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Acute ischemic stroke due to floating thrombus of ascending aorta: An acute and subacute complication of SARS-CoV-2 infection

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ABSTRACT

Objective: To describe ischemic stroke due to floating thrombus of ascending aorta occurring as acute and subacute complication of SARS-CoV-2 infection.
Material and Methods: consecutive identification in clinical practice of ischemic strokes secondary to aortic arch thrombosis and history of acute or recent Covid-19 infection.
Results: two patients had ischemic stroke with evidence of aortic arch thrombosis. The first case had concomitant acute Covid-19 infection, the second had recent Covid-19 infection. Both patients underwent intravenous thrombolysis, and subsequent anticoagulation. One patient died due to cerebral hemorrhage.
Discussion and Conclusions: aortic arch thrombosis can be an incidental finding in acute ischemic stroke in patients with concomitant and recent COVID-19 disease. However, the infection may lead to thrombosis in non-atherosclerotic vessels and to cerebral embolism. Our findings support active radiological search for aortic thrombosis during acute stroke in patients with acute or recent COVID-19 disease.

Introduction

Patients hospitalized with severe COVID-19 have an estimated five-fold increased risk of developing ischemic stroke compared to non-COVID-19 patients. Typical clinical features include younger age, male sex, and more severe neurological deficit at admission (Yaghi et al., 2020). The most frequent presentation (80%) is large vessel occlusions, while etiology is cryptogenic in 45% and cardioembolic in 22% of cases (Nannoni et al., 2020). Embolic stroke of unknown source (ESUS) is frequent in COVID-19 and may explain up to 50% of cases (Grewal et al., 2020). Aortic arch thrombi are a possible cause of ESUS, although usually a rare finding in absence of aortic wall damage (Fayad et al., 2013).

We hereby report two cases of ischemic stroke due to embolization of a floating thrombus in the ascending aorta in patients with concomitant and recent COVID-19 infection and without signs of aortic wall damage.

Case 1

A 64-years-old male was brought to our Emergency Department (ED) for sudden onset dysarthria, left hemiparesis and hemisensory syndrome. The patient reported ongoing generalized asthenia from two weeks while fever and dyspnea had been present for two days. Upon arrival he was afebrile, tachypneic, and NIH Stroke Scale (NIHSS) was 10. Urgent laboratory tests showed neutrophilic leukocytosis with elevated C-reactive protein and D-dimer levels; COVID-19 molecular swab test was positive. Head computed tomography (CT) scan revealed no abnormalities whereas CT angiography (CTA) of the cervical and intracranial vessels showed a complete filling defect of the right middle cerebral artery (MCA) M3 segment. CT perfusion revealed an area of ischemic core with penumbra in the right parieto-occipital region, while a floating thrombus of the ascending aorta was identified in the thoracic planes included in the examination. A thoracic CT scan confirmed the latter finding and demonstrated bilateral interstitial pneumonia with pulmonary embolism. Considering the patient's critical conditions, urgent surgical removal of the aortic thrombus was deemed at high risk and mechanical thrombectomy for M3 thrombosis was not performed due to the distal location of the occlusion. Intravenous fibrinolysis with alteplase was administered. Control head CT scan at 24 h showed a

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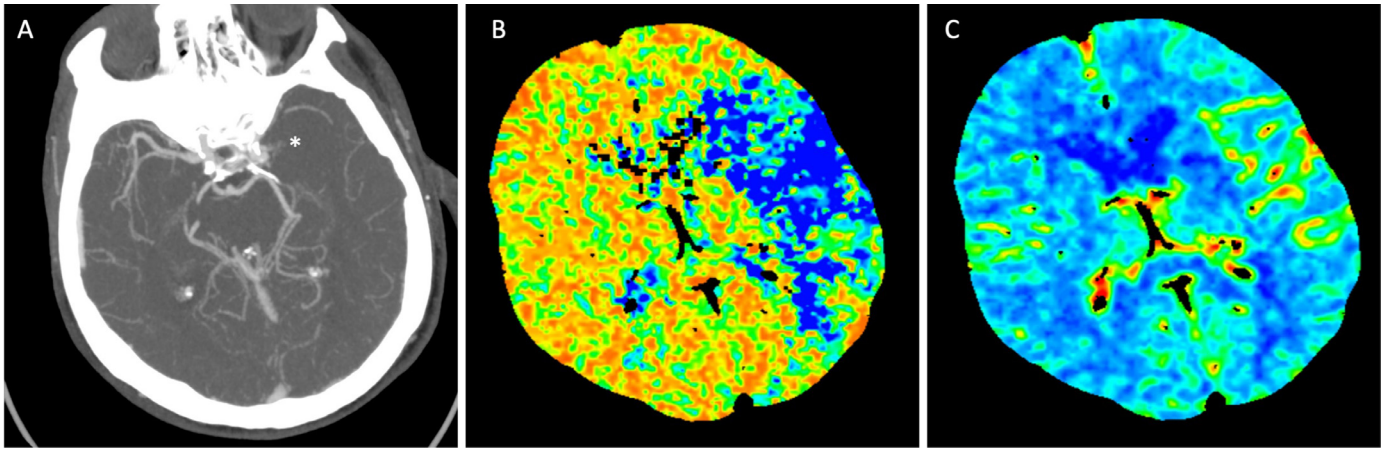

Fig. 1. Case #2 (A) Axial section of a maximum intensity projection reconstruction CT angiography of intracranial circulation demonstrating the occlusion of the M1 segment of left ACM (asterisk). (B) CT perfusion scan maps showing increased mean transit time and (C) increased cerebral blood volume in the left ACM territory demonstrating ischemic penumbra.

parenchymal hematoma and acetylsalicylic acid was initiated. Follow-up head CT scan at day 11 demonstrated progressive reabsorption of the hematoma, therefore anticoagulation with low weight molecular heparin (LWMH) was started and subsequently switched to warfarin. Thoraco-abdominal CT scan on day 27 showed aortic thrombosis resolution but demonstrated spleen and kidney embolism without clinical or laboratory involvement. No further treatment was initiated, and the patient underwent good neurological recovery with only mild left tactile sensory loss persisting at discharge on day 39.

Case 2

A 69-year-old male was admitted to our ED 100 days after COVID-19 infection, for sudden onset of global aphasia, right hemiplegia and hemianopsia. Upon arrival he presented fever, tachycardia, hypertension, and tachypnoea while NIHSS score was 18. Urgent laboratory tests revealed microcytic anemia, leukocytosis, elevated C-reactive protein, and mildly elevated D-dimer levels; COVID-19 molecular swab test was negative. Head CT scan and CTA showed a complete filling defect of the left MCA M1 segment with early signs of ischemic stroke, while CT perfusion revealed ischemic penumbra correspondingly (Fig. 1). Incidentally, a floating thrombus was identified in the ascending aorta. Due to the concomitant ischemic stroke, urgent surgical removal and percutaneous thromboaspiration of the aortic thrombus were deemed at high risk. Intravenous fibrinolysis with alteplase was administered and endovascular thrombectomy of the left MCA occlusion was performed with complete revascularization of M1 segment. Head CT scan at 24 h demonstrated an hypodensity in the left parieto-insular region, and on day 3, anticoagulation therapy with LMWH was initiated. To complete the study of aorta, an abdomen CT scan was performed revealing a colonic polypoid mass. Due to anemia worsening after initiation of anticoagulation, the patient underwent urgent colonoscopy with biopsy of the lesion which confirmed an infiltrating local adenocarcinoma. Despite the disappearance of aortic thrombus at follow up CT scan on day 11 (Fig. 2), the patient clinical conditions progressively worsened and on day 12 he was found comatose. Head CT scan showed a massive left nucleocapsular intracerebral hemorrhage extending into the ventricular system, with mass signs. The patient died on day 21 despite best medical therapy.

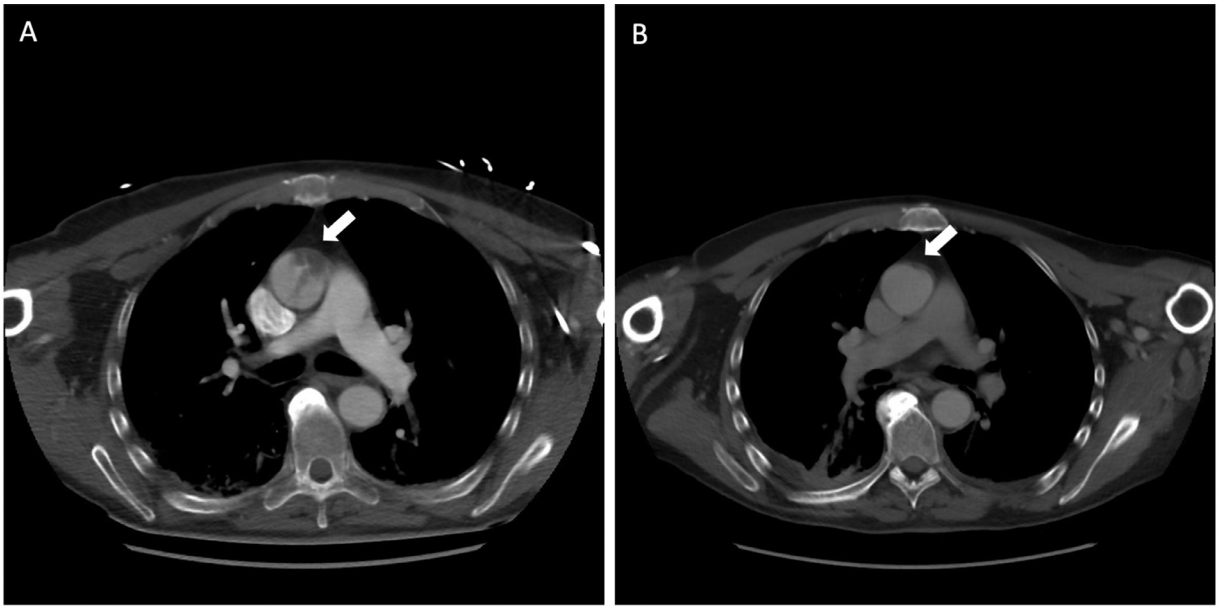

Fig. 2. Case #2 (A) Axial section of the baseline CT thoracic angiography showing the floating thrombus (arrow) located in the ascending tract of the aorta (B) Follow-up CT scan obtained on day 11, showing disappearance (arrow) of the thrombus after anticoagulation treatment.

Table 1
Clinical, laboratory and radiological characteristic of patients.

Clinical characteristics	Case 1	Case 2
Sex	M	M
Medical history	Lower limbs obliterating arteriopathy Former smoker	Arterial hypertension Chronic gastritis Microcytic anemia Glaucoma
Concomitant therapy	Acetylsalicilic acid	Ramipril Hydroclorotiazide
Laboratory findings at admission		
Hb (g/dL)	16.1	7
WBC (n/μL)	12,580	9930
N (n/μL)	10,560	7750
L (n/μL)	1430	920
CRP (n/μL)	276.6	55.2
IL-6 (pg/mL)	115.0	101.2
Coagulation studies**		
PLT (n/μL)	441,000	***531,000***
D-Dimer (FEUng/mL)	2753	932
INR	1.3	1.2
Fibrinogen (mg/dL)	419	470
Factors II, V, VII, VIII, X and XII activity (%) †	***V:160*** (n.v. 60–140) ***VIII:349*** (n.v. 55–150) ***XII: 217*** (n.v. 50–150)	***VIII:182*** (n.v. 55–150)
PAI (ng/mL)	***131***(n.v. 1–25)	***107*** (n.v. 1–25)
Antitrombin (%)	Normal	***78*** (n.v. 80–120)
Radiological findings		
ASPECT*** at admission	10	9
Aortic thrombus (length x width in mm)	15 × 20	30 × 10
Aortic arch wall	Normal	Normal
Stroke diagnostic work-up		
Cardiac telemetry	Negative	Negative
Echocardiography	Negative	Negative
CTA	Carotid atherosclerosis of without severe stenoses or unstable plaques	Negative

Legend: *Hb=hemoglobin; WBC=white blood cells; L=leukocytes; N=neutrophils; CRP=C-reactive protein. ** PLT=platelets; PAI=plasminogen activator inhibitor; n.v.=normal values; †=only factors with abnormal values are reported. *** Alberta Stroke Program Early CT score.

Table 1 summarizes the clinical and laboratory findings and the diagnostic work-up performed to rule out other potential stroke etiologies.

Discussion

The cases reported highlight how aortic arch thrombosis can be an incidental finding in the acute stroke setting in patients with concomitant and recent COVID-19 disease. In fact, it has been estimated that over 30% of patients admitted to intensive care with COVID-19 suffer from systemic thromboembolism, including from aortic thrombi (Klok et al., 2020; Buikema et al., 2021). In addition, the infection often leads to thrombosis in non-atherosclerotic vessels (de Roquetaillade et al., 2021): this occurrence is likely mediated by the viral-induced apoptosis of vascular endothelial cells and subsequent mononuclear infiltration with development of a severe leukocytoclastic vasculitis; newly formed antiphospholipid antibodies along with COVID-19-coagulopathy then promote local vascular thromboses (Roncati et al., 2021). Nevertheless, aortic thrombosis could also be an innocent bystander in the case of acute ischemic stroke, even in COVID-19 patients (Kashi et al., 2020). However, the occurrence of renal and spleen thrombosis in patient #1, support the hypothesis of embolization from the aortic thrombus, as described during COVID-19 infection (Sztajnbok et al., 2021), and in line with the finding that recurrent embolization from aorta is more frequent when stroke is the presentation syndrome (Fayad et al., 2013).

Early recognition of aortic thrombosis during acute stroke impacts treatment decision and, although no definitive consensus exists, there are numerous therapeutic options for its management including pharmacological thrombolysis, interventional or surgical removal, and anticoagulation (Fayad et al., 2013). Considering the severity of COVID-19 disease and concomitant ischemic stroke in our patients, pharmacological thrombolysis was performed followed by anticoagulation initiated after balancing the risk of hemorrhagic transformation of the ischemic lesion and the risk of embolic stroke relapse. Nevertheless, the co-existing coagulopathy adds further complexity to this clinical scenario, and the ideal time window to initiate anticoagulation should be evaluated case by case.

We acknowledge that our conclusions are limited by the number of observations, and we are aware that in patient #2 the concomitant adenocarcinoma could have acted synergistically in the stroke pathophysiology. Nevertheless, our findings suggest active radiological search for aortic arch thrombosis during the acute phase of stroke in patients with concomitant or recent COVID-19 infection.

Declaration of Competing Interest

The authors declare that they have no financial nor personal conflicts of interest related to the manuscript.

CRediT authorship contribution statement

Nunzio Davide de Manna: Conceptualization, Writing – original draft. **Francesco Bax:** Conceptualization, Writing – original draft. **Sandro Sponga:** Conceptualization, Methodology. **Francesco Toso:** Investigation. **Mariarosaria Valente:** Supervision, Writing – review & editing. **Serena D'Agostini:** Investigation. **Igor Vendramin:** Investigation. **Andrea Lechiancole:** Investigation. **Esmeralda Pompei:** Investigation. **Gian Luigi Gigli:** Conceptualization, Writing – review & editing. **Ugolino Livi:** Conceptualization, Writing – review & editing.

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