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A case of stroke as a unique sign of subclinical infective endocarditis by *Abiotrophia defectiva*: a case report

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Abstract

Purpose Here we describe a patient admitted for a stroke that was unexpectedly correlated with subclinical infective endocarditis attributable to a rarely opportunistic pathogen, *Abiotrophia defectiva*.

Case report A 75-year-old man presented with a stroke. Transesophageal echocardiography suggested vegetation on all aortic valve cusps, despite the absence of clinical or laboratory signs of infection. Surprisingly, three sets of blood cultures collected without fever were positive for *A. defectiva*. Although the patient did not exhibit classic signs of infection during hospitalization, the severity of the valve condition necessitated replacement with a bioprosthesis.

Conclusions This clinical case underscores the importance of investigating the infective origin of endocarditis, even in the absence of clinical or laboratory evidence. Physicians should maintain a high level of suspicion, especially in patients with highly suggestive anamnestic characteristics.

Keywords Abiotrophia defectiva, Infective endocarditis, Valve replacement, Blood cultures, MALDI-TOF, Case report

Background

Among endocarditis cases, approximately 90% are of infective origin [1]. Infective endocarditis (IE), particularly bacterial forms, primarily involves the heart valves, but can also affect the endocardium or intracardiac devices. Most bacterial endocarditis are caused by viridans streptococci, *Streptococcus gallolyticus*, *Staphylococcus aureus*, coagulase-negative staphylococci, enterococci, and the HACEK group (*Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella)*. Less commonly, IE is caused by pneumococci, *Candida* spp, polymicrobial infections, and non–HACEK Gram-negative bacilli [2]. Among the latter, *Serratia marcescens* [3], *Coxiella burnetii*, *Bartonella* spp., and *Brucella* spp [4, 5] are the most significant culture-negative pathogens to be identified. *Serratia marcescens*

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typically affects intravenous drug users and can lead to rapid and severe infections [6, 7]. *Coxiella burnetii* and *Bartonella* spp. account for 61.4% and 20.7% of culture-negative IE, respectively [8, 9], characterized by aortic valve vegetation more than *S. aureus* and *Streptococcus* spp [10]. Finally, *Brucella* prosthetic valve endocarditis is a rare but life-threatening complication of brucellosis which remains a diagnostic challenge and the optimal treatment is still debated [11]. In high-income countries, the incidence of IE ranges from 3 to 10 cases per 100,000 inhabitants per year [12] with an average patient age of 58 years. Beyond age 60, risk factors include male sex, intravenous drug use, history of previous IE, poor dental hygiene, odontoiatric treatments and intervention procedures, prosthetic valves or intracardiac devices, history of valvular disease (e.g., rheumatic heart disease, mitral valve prolapse, aortic valve disease, mitral regurgitation), congenital heart disease (i.e., aortic stenosis, bicuspid aortic valve, pulmonary stenosis, ventricular septal defect, ductus arteriosus patency, coarctation of the aorta and tetralogy of Fallot), indwelling intravenous catheter, immunosuppression, and hemodialysis [13]. Currently, increasing rates of antibiotic resistance, opportunistic germs, and even fungi affect a significant proportion of all IE patients [14]. Viridans streptococci-like organisms, such as Nutritional Variant Streptococci (NVS) of the *Lactobacillales* order account for 4–8% of IE cases and require thiol-enriched culture media [15, 16]. The genus *Abiotrophia*, identified through 16 S ribosomal rRNA sequencing in 1995, also belongs to this group [17]. *Abiotrophia* includes variable Gram-positive, catalase-negative, and facultatively aerobic bacteria often forming chains, and responsible for approximately 5–6% of streptococcal endocarditis cases [18]. *A. defectiva*, part of the normal oropharyngeal, genitourinary, and intestinal flora, is notable in this group [19]. Due to their specific nutritional requirements, these bacteria are often misdiagnosed as culture-negative, which leads to underreporting of their role in endocarditis.

Case presentation

Figure 1 depicts the historical and information timeline from the case of a 75-year-old man who was admitted to the Stroke Unit with verbal expression deficits, right limb hypoesthesia, right hemianopsia, central paresis of the right VII cranial nerve, right limb slivering, and a score of 12 on the National Institute of Health Stroke Scale (Italian version) [20]. The patient's home therapy was reported to include Rivaroxaban and approximately six months prior, the patient had undergone aortic valve replacement and a Dacron patch placement for the enlargement of the ascending aorta, alongside atrial fibrillation, splenic infarction, and transient ischemic attack. CT angiography of the brain revealed a proximal thrombotic occlusion of the inferior, dominant M2 branch of the ipsilateral middle cerebral artery, with a relatively poor parenchymogram of the relevant territory. Blood tests showed no signs of infection (WBC $10.22 \times 10^3/\mu L$, CRP 5.83 mg/dL,

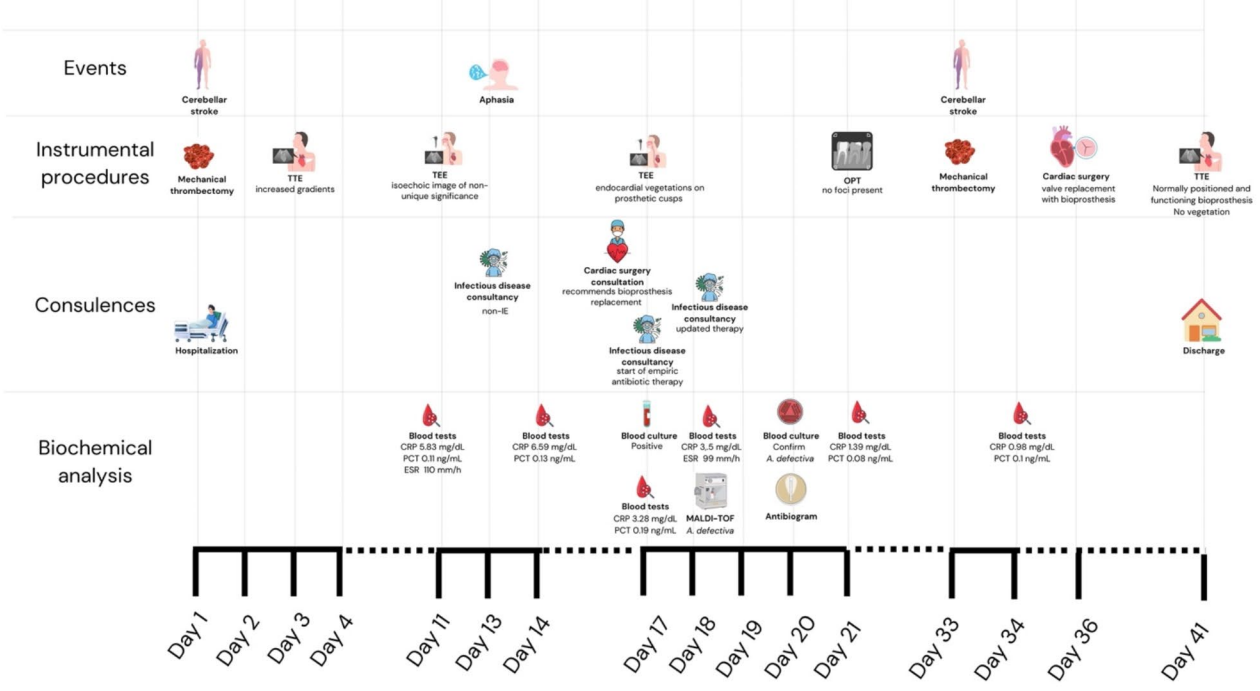

Fig. 1 Historical and information timeline from this case

PT (INR) 1.20, APTT 36 s/1.2 ratio, fibrinogen 439 mg/dL, ESR 110 (1 h), procalcitonin 0.11 mg/dL). Transthoracic echocardiography (TTE) was performed revealing an increase in transvalvular gradients compatible with aortic stenosis. TEE, subsequently performed due to its higher sensitivity and specificity, showed degeneration of the bioprosthesis and an 8 mm mobile isoechogenic image adherent to the non-coronary cusp along with other smaller images on the other two cusps, compatible with endocardial vegetations (Fig. 2). This finding raised suspicions of an ongoing IE, thus 3 sets of blood culture bottles were drawn [21] and processed by BactAlert®. Both aerobic and anaerobic blood cultures resulted positive after 15.2/15.7 and 16.2/15.5 h, respectively. Following the European Society of Cardiology (ESC) guidelines [22], and due to strong suspicion of stroke caused by IE, empirical antibiotic therapy was initiated with vancomycin (1 g x 2 times/day) and ceftriaxone (2 g/day) starting on the same day, a choice based on literature recommendations [15] and the epidemiology of our hospital indicating staphylococci as the first cause of IE. Gentamicin was avoided due to imminent surgery, and because the recent supporting evidences that there is no benefit in terms of mortality reduction by using gentamicin in association with ceftriaxone [23], while add nephrotoxicity and hepatoxicity [24]. To identify the etiological agent, blood samples from positive bottles were processed using the Walk Away Specimen Processor (WASP), which highlighted the presence of Gram-positive cocci arranged in chains, suggestive of streptococci-like organisms (Fig. 3A). At the same time, cultures on Chocolate Agar + PolyVitex® Biomerieux and Columbia Agar supplemented with 5% sheep blood showed insufficient growth after 24 h at 37 °C. Reincubation on Chocolate Agar + PolyVitex at 5% CO_2 for 48 h resulted in appreciable growth (Fig. 3B). Being a particularly demanding pathogen, Matrix-Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF®) was used for its identification as previously reported [25, 26]. MALDI-TOF® revealed the presence of *A. defectiva* confirming the suspect of IE despite the absence of symptoms and blood infection markers. Following the identification of the pathogen, the therapy was adjusted to ceftriaxone (2 g daily) for six weeks, discontinuing vancomycin. Although empirical therapy was already in progress, an antibiogram identification was carried out using E-TEST® (Biomerieux) (Fig. 3C-F) as per EUCAST 2023 [27], allowing for the evaluation of the Minimum Inhibitory Concentration (MIC) and the antibiotic susceptibility interpretation by referring to the non-species related PK/PD breakpoints set by EUCAST [27] as reported in Table 1. The antibiogram revealed resistance to amikacin, gentamicin, and tobramycin while showing susceptibility to aztreonam, ciprofloxacin, levofloxacin, piperacillin/tazobactam and ticarcillin/clavulanic acid (Table 1). Regrettably, MIC for ceftriaxone could not be tested due to unavailability at the time. Given that *A. defectiva* is a common resident and opportunistic pathogen of the oral cavity, orthopantomography (OPT) of the dental arches was performed, revealing a weak area of osteo-rarefaction in the periradicular region of tooth 45, suggestive of a resolving inflammatory process. Finally, due to the IE-related inflammatory process, the aortic valve was compromised and required replacement with a bioprosthesis. Before discharge the newly implanted bioprosthesis appeared free of vegetation and transvalvular gradients were normal on TTE.

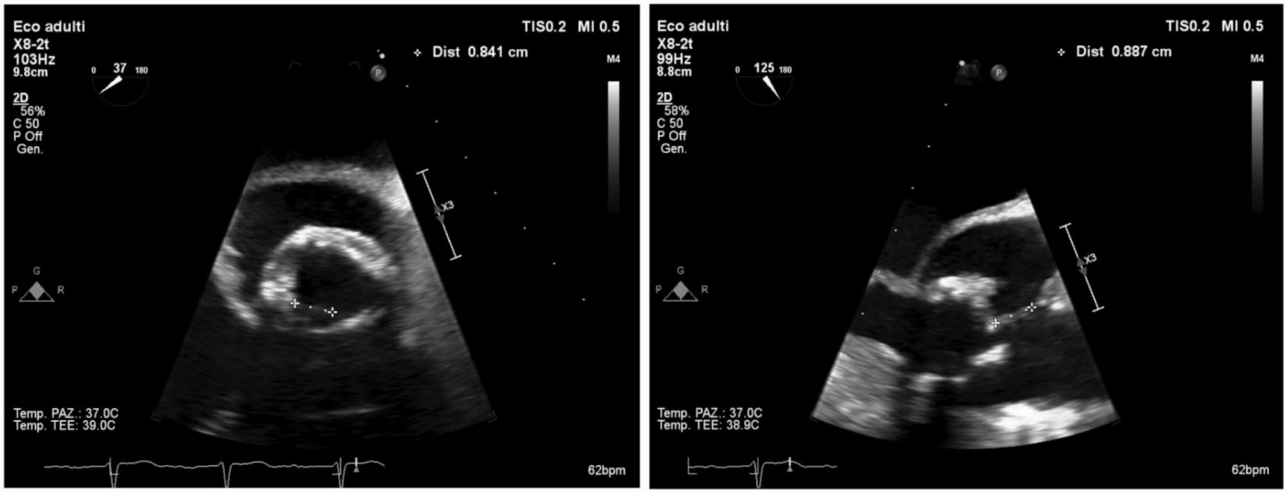

Fig. 2 Transesophageal echocardiogram (TEE) imaging indicating the presence of a linear image with passive movement adherent to the non-coronary cusp (about 8 mm) associated with other small images on the other two cusps, compatible with endocardial vegetations on the prosthetic cusps

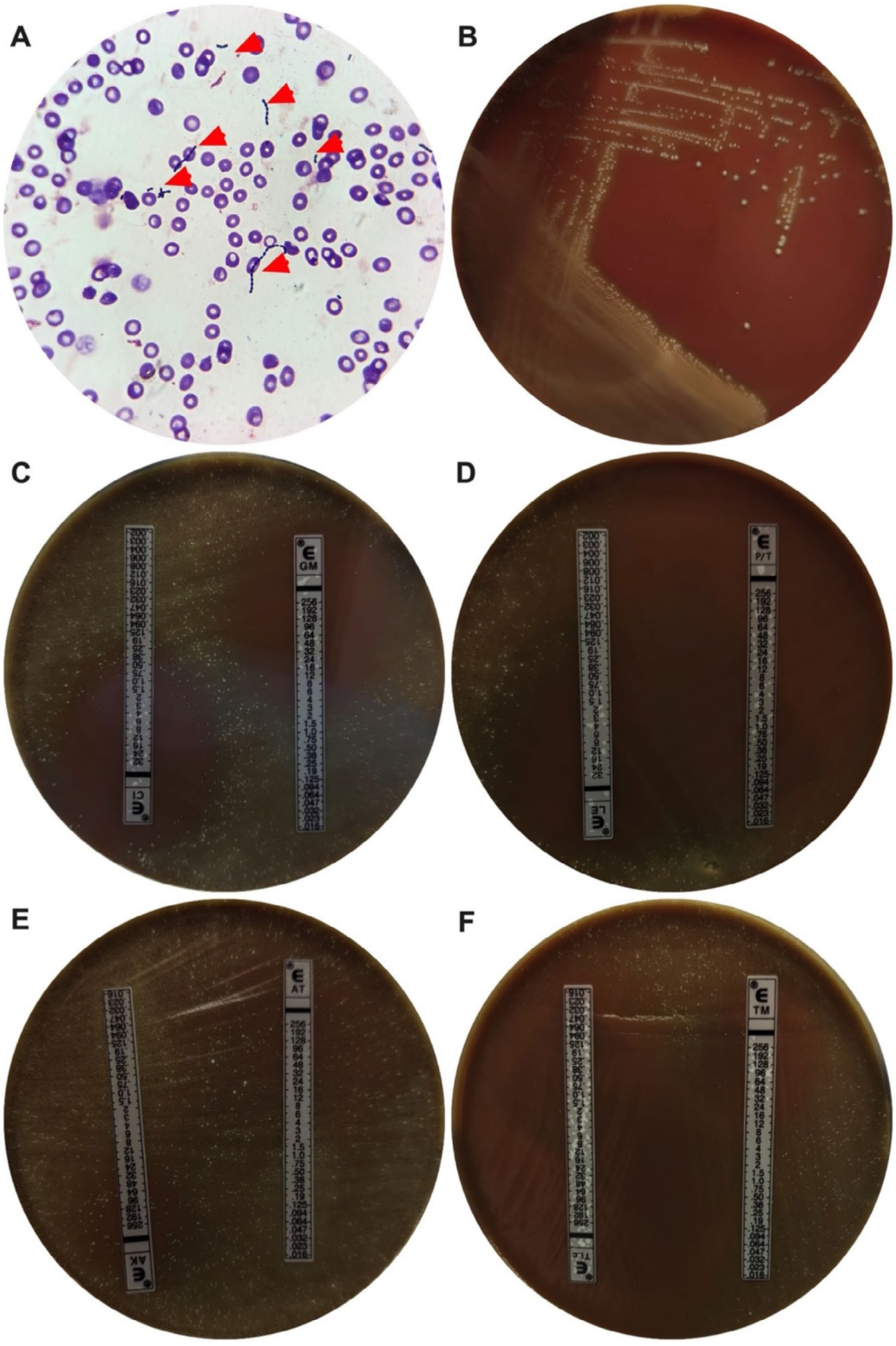

Fig. 3 (**A**) Peripheral blood smear by Walk Away Specimen Processor (WASP) highlighting the presence of Gram-positive cocci organized in chains (red arrows). (**B**) Chocolate Agar + PolyVitex® Biomerieux culture medium with *A. defectiva* visible growth. Colonies appear surrounded by a halo with greenish fuzzy contours. Antibiogram was performed by E-TEST method inoculating a pure culture of *A. defectiva* on Chocolate Agar + PolyVitex® Biomerieux. The susceptibility was evaluated against (**C**) ciprofloxacin (CI), gentamicin (GM), (**D**) levofloxacin (LE) and piperacillin/tazobactam (PT), (**E**) amikacin (AK) and aztreonam (AT), (**F**) tobramycin (TM) and ticarcillin/clavulanic acid (TLc)

Table 1 Minimal inhibitory concentration (MIC) values of *A. defectiva* obtained by E TEST method

ANTIBIOTIC	MIC (mg/L)	interpretation	EUCAST MIC breakpoint (mg/L)	
			Susceptible ≤	Resistant >
Amikacin	32	R	1	1
Aztreonam	2	S	4	8
Ciprofloxacin	0.25	S	0.25	0.5
Gentamicin	3	R	0.5	0.5
Levofloxacin	0.19	S	0.5	1
Piperacillin/tazobactam	0.47	S	8	16
Tobramycin	8	R	0.5	0.5
Ticarcillin/clavulanic acid	< 0.16	S	8	16

EUCAST: European Committee on Antimicrobial Susceptibility Testing; S: susceptible; R: resistant

Discussion and conclusions

According to the guidelines for the diagnosis and management of IE [22, 28], the use of modified Duke criteria, which integrates clinical characteristics, biomarkers, and imaging, is recommended for suspected IE. In this case, both clinical characteristics and biomarkers were negative, although IE was strongly indicated by imaging and the patient's clinical history. It is well established that patients undergoing valve replacement within the previous six months have a higher risk of developing IE [29]. The peculiarity of this case lies in the fact that, because of the absence of clinical or laboratory indications of infection, the diagnosis of IE due to *A. defectiva* occurred late. In such scenarios, the only alternative is to perform blood cultures a priori to resolve the diagnostic uncertainty [21, 30]. Two large observational studies have suggested that the maximum yield for the detection of a pathogen from culture bottles is achieved with 3 or 4 sets of blood cultures over a 24-hour period, preferably with samples taken before the start of antibiotic therapy [31]. In this report, 2 sets of blood cultures were analyzed and tested positive after 16 and 17 h, respectively. Due to the high mortality associated with IE, antibiotic therapy should be initiated as soon as the IE diagnosis is considered likely [22]. Ceftriaxone represents one of the standard options for the treatment of streptococcal IE according to the ESC guidelines [28] with teicoplanin and vancomycin as valid alternatives [32]. In the case of suspicion, treatment consists of intravenous antibiotics for up to six weeks and control of the infectious source [22]. Following these guidelines, ceftriaxone and vancomycin, were administered empirically and the patient's therapy was continued for six weeks with ceftriaxone as per protocol. Gentamicin was avoided due to the nephrotoxic risk associated with this drug, especially given the patient's creatinine values of 1.30 mg/dL and the imminence of the surgery [33]. This choice proved correct as the *A. defectiva* isolate showed resistance to gentamicin on the antibiogram.

Overall, this case highlights the importance of considering infections by fastidious pathogens in situations where the Gram staining of positive samples (in this case blood cultures) shows streptococcal-like organisms that fail to grow in subsequent cultures or subcultures. It further emphasizes the necessity for stringent communication between clinicians and microbiologists to better define an early and effective therapeutic strategy.

The strength of this work lies in its proposed approach of evaluating blood cultures even in cases where overt signs of infection are absent (e.g., fever, biochemical markers), but where clinical presentation or patient history is strongly suggestive. This methodology facilitates the early and timely detection of IE, which would otherwise remain undiagnosed until significant systemic damage occurs. On the other hand, this study faced several limitations, namely the challenges in accessing comprehensive clinical information during hospitalization, due to the involvement of multiple departments, as well as challenges in testing ceftriaxone in accordance with the 2023 guidelines, which recommend the E-test method. Finally, follow-up microbiological analyses could not be performed, and patient perspective data could not be obtained.

Abbreviations

ESC	European Society of Cardiology (ESC)
EUCAST	European Committee on Antimicrobial Susceptibility
IE	Infective endocarditis
MALDI-TOF	Matrix-Assisted Laser Desorption Ionization Time-of-Flight
OPT	orthopantomography
TEE	Transesophageal echocardiogram
TTE	Transthoracic echocardiography
WASP	Walk Away Specimen Processor

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Author contributions

MD, VV, DS, LP, MDR, SV, AMA, GA, EMC, and CM carried out the routine diagnostics; SP, MD, VV, and DS collected patient data; SP, VV, DS and MD carried out the data analysis, interpretation and prepared the figures; SP, VV, DS, MD and FA have written the main manuscript text; FA, AM, EMC and CM have revised the article critically for important intellectual content. All authors read and approved the final version of the manuscript. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Consent for publication

The patient's written consent was obtained for the publication of any potentially identifiable images or data included in this article and for the publication of this case report.

Competing interests

The authors declare no competing interests.

Clinical Trial

Not applicable.

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