseria gonorrhoeae and N. meningitidis are the 2 most known pathogenic Neisseria species. Other Neisseria species are common commensal inhabitants of the upper respiratory tract and oral cavity of humans and other animals, but they have been implicated in clinical disease in occasional cases, particularly in immunocompromised patients.(5)
currently no records have been maintained for the assessment of the frequency of infective endocarditis of Neisseria SP in general. Among Neisseria species, N. gonorrhoeae and N. elongata are known to affect cardiac valves.

A review of the literature from 1966 to 2007 revealed that only 18 cases of endocarditis due to N. elongata met the modified Duke criteria (Lamas & Eykyn, 1997) for definite or possible infective endocarditis (Table 1). Of the 18 cases, 15 were caused by N. elongata subsp. nitroreducens, two by N. elongata subsp. elongata, and one by N. elongatagladytica.(6)

Table 1:- Various studies showing the prevalence and characteristics of infectious endocarditis due to N. ELONGATA(6).

Valvular involvement seen in gonococcal endocarditis prior to the antibiotic era is well-documented in 120 cases. The aortic valve was involved in 50% of cases; the mitral valve in 40%, and the pulmonic valve in 15%. Purely left-sided involvement occurred in 80% of cases. Gonococcal endocarditis became exceedingly rare following the advent of effective antimicrobial therapy.

During a 30 year period from 1942-1972, eight cases appeared in the literature. During this period, two patients underwent valve replacement, and seven of the eight survived. Interestingly, the only two cases displaying a double quotidian fever curve in the antibiotic era occurred during this period.(7)
Conclusion:
Infectious endocarditis caused by neisseriaspp remains relatively rare, especially after the advancements made with the arrival of the different families of antibiotics. However, under certain conditions, this family of bacteria can emerge and give rise to severe infectious endocarditis. Neisseria elongata and gonorrhoeae remain the strains with more affinity for cardiac involvement. Awaiting the various studies grouping the different strains of neisseriaspp and their role in the occurrence of infectious endocarditis, this family of bacteria should always be suspected in the presence of patients with a high clinical probability and negative blood cultures so as not to miss out on a diagnosis that may affect the prognosis of the patient.

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