

Let's Talk About a New Urogenital Pathogen: *Actinomyces Neuii*

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Abstract

In traditional bacterial cultures of clinical samples, the presence of coryneform has often been considered as local flora, but it is well known that in patients with predisposing factors, these micro-organisms may have a pathogenic implication that would be underestimated. Among other causes, this is due to the difficulty in making an adequate identification to species level. The advent of mass spectrometry in clinical laboratories has greatly facilitated this task. We describe a clinical case of *Actinomyces naoi* urinary tract infection in an elderly multipathological patient with urinary catheterization.

For this purpose, a descriptive clinical-microbiological study of *A. naoi* as a pathogen was performed. It was identified by Maldi-TOF mass spectrometry. The clinical course was satisfactory after antibiotic treatment with amoxicillin/clavulanic acid.

In urine cultures, if there is a significant monomicrobial count of coryneform micro-organisms, we should rule out micro-organisms potentially involved in infection before reporting the result as local microbiota.

Keywords: *Actinomyces Neuii*, Uropathogen, Amoxicillin/Clavulanic Acid, Urogenital Microbiota.

1. Introduction

Classically, coryneforms have been considered to be skin and mucosal flora found contaminating cultures, but about 20% of these isolates may have pathogenic involvement. Proper identification of the different species of *Actinomyces* spp. in clinical microbiology has long been a challenge, until the widespread use of mass spectrometric techniques in clinical laboratories, such as Maldi-TOF, which has facilitated their increased involvement in various types of infections [1-4].

Actinomyces neuii is a small, catalase-positive, unbranched, gram-positive bacillus that does not produce sulphur granules. It can grow in both aerobiosis and anaerobiosis. It has been isolated from many different types of specimens such as infected atheroma's, abscesses, endophthalmitis, endocarditis and chorioamnionitis [1,5-7]. *A. neuii* is the only species of *Actinomyces* spp. so far associated with urinary pathology, especially in patients with

uroolithiasis or urinary catheterization [3,8,9].

We present a case of a urinary tract infection caused by *A. neuii* in an elderly patient with extensive underlying pathology and urinary catheterization, with a good clinical course.

2. Presentation of the Case

The patient was an 89-year-old man admitted to the neurology department for an ischaemic stroke. His medical history included hypertension, dyslipidemia, cataracts, type 2 diabetes mellitus and benign prostatic hyperplasia.

Three days after admission, he presented with frank hematuria in the urine collection bag and purulent exudate around the urinary meatus. Samples of exudate from the meatus and urine were sent to Microbiology for culture. The analytical data presented at that time are shown in table 1.

	Patient	Normal
Biochemistry:		
Urea	27 mg/dl	< 40mg/dl
Creatinine	0.95 mg/dl	0.5 – 1.1 mg/dl
C reactive protein	34.8 mg/dl	< 2mg/dl
Procalcitonin	0.1 nanog/dl	<0.5 nanog/dl
Blood count:		
Hemoglobin	14.2 g/dl	14 – 16 g/dl
Leucocytes	7,988/mm ³	4,000 – 10,000/mm ³
Percentage of neutrophils	86%	40 – 70%
Platelets	283,000/mm ³	150,000 – 400,000/mm ³
Coagulation:		
Prothrombin time	13.5 s	11.5 -14.5 s
INR	1.17	0.9 – 1.5
Fibrinogen	383 mg/dl	200 – 400 mg/dl

Table 1: Analytical values of the patient:

Immediately after obtaining the clinical samples, antibiotic treatment with amoxicillin/clavulanic acid 1000/62.5 mg intravenous every 8h was prescribed. Five days later, due to a good clinical evolution with absence of urinary symptoms and stability of the underlying pathology, the patient was discharged to the chronic patient area. Urine and periurethral exudate cultures were taken as described below.

3. Periurethral Exudate

The swab sample was seeded on Chocolate and Thayer-Martin agar (Becton-Dickinson, Spain), in a 10% CO₂-enriched aerobic atmosphere at 37°C for 48 hours. Pure growth of small greyishwhite, alpha-haemolytic, catalase-positive and oxidase-negative colonies could be observed on chocolate agar. A subculture on blood agar (BD Columbia Agar 5% sheepblood®, Becton Dickinson) was performed for identification by mass spectrometry (Vitek MS) resulting in *Actinomyces neuii* with high reliability.

An antibiogram was performed using the disc-plate technique against penicillin, meropenem, imipenem, amoxicillin/ac. clavulanate, piperacillin/tazobactam, clindamycin and vancomycin, being sensitive to all of them according to EUCAST 2022 (*European Committee on Antimicrobial Susceptibility Testing*) criteria. E-test strips (Liofilchem, Roseto degliAbruzzi, Italy) were used for sensitivity to moxifloxacin and metronidazole, the latter being the only resistant antibiotic.

4. Urine

In the urine culture, on CHROMagar Orientation chromogenic medium with semi-quantitative grid seeding, more than 100,000 CFU/ml of *A. neuii* grew predominantly as flat greyish-white colonies. Subculturing was performed on blood agar for subsequent identification by mass spectrometry.

5. Discussion

Actinomyces neuii is an opportunistic gram positive, its isolate represents 17% of all clinically significant *Actinomyces*

spp. Isolates [1,2]. In *A. neuii* subsp. *neuii*, the predominant morphology is diphtheroid forming V-shaped clusters. Colonies are circular and smooth, alpha-hemolytic, convex, opaque and white with well-defined borders. The subspecies *A. neuii* subsp. *anitratus* has the same characteristics except for haemolysis and the absence of nitrate reduction [3,10]. In our case it was *A. neuii* subsp. *neuii* as it was haemolytic.

A. neuii is an exception within its genus due to its ability to grow in aerobic atmosphere, and thus to be able to grow in a wide range of tissues. The location of the abscesses it forms, usually together with mixed anaerobic flora, is similar to those caused by other *Actinomyces* spp, supporting it as an opportunistic pathogen of endogenous origin⁴. However, it is very rare to isolate *A. neuii* from clinical specimens of intra-abdominal or intrathoracic infections, where the presence of other *Actinomyces* spp. is relatively common [4,5,11].

A. neuii can be found in the female urinary tract, being more frequent in women with overactive bladder and incontinence [6,12].

Recent studies have shown that some diphtheroids isolated in urine may have clinical relevance, such as *Agtinotignum schaali* and *Actinomyces neuii*, as in the present case, whose involvement in the infection was considered due to their growth in pure and abundant culture.

The potential link between diphtheroids and infection has classically been hampered by the limited capacity of clinical microbiology laboratories to make an adequate identification to species level. Today, despite the widespread availability in clinical laboratories of more accurate identification methods such as mass spectrometry, or even sequencing in some of them, it has been difficult to identify the species or even sequencing for some of them, the information on the presence of a potentially pathogenic diphtheroid in a clinical sample culture depends on its predominance in culture [4]. That is to say, generally, if

its presence is not predominant, it will be reported as part of the local flora, leaving it entirely to the clinician's discretion to establish an antibiotic treatment that can cover it [3,7]. About 20% of diphtheroids suspected of involvement in a soft tissue infection meet the criteria to be really implicated in it, while in blood cultures, the significance of these increases to over 40% [7].

Although the gold standard bacterial identification method, with some exceptions, is the identification by 16s rRNA gene sequencing, its diagnosis has increased thanks to the presence of mass spectrometry equipment in clinical laboratories, as it is cheaper, faster and does not require specially trained workers [4,13]. When identification by biochemical or phenotypic testing is used, classification as another species or another closely related genus is very frequent. With the experience of the microbiologist in our case, a diphtheroid was suspected by naked eye recognition of compatible colony morphology and by fresh visualisation, and culture isolates were prepared for identification by MALDI-TOF, with high confidence identification [4].

The correct identification of a micro-organism involved in the infection guarantees the establishment of a more appropriate treatment by the clinician. The clinical microbiologist must not only identify the micro-organism, but must also report the possible degree of its involvement in the infection through knowledge of the patient's clinical data and history, which is one of his main functions. It must be taken into account that any commensal micro-organism can act as a pathogen depending on the degree of immunity of the patient, presence of comorbidities and medical procedures performed.

Infections caused by *Actinomyces* spp. have an indolent course, including actinomycosis, and usually resolve favourably with appropriate antibiotic treatment [3]. Treatment of abscesses with antibiotic therapy alone is usually not sufficient, requiring drainage and prior debridement for complete resolution [3,14]. In this case, it was a focus without underlying collection, a lower urinary tract infection, and with possible origin in the placement of the urinary catheter, so the appropriate treatment should be based on a replacement of the catheter and antibiotic treatment with good urinary elimination (amoxicillin/ac. Clavulanic acid). *A. neuii* is usually susceptible to beta-lactams, vancomycin, erythromycin and clindamycin. According to the literature, antibiotic treatment used in this type of infection has in most cases included beta-lactams and/or vancomycin [4,15]. *Actinomyces* spp. is very susceptible to all antibiotic groups except metronidazole [8,15, 16].

6. Conclusion

In the presence of a monomicrobial choriomycete in a clinical culture, it is advisable to investigate the underlying pathology of the patient, as well as other possible predisposing factors, as in a non-negligible percentage it may be a micro-organism that is truly involved in the infection. Although *Actinomyces neuii* colonises skin and mucous membranes, we should not forget that it could also be involved in genitourinary infections.

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