


CASE REPORT

Neuropsychiatric disorder as early clinical presentation of marantic endocarditis in patient with newly diagnosed poorly differentiated esophago-gastric junction adenocarcinoma: A case report

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Key Clinical Message

Neuropsychiatric symptoms, depression, and progressive mental confusion should not be overlooked as onset symptoms of multiple cerebral ischemic lesions due to cardiac embolization. Comprehensive clinical evaluation due to progressive anemia led to the diagnosis of poorly differentiated adenocarcinoma of the esophagogastric junction as cause of embolizing nonbacterial mitral endocarditis.

KEYWORDS

cerebral embolism, gastric cancer, marantic endocarditis, neuropsychiatric symptoms

1 | INTRODUCTION

Nonbacterial thrombotic endocarditis (marantic endocarditis) is a sterile thrombotic disease related to hypercoagulable conditions like cancer or chronic inflammatory syndromes (such as systemic lupus erythematosus and antiphospholipid syndrome).

The most common malignancies associated with NBTE include lung, pancreas, and gastric adenocarcinoma and adenocarcinoma of unknown primary site.¹

The aseptic masses, composed of platelets and fibrin, are located on heart valves and usually are demonstrated at necropsy. Between 15% and 50% of cancer patients show thrombotic phenomena in autopsy series.² Some studies reported that NBTE occurs in approximately 4% of patients with terminal malignancies, and up to 19% in metastatic adenocarcinomas. The postmortem prevalence of NBTE among malignancy patients has been reported to be up to 1.3%, whereas the prevalence in the general population ranges from 0.3% to 9.3%.^{3,4}

The pathogenesis of NBTE is incompletely understood. Elevated levels of circulating cytokines associated with cancers, such as tumor necrosis factor or interleukin-1 may also result in local tissue damage that instigates vegetation formation. Perhaps the most important factor in the formation of these valvular vegetations is the hypercoagulable state associated with malignancies.^{1,5}

Vegetations in NBTE are neither associated with bacteremia nor with destructive changes of the underlying valve. The diagnosis is based on strong clinical suspicion in the context of a disease process associated with NBTE, the presence of a heart murmur, negative blood cultures, the absence of response to antibiotic therapy, and evidence of multiple systemic emboli (in brain, spleen, kidney, skin, or extremities). Up to 15% of cancer patients have thrombotic phenomena and the most common presentation was stroke (54%)⁶ which determines a wide spectrum of manifestations, in rare cases insidious and nonspecific like cognitive changes and mental slowdown.

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There are few reported cases of NBTE as a presenting manifestation of gastric cancer, and the majority occur in advanced disease.⁷

In this case, we report an atypical presentation of marantic endocarditis associated with signet ring cell esophagogastric junction carcinoma. Signet ring cell adenocarcinomas (SRCCs) are a rare histological subtype of adenocarcinomas with a poor prognosis, typically due to advanced disease at diagnosis. SRCCs comprise 16.8% of all cases of gastric cancer, and nearly 57% of all SRCC cases; these cancers are most often detected at a distant or metastatic stage (43.0% vs. 37.3%) with a poor tumor grade (75.4% vs. 52.1%).⁸

2 | CASE HISTORY

We describe the case of a 64-year-old man, presenting to the ED for general conditions impairment starting 2 months before with progressive mental confusion, asthenia, and inappetence conditioning weight loss, until then attributed to work-associated stress. For intercurrent pre-syncopal episode and acute confusional state, he performed several assessments including cardiac echo color-Doppler (repeated several times), supra-aortic trunks ultrasound, coronarography, brain CT scan, neurological examination, and internist examination, all of which showed no pathological findings; he therefore started psychoactive therapy after psychiatric counseling.

His medical history was notable for quiescent ulcerative recto colitis, type 2 diabetes, and hypertension.

On emergency room examinations have been detected normocytic anemia (Hb 10.4 g/dL; hemoglobin value in the previous month was 14.8 g/dL); hypokalemia (K 3.1) and INR 1.4 (spontaneous).

3 | METHODS

During hospitalization, a total body CT scan was performed that showed several hypodense subcortical lacunar lesions in the semi oval centers, the most voluminous in the left frontal site, rather well defined, compatible with ischemic outcomes, in the absence of pathological significance encephalic impregnations after contrast medium by vein; at thoracoabdominal level multiple diffuse lymphadenopathies, some colliquated and tending to confluence, with likely infiltration of surrounding structures (kidneys, spleen, pancreas); also consolidative parenchymal thickening at lingula of likely inflammatory-infective and partly poorly aerated/collapsed segments of the lungs with bilateral mid-basal pleural effusion.

For the appearance of fever, empiric therapy with ceftriaxone 2 g/day was undertaken. Repeated blood cultures however resulted in negative.

To better investigate brain lesions an EEG was performed, which showed no epileptiform abnormalities; Angio-CT of the intracranial vessels showed only anatomic variants (right vertebral artery terminating in PICA and fetal origin from the carotid siphon of the right posterior cerebral artery); encephalic MRI showed supra and sub tentorial encephalic signal changes referable to embolic-based ischemic lesions (Figure 1).

To rule out potential embolic sources transesophageal cardiac echocolor-Doppler was performed and showed the presence of mitral valve endocarditic vegetations (the largest about 1 cm in size—Figure 2) with moderate valve insufficiency and interatrial septal aneurysm with foramen ovale patency and massive right-left interatrial shunt.

Therefore, new cold blood cultures were collected (3+1 for KB, which were later found to be negative) and antibiotic therapy was modified by increasing the dosage of ceftriaxone to 2 g 2 times/day and adding vancomycin 1 g/day ev. To exclude the hypothesis of an infectious etiology we also collected samples for serology for cysticercosis (WB), Toxocara, Strongyloides, Trichinella, culture test for helminths, PCR for toxoplasma on blood, serologies for syphilis, CMV DNA, EBV DNA, Parvovirus B19 DNA. All resulted negative. The case was also discussed with heart surgeons who excluded urgent surgery due to severe brain involvement.

An FDG PET scan confirmed multiple areas, some confluent, of intense glucose hypermetabolism referable to lymph node involvement; another macro area of intense hypermetabolism was found in the esophagogastric region (Figure 3).

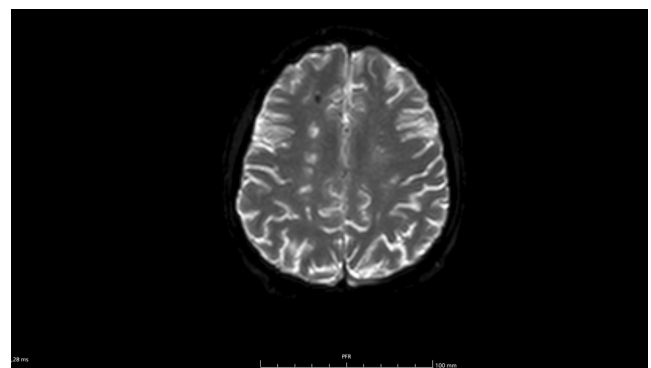


FIGURE 1 Contrast-enhanced encephalic MRI—DWI sequence demonstrating parieto-occipital cerebral cortex embolic-based ischemic lesions.



FIGURE 2 Transesophageal cardiac echocolor-Doppler: large package of endocardial vegetations encompassing the posterior mitral leaflet, especially at P2-P3 level; similar lesions also at the free edge of the anterior mitral flap in A2.

4 | OUTCOME AND FOLLOW-UP

A left lateral-cervical lymph node was excised for histologic examination.

In addition, the patient underwent gastroscopy which showed a vegetating and sub-stenosing lesion of esophago-gastric junction, with difficult passage of the endoscopic instrument. The mass was fragile and easily bleeding. Due to progressive worsening of anemia two RBC units were transfused.

Histologic examination of lymph nodes and of the gastric samples demonstrated a low-grade adenocarcinoma with signet ring cells.

A multidisciplinary evaluation, in consideration of the poor general clinical conditions, the severe cognitive impairment, and the poor outcome did not suggest active treatment and suggested only supportive therapy.

The patient had a further worsening of the neurocognitive conditions, with alternance of phases of alertness with phases of drowsiness and disorientation with slurred and dysarthric, poorly comprehensible speech. He remained afebrile. He was finally transferred to hospice and died 11 days after discharge.

5 | DISCUSSION

In this patient, at clinical presentation the absence of frank side neurological symptoms did not lead to suspect of organic brain involvement, and in first instance a primary psychiatric disorder was considered. Multiple ischemic brain lesions found at CT scan at hospitalization suggested a cardioembolic cause. Echocardiographic confirmed the presence of mitral valve vegetations with negative blood

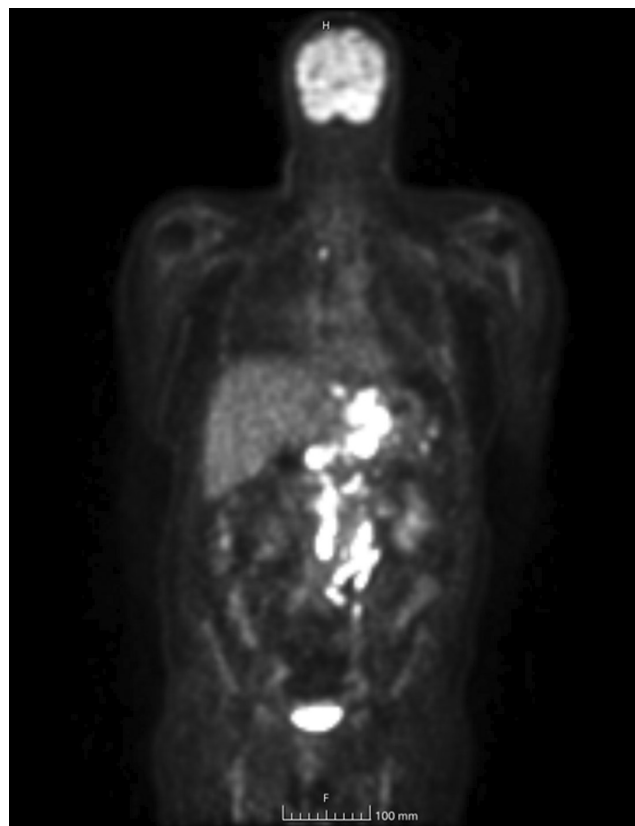


FIGURE 3 FDG PET scan demonstrating macro area of intense hypermetabolism in esophago-gastric region extended to the small gastric curvature and multiple areas of intense glucose hypermetabolism, some confluent, of abdominal lymph node relevance.

cultures. The diagnosis of non-infective endocarditis is challenging, and clinical presentation and likelihood of infective endocarditis should guide in further clinical investigations. In this patient the repeated negativity of blood cultures was not consistent with infective endocarditis: moreover, the significant decrease of Hb levels raised the suspect of occult bleeding and of a gastroenteric neoplasm. According to guidelines,⁹ the diagnosis of non-bacterial endocarditis relies on strong clinical suspicion in the context of a disease known to be associated with marantic endocarditis. The reported case emphasizes the heterogeneous clinical presentation of marantic endocarditis since cerebral embolization was not associated with side neurological signs but with nonspecific neuropsychiatric symptoms that hampered significantly to achieve rapidly the correct diagnosis.

AUTHOR CONTRIBUTIONS

Filomena Ferrentino: Conceptualization; data curation; writing – original draft; writing – review and editing. **Sara Campana:** Conceptualization; data curation; resources; writing – original draft. **Marco Torri:** Conceptualization; data curation; validation; writing – review and editing.

Carlo Rostagno: Data curation; supervision; validation; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data are available on electronic clinical records of our hospital.

CONSENT

Written informed consent was obtained from the relatives of patient to publish this report in accordance with the journal's consent policy.

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