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Combined Intestinal Ischemia, Cerebral Stroke and Thrombosis of Thoracoabdominal Aorta and Splenic Artery in a Thrombophilic Woman: A Case Report

Carolina Giordano[1], Olivia Penna[1], Antonio Amato[1], Rosario Bruno[1], Vincenzo F. Tripodi[1], Eugenio G. Vadalà[1], Natalino C. Pennisi[2], Epifanio Mondello[1] and Vincenzo Fodale[1*]

[1]Department of Human Pathology, Section of Anesthesiology, University of Messina, Italy.
[2]Residency Program in Diagnostic Radiology, University of Messina, 98125 Messina, Italy.

Authors' contributions

Authors CG and VF conceived the study and drafted the manuscript. Authors OP, AA and RB reviewed the literature and also drafted the manuscript. Authors VFT, EGV and NCP collected and elaborated the data used for writing the paper and authors EM and VF revised the paper. All authors were equally involved in the final reading and appraisal for publication.

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Case Study

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ABSTRACT

Aim: To present an uncommon, life-threatening case of intestinal ischemia complicated by cerebral stroke, thoraco-abdominal aorta and splenic artery thrombosis, in a woman with thrombophilia presenting common clinical signs.
Presentation of Case: A 42-year-old woman was admitted to hospital for lower abdominal pain, vomiting and fever. Emergency abdominal surgery evidenced intestinal ischemia requiring 80 cm ileum resection. The day following surgery, the patient lost consciousness and was admitted to the stroke unit. Thereafter, the patient was transferred to the intensive care unit due to respiratory failure. A brain-thoracic-abdominal CT-angiography showed occlusion of left medium cerebral artery, a thrombotic formation in thoracic and abdominal aorta, and partial occlusion of splenic

**Corresponding author: Email: vfodale@unime.it;*

artery. Homocysteine levels were 56.8mmol/l, screening for homozygosis mutation MTHFRC677T positive. Resolution of systemic thrombosis lasted one month. Patient was finally transferred to a rehabilitation center.

Discussion: Vascular disease and ischemic stroke have rarely been reported in subjects with thrombophilia and MTHFR polymorphisms. Our patient, affected by thrombophilia and high homocysteine levels, faced multiple vascular and cerebral complications. High concentration of homocysteine, with consequent vessel deposits, was detrimental for endothelium and vessel walls, due to action on blood coagulation factors and lipoproteins, with increased platelet adhesion and aggregation.

Conclusion: This case report represents an uncommon, sudden, life-threatening complication in thrombophilic patients, in spite of the common clinical signs presented. This clinical report should alert physicians to the importance of carrying out a careful clinical examination in the presence of thrombophilic patients presenting with apparently common clinical signs, such as abdominal pain, vomiting and fever.

Keywords: Aorta; artery thrombosis; cerebral stroke; homocysteine; intestinal ischemia; MTHFRC6 mutation; splenic artery; thrombophilia.

1. INTRODUCTION

Thrombophilia is an abnormality of blood coagulation leading to an increased risk of obstructive arterial or venous clots [1,2].

The existence of inherited or acquired thrombotic disorders is described in rare cases of symptomatic young subjects, in pregnancy and puerperium, in women taking oral contraceptives, or subjects with a genetically determined family history [3].

Thrombophilia as a cause of ischemic stroke was previously considered extremely rare, often remaining under-diagnosed, also considering the low likelihood of genetic predisposition to multiple thrombosis at atypical sites in an individual who has suffered multiple strokes [4-6]. However, vascular disease and ischemic stroke have been reported in subjects with thrombophilia and MTHFR polymorphisms [4,7,8].

An uncommon case report of life-threatening intestinal ischemia, complicated by cerebral stroke, thoracoabdominal aorta and splenic artery thrombosis is here presented, regarding a woman with thrombophilia reporting to the emergency department with common clinical signs.

2. PRESENTATION OF CASE

A 42-year-old woman (165 cm, 100 kg, BMI 36), ex-smoker, with Hashimoto thyroiditis and untreated diabetes, but without any familiar history for venous thrombosis and thrombophilia, was admitted to the emergency department due to sudden onset of fever, vomiting and painful distended abdomen.

Orthostatic abdominal X-ray revealed gaseous distention in various intestinal loops, mainly ileum-jejunum with multiple air fluid levels and a marginal involvement of the colic frame, except for the cecum and ascending colon, where signs of coprostasis were evident. The entire peritoneum was affected.

The patient was admitted to the surgical unit and underwent emergency abdominal surgery, which revealed intestinal ischemia requiring resection of the ileum (80 cm) and anastomosis. Pre-operative evaluation of global thromboembolism risk was 2/5 (moderate risk) with 10-20% venous thromboembolism risk. Glycemia was 129 mg/dL, LDH 652 µ/L, CPK 56 µ/L, PT 13.1 sec, AP 113%, PTT 24.8 sec, INR 0.94, platelets 489,000 mmc, erythrocyte sedimentation rate (ESR) 100 mm/hr.

After surgery, the following medical treatment was prescribed: low-molecular-weight heparins 3800 U.I. 0.4 mL, imipenem 500 mg and cilastatin 500 mg, metronidazole 500 mg/100 ml, omeprazole 40 mg.

The day following surgery (day 2), the patient lost consciousness. Neurological examination revealed lack of response to verbal stimuli, and a right-sided hemiparesis. The right-sided Babinski sign was present.

A brain CT without contrast did not show altered density in the parenchyma, above or below the tentorium, but showed mild flattening of the gyri with narrowing of the sulci in the left

frontoparietal lobe. Hematological values were PT 15.8 sec, AP 76.3%, PTT 24.9 sec, international normalized ratio 1.14, platelets 383,000 mmc, glycemia 122 mg/dL. Mannitol 10% infusion 150 mL x 3 was added to medical treatment.

However, another brain CT scan, repeated the day after (day 3), showed an extended, non-homogeneous area of hypodensity in the left temporoparietal lobe, with a consequent median line shift. Homocysteine in blood sample was 56.8 micromol/L (normal values 0-15), fibrinogen 688 mg/dl (normal values 220-496). The patient was therefore transferred to the Stroke Unit.

On day 4, the patient exhibited acute respiratory failure. Analysis of arterial blood gas showed impaired values (pH 7.468, pCO_2 31.4 mmHg, pO_2 52.9 mmHg, sO_2 86.3%, HCO_3 22.2 mmol/l, and P/F ratio 251 mmHg). Thoracic CT scan presented multiple parenchymal densities due to bilateral filling of alveolar spaces, in the hilar, perhilar and apical regions of the lungs. In addition, air bronchogram showed consolidations in both dorsal segments.

The patient was transferred to the intensive care unit (ICU), where endotracheal intubation and mechanical ventilation were carried out.

After admittance to ICU, brain CT-angiography showed a vast hypodense parenchymal area, in the cortical and subcortical regions, in the frontoparietal lobe, attributed to an ischemic attack caused by complete occlusion of the left middle cerebral artery at the level of the third distal artery.

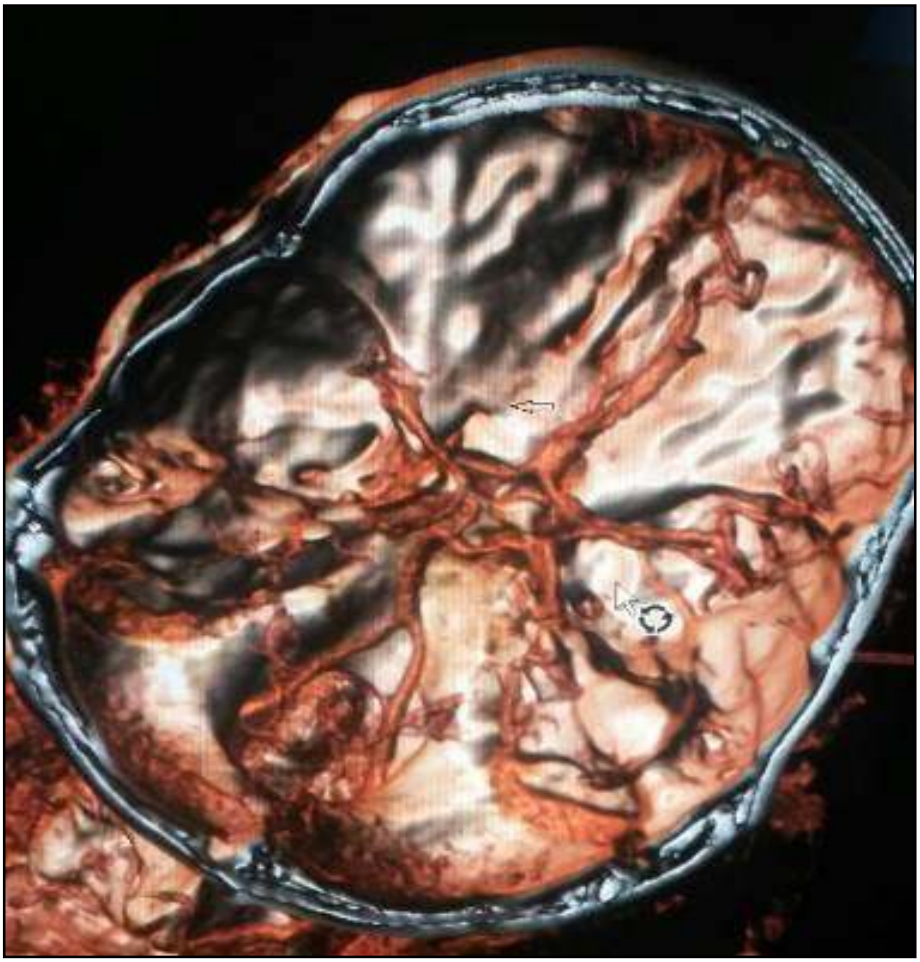

Fig. 1. Brain 3D-CT angiography shows complete occlusion of left medium cerebral artery (arrow)

The abovementioned lesion led to significant constriction of the third ventricle on the same side of the brain, and mild flattening of the sulci in the near gyri, with the structure along the median line shifting slightly towards the right.

Thoracic CT-angiography showed a coarse, fluctuating thrombus formation in the middle third of the thoracic aorta, occupying more than 60% of the lumen, extending in the cranio-caudal direction for about 15 mm.

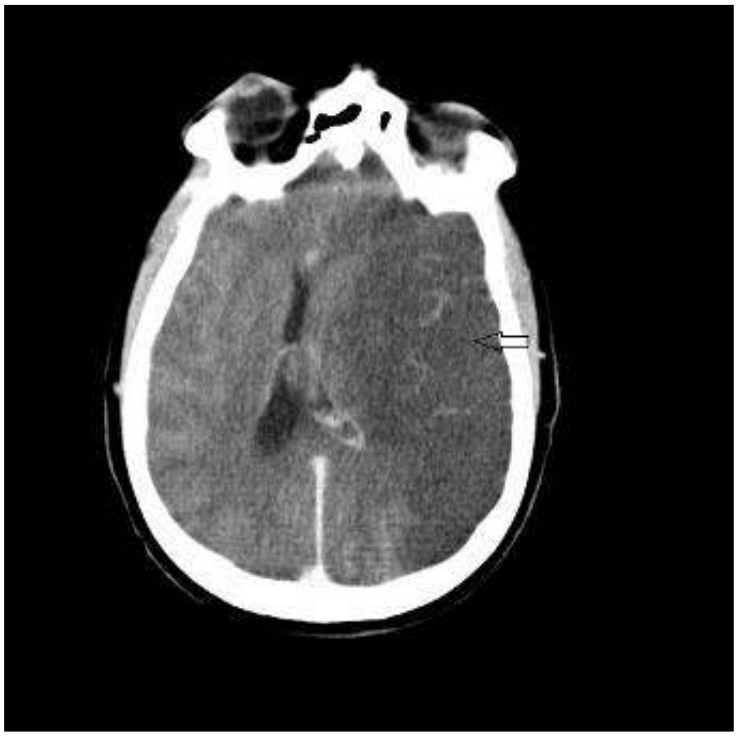

Fig. 2. Brain CT shows extended left frontotemporoparietal hypodense area with midline shift (arrow)

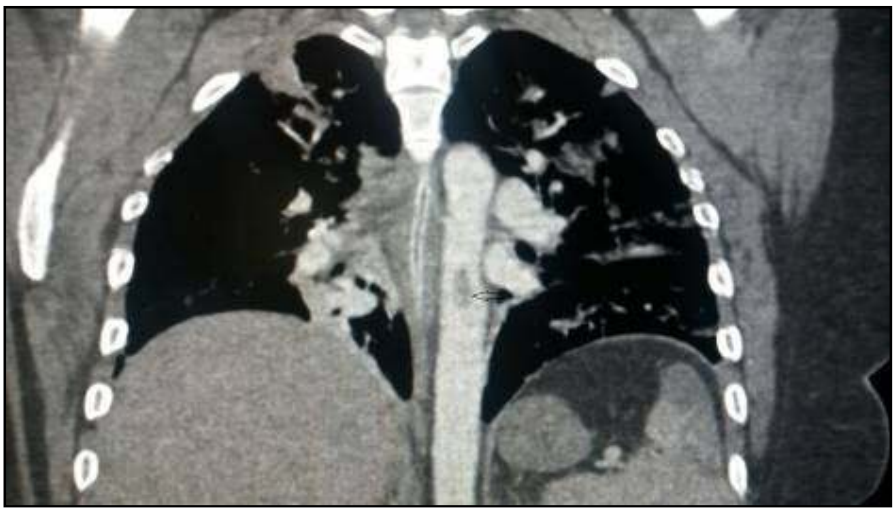

Fig. 3. Thoracic-Abdominal CT angiography showing partial occlusion of the III medium of the thoracic aorta (a 15 mm fluctuating thrombus formation occluding 60% of endovascular space)

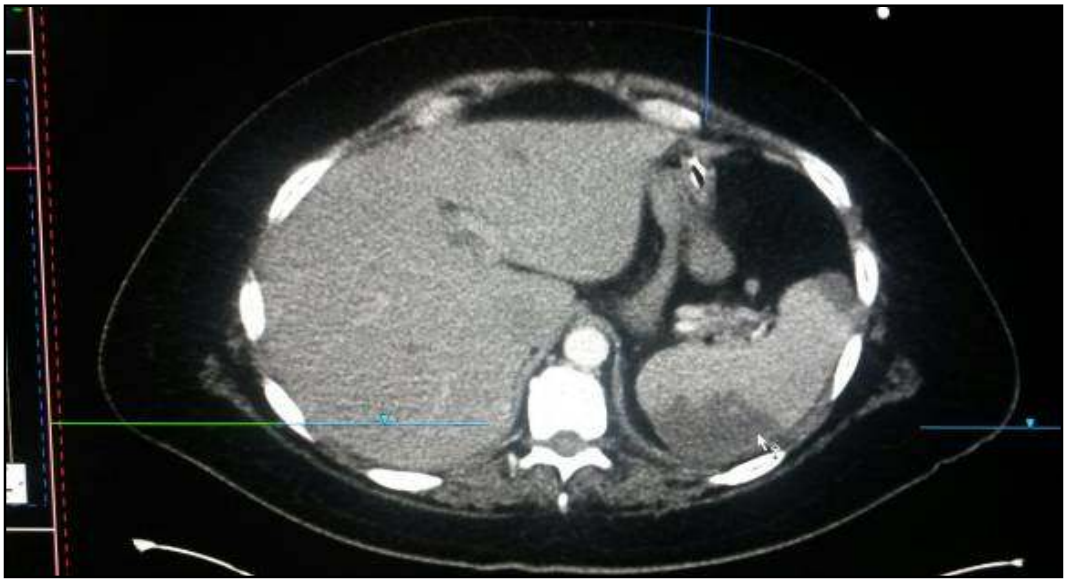

Fig. 4. Partial occlusion of splenic artery with stroke involving 70% of splenic parenchyma

Table 1. Laboratory screening details

Laboratory test	Result
MTHFR*C677T*	Positive (TT genotype)
MTHFRA1298C	Negative
Antiphospholipid autoantibodies (aPL)	Negative
Anticardiolipin antibodies (aCL)	Negative
Anti-*neutrophil* cytoplasmic antibodies (ANCAs)	Negative
Anti-*nuclear* antibodies (*ANA*)	Negative
Anti-Smooth Muscle Antibodies (ASMA)	Negative
Anti-nDNA autoantibodies	Negative
Antiphospholipid antibodies (APLAs)	Negative
Extractable *nuclear* antigens (ENA)	Negative

There were no signs that indicated pulmonary embolism, and perfusion from pulmonary arteries through to segment branches was regular.

In addition, abdominal CT-angiography showed a partial obliteration of the splenic artery at the hilum, with a series of coarse infarctions across over 70% of the splenic parenchyma.

Thrombosis was also observed on the anterior wall of the abdominal aorta, close to the diaphragmatic pillars. Antiplatelet drugs and anticoagulants were added to medical treatment. Screening for genetically determined thrombophilia mutation in homozygosis MTHFRC677T was positive.

On day 8 in ICU, based on the results of a brain CT scan showing an increase in the extension of the hypodense parenchymal area, affecting the entire left parietal and occipital lobes, with an increase in the mass and consequent contralateral dislocation of the median line, the patient underwent a left decompressive craniotomy. A tracheotomy was performed on day 20.

A CT-angiography, performed on day 28, showed resolution of aorta thrombotic formations, while pulmonary resolution of multiple hypodense parenchymal area was documented on day 30.

The patient, with a GCS 4+4+1 and tracheotomy, was finally transferred to a Rehabilitation Center on day 64.

3. DISCUSSION

Genetic abnormalities predisposing arterial thrombosis are independent of obesity, smoking, hypertension, or hypercholesterolemia [9].

Multicenter clinical and laboratory screening-tests have helped ascertain that mutations are associated with a high incidence of thrombotic events. Predominant thrombophilic mutations include factor V Leiden mutation, prothrombin gene mutation G20210A, deficiencies of the natural anticoagulant proteins C and S, antithrombin and methylene tetrahydrafolate reductase-MTHFR-mutation, elevated clotting factors (factors VIII and IX-XI) and high levels of circulating lipoprotein and fibrinogen [8,10]. Patients with suspected antiphospholipid syndrome should be tested for lupus anticoagulants, anti-cardiolipin antibodies, and anti-β2-glycoprotein I-antibodies [10].

Regular screening tests can reduce the risk of venous thrombosis in individuals with risk factors [3], while a causal relationship between tests and arterial thrombosis has not been distinctly demonstrated [11].

Our patient showed high levels of homocysteinemia. Screening for mutation in homozygosis MTHFRC677T was positive.

Multiple mechanisms for homocysteine are associated with endothelial damage: deposit of homocysteine on the vessel walls was detrimental to both endothelium and vessel walls through its direct action on blood coagulation factors, lipoproteins and platelets, with an increase of platelet adhesion and aggregation. Hyperhomocysteinemia, due to MTHFR mutation, caused the formation of widespread thromboses in the intestinal artery, left medium cerebral artery, and splenic artery, fluctuating thrombus formation in the thoracic aorta and plaque formation in the abdominal aorta.

The mutation of thermolabile MTHFR enzyme, caused by an alanine to valine residue substitution (missense mutation), determines hyperhomocysteinemia. Vascular damage is a potential consequence of high levels of homocysteine, with an increased risk of occlusive vascular disease [12]. This mutation is linked to increased predisposition to venous [12] or arterial thrombosis [13-15] but association with arterial stroke [16], peripheral arterial disease [17] and ischemic stroke in young adults [18-20] has unquestionably been proven.

Although MTHFR polymorphisms and hyperhomocysteinemia are well-known risk factors of thromboembolism, possessing an abnormal or mutant gene does not necessarily mean an individual will experience a thrombotic episode. However, in certain at-risk individuals, the combination with family or personal history and/or biochemical factors, or coagulation modified testing, may impact upon the development of an acute thrombotic episode [8,9]. This is in accordance with our patient presenting, in addition to genetic risk factors, with many other non-genetic risk factors such as obesity, diabetes, past smoking habit and, possibly, hypothyroidism.

This case report is a paradigmatic example of the predictive role of investigating thrombophilic disorders in young people affected by stroke. However, the actual benefit of routine testing for thrombophilic disorders in young subjects affected by stroke remains uncertain. Moreover, screening tests are less used due to high costs and low prevalence of thrombophilic disorders among the general population. A careful selection of high-risk patients and type of testing often contribute to reducing the probability of arterial and venous thrombosis and ischemic stroke [21].

4. CONCLUSION

This case report represents an uncommon, sudden life-threatening complication in a thrombophilic patient, in spite of the common clinical signs presented. This clinical report should alert physicians to the importance of carrying out a careful clinical examination of thrombophilic patients presenting apparently common signs such as abdominal pain, vomiting and fever.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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