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VALVULAR HEART DISEASE

CASE REPORT: CLINICAL CASE

Cat Scratch Endocarditis

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ABSTRACT

We reported a case of blood culture–negative infective endocarditis on a native valve, where the clinical presentation was exclusively related to extensive cerebral ischemia secondary to multiple systemic septic cardioembolic events. The cause was ascribed to subacute *Bartonella henselae* infection, presumably transmitted by cat scratch, documented by positive serologic findings. (J Am Coll Cardiol Case Rep 2024;29:102201) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 71-year-old man was admitted to the emergency department after being found on the floor in a state of confusion, following an episode of loss of consciousness that likely arose within the previous 24 hours. Vital parameters were stable, and only moderate hypertension (arterial blood pressure, 160/80 mm Hg) was recorded. The patient presented apyretic, awake, disoriented, and unable to recall in detail what had happened. On physical examination, ecchymosis, palpebral contusion, and scabbed lesions of the upper limbs were noted. Signs of scratching lesions were observed on the lower extremities. No other peculiar signs were detected. Cardiopulmonary and abdominal objectivity were normal. Neurologic examination documented the presence of ideomotor slowing and proximal motor sparing of the right upper limb. In the following hours, a progressive deterioration of the state of consciousness was observed.

LEARNING OBJECTIVES

- To be able to make a diagnosis of IE with multimodality imaging in absence of typical clinical symptoms and features.
- To be able to exclude the role of insidious or difficult-to-cultivate bacteria in a case of blood culture–negative IE by mainly focusing on the patient's clinical history and risk factors.

PAST MEDICAL HISTORY

The patient's medical history was positive for arterial hypertension and a smoking habit. Home medical therapy included antihypertensive drugs and aspirin taken for cardiovascular indications. Relatives reported that the patient was previously autonomous, living alone with a cat. They reported other episodes of sudden fall without loss of consciousness in the previous few days and recent radiologic investigations for back pain with documented lumbar disc herniation.

DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis included an acute severe cerebral ischemic or hemorrhagic event, a primitive cardiac ischemic or arrhythmic event with secondary cerebral involvement, and a subacute

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ABBREVIATIONS AND ACRONYMS

BCNIE = blood culture-negative infective endocarditis

CT = computed tomography

ECG = electrocardiogram

IE = infective endocarditis

MI = myocardial infarction

MRI = magnetic resonance imaging

PCR = polymerase chain reaction

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

infectious disease. In the absence of known risk factors and Duke criteria positivity, infective endocarditis (IE) was not considered until suspicion of cerebral embolic events of potential cardiac origin was raised by brain magnetic resonance imaging.

INVESTIGATIONS

Initial blood tests revealed leukocytosis (white blood cell count, 27.4 $\times$ 10^9/L; 87.4% neutrophils, 3.6% lymphocytes, 8.7% monocytes), normal hemoglobin and platelet count (hemoglobin, 17.4 g/dL; platelets, 185 $\times$ 10^9/L), mild acute kidney injury (creatinine, 1.34 mg/dL; estimated glomerular filtration rate, 52.5 mL/min/1.73 m^2), elevated C-reactive protein (157 mg/L), and elevated creatine phosphokinase (6,091 U/L) and troponin I (1,174 ng/L) values. Urinary toxicology test results were negative. On a brain computed tomography (CT) scan, no signs of acuity emerged, but only focal hypodensities of chronic vascular significance. Radiologic examinations of the pelvis, whole spine, and facial massif excluded the presence of severe traumatic injuries and demonstrated mild discopathy at the cervical and lumbar levels. The chest radiograph was also normal. Color Doppler imaging of the supra-aortic trunks showed the presence of bilateral carotid stents in the absence of critical stenosis or intrastent thrombosis.

During the electrocardiogram (ECG) examination, sinus rhythm and an isoelectric ST-segment were observed. Transthoracic echocardiography (TTE) showed mild left ventricular systolic dysfunction (left ventricular ejection fraction, 45%) secondary to apex and anterior wall hypokinesia and moderate mitral regurgitation. Because the patient's neurologic status was severely impaired, coronary angiography was delayed despite the significantly increased troponin levels on admission. Clinical, ECG, and laboratory monitoring was performed. No significant changes in ECG configuration or arrhythmias were observed, whereas troponin levels subsequently decreased.

Two sets of blood cultures and urine culture were performed, and all results were negative. Results of a 24-hour brain CT scan were unchanged. For a seizure electroencephalographic pattern finding, antiepileptic therapy was started. Lumbar puncture and cerebrospinal fluid examinations were performed as well, with no relevant findings. On suspicion of a primary central nervous system infection, empirical therapy with ceftriaxone (4 g/day), ampicillin (12 g/day), and acyclovir (1.95 g/day) was started. The patient remained afebrile.

Two days after hospital admission, the patient's neurologic status was unchanged. Brain MRI was performed, showing bilaterally supratentorial and subtentorial multiple embolic ischemic lesions, characterized by hyperintensity in diffusion-weighted imaging and T2-weighted fluid-attenuated inversion recovery sequences (**Figure 1**). At this point, TEE was performed, and a vegetation was detected on the native mitral valve, most evident at the anterior leaflet level, with extension to the posterior leaflet, and leading to moderate to severe regurgitation (**Figure 2**).

Total-body CT showed multiple mediastinal adenopathies and hepatic, splenic, and renal embolic ischemic lesions. On cardiac CT, the presence of vegetations on the anterior (12 $\times$ 7 $\times$ 6 mm in size) and posterior (7 $\times$ 5 $\times$ 6 mm) mitral leaflets was confirmed. No extra-annular complications or critical coronary artery stenoses were revealed. Intracranial CT angiography excluded mycotic aneurysms or arterial occlusions.

An ophthalmologic examination was not conducted because of the patient's neurologic state.

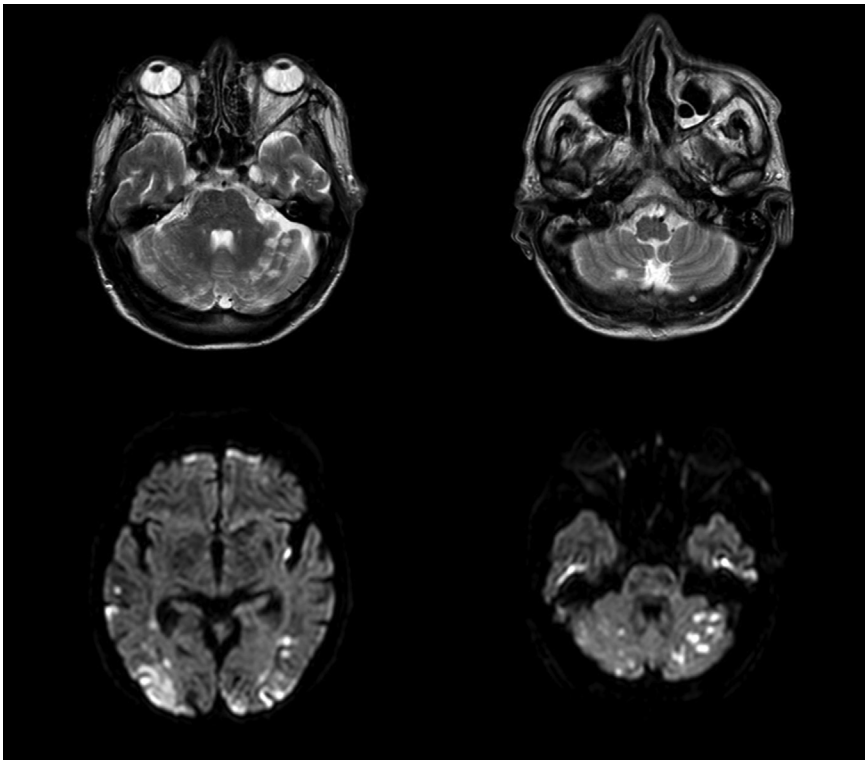
MANAGEMENT

A different empirical antibiotic therapy was instituted with ceftriaxone (4 g/day) and daptomycin (700 mg/day). On the basis of the patient's neurologic status, which was severely and persistently impaired, in the absence of acute heart failure or periannular complications, cardiac surgery was deferred. A tuberculosis test, a *Staphylococcus aureus* search on nasal swab, and a gram-negative multidrug resistant strain search on rectal swab were performed, all with negative results. An antiphospholipid syndrome antibody search also had negative results. Suspecting native valve blood culture-negative IE (BCNIE) with disseminated infection, given the known anamnestic finding of exposure to cats, serologic testing for *Bartonella henselae* by indirect chemiluminescent immunoassay was performed and showed positivity for immunoglobulin M antibodies (index, 1.2; positive if >1.1). On the basis of imaging and serologic findings, the case was classified as possible IE.[1] Targeted treatment with doxycycline and rifampin was then started. Two weeks later, serologic testing gave the same result. The hospital's laboratory was unable to perform a specific polymerase chain reaction (PCR) assay. Blood culture results remained negative after 21 days.

DISCUSSION

IE is a rare condition whose mortality rate has been significantly reduced over the years.[1,2] However, it

FIGURE 1 **Brain Magnetic Resonance Imaging**



Bilaterally supratentorial and subtentorial multiple embolic ischemic lesions, characterized by hyperintensity in diffusion-weighted imaging and T2-weighted fluid-attenuated inversion recovery sequences were observed.

remains a life-threatening condition, especially when the correct diagnosis is not promptly made or the responsible microorganism is not identified and effective antibiotic therapy is not begun in time.[1,2]

In the present case, difficulties in anamnestic collection, severe neurologic impairment concurrently with nuanced findings of myocardial damage, in the absence of fever or other findings suggestive of IE on objective examination or TTE, initially made the diagnostic process complex, leading to a relative delay in definitive diagnosis.

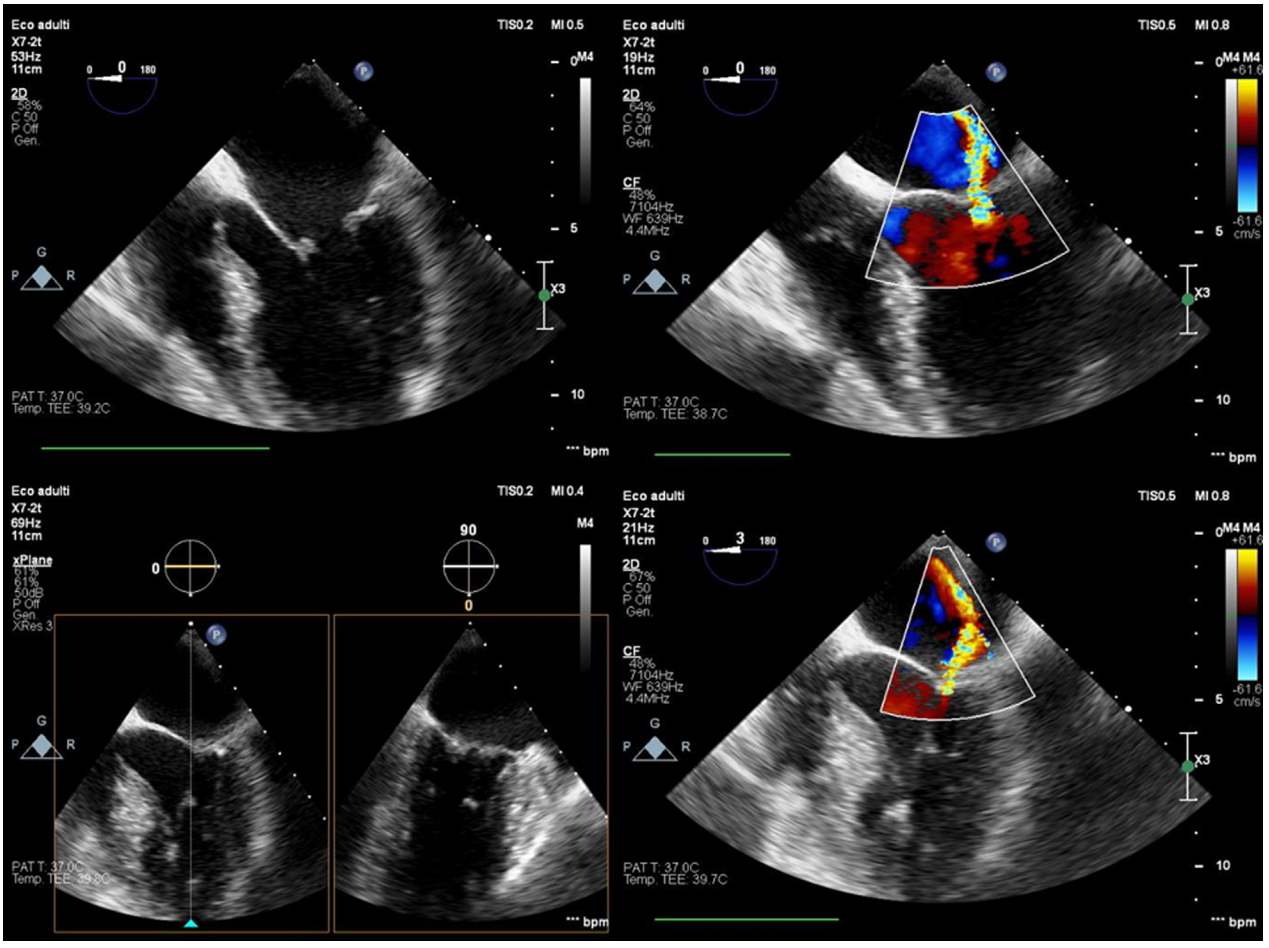
Neurologic sequelae are the most frequent and severe extracardiac complications of IE, occurring in 25% to 80% of established cases, including silent cerebral complications detected by brain MRI. As many as 40% of patients present with a clinically evident neurologic event, which occurs before or at IE diagnosis, especially in the form of embolic stroke, and poses an independent risk factor for mortality in IE.[1-5] The risk of developing embolic complications depends mainly on the characteristics of the vegetation and the duration of antibiotic therapy. Large left-sided lesions, especially on the mitral valve, are those at greatest risk of embolizing.[3-5]

In our patient, brain MRI played a key role in establishing the diagnosis of embolic stroke and directing clinicians to search for the underlying focus by TEE, which is confirmed to be a significantly more sensitive diagnostic modality than TTE in identifying the presence of valvular vegetations.[1,2]

A further crucial issue was the patient's candidacy for valve surgery. The impact of valve surgery on the outcome in IE patients with cerebrovascular complications is a subject of debate. There is major concern about the risk of postoperative neurologic compromise when surgery is performed early after an ischemic or hemorrhagic episode. Clinical judgment of the patient's neurologic status is mandatory, but the generally accepted advice is to delay surgery for ≥4 weeks in the case of major ischemic stroke or intracranial hemorrhage.[1-3]

An additional challenge was identifying the responsible etiologic agent in consideration of

FIGURE 2 **Transesophageal Echocardiography**



A vegetation was detected on the native mitral valve, most evident at the anterior leaflet level, with extension to the posterior leaflet, and leading to moderate to severe regurgitation.

negative blood culture results and the absence of obvious risk factors except for exposure to a cat.

BCNIE can occur in up to 31% of all cases of IE.[2] This may be attributable to infection with highly fastidious or noncultivatable bacteria or to previous administration of antimicrobial agents before blood cultures were obtained. *Bartonella* species are small, intracellular gram-negative bacilli transmitted by arthropod vectors and represent the second most common cause of BCNIE following *C. burnetii*.[1,2,6,7]

B. henselae is globally distributed in domestic and feral cats, and the major arthropod vector is the cat flea.[6,7] It is the main etiologic agent of cat scratch disease and is the second most common *Bartonella* species known to cause endocarditis. The clinical course of endocarditis is subacute, manifesting with nonspecific symptoms even though it typically causes extensive valve damage and embolizations. Serologic testing is often used for the diagnosis, although rapid detection of *Bartonella* DNA in blood or in samples of resected valve by real-time PCR is the most sensitive test.[6,7]

Our case stands as one of the few cases of *B. henselae* endocarditis described in Italy.[8] Its clinical presentation aligns with previous data,[9] with diagnostic suspicion guided by known cat exposure. In this case, IE was associated with myocardial infarction (MI) with nonobstructive coronary arteries,

supported by elevated troponin, wall motion abnormalities, and open coronary arteries on cardiac CT. A type 2 MI caused by coronary emboli was hypothesized, given the documented systemic embolization.[10]

In this setting, the first-line antibiotic is doxycycline or ceftriaxone used in combination with an aminoglycoside.[1,2,6,7] In our case, oral rifampin was preferred, considering aminoglycoside's risk of nephrotoxicity.

FOLLOW-UP

One week after the IE diagnosis, partial improvement in the patient's neurologic status was observed; on follow-up brain MRI, a reduction in the extent of ischemic lesions was found, and new subclinical embolic cerebral infarcts were excluded. The patient remained hemodynamically stable. Myocardial enzymes progressively normalized.

CONCLUSIONS

This case emphasizes how IE could be an insidious disease that can manifest directly with symptoms related to extracardiac complications, especially in the form of neurologic sequelae, and in the absence of the typical findings described by the Duke criteria. In particular, in the case of BCNIE, it is necessary to focus on epidemiologic and patient risk factors, to quickly identify infection promoted by fastidious pathogens such as *Bartonella* spp.

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KEY WORDS ***B. henselae*, blood culture-negative infective endocarditis, neurologic impairment**