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Symptomatic Common Carotid Free-Floating Thrombus in a COVID-19 Patient, Case Report and Literature Review

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Carotid free-floating thrombus is an uncommon entity that usually presents with neurologic symptoms. Crescendo transient ischemic attack is an accepted indication for urgent carotid endarterectomy. COVID-19 is associated with severe thromboembolic complications. We report the case of a 61-year-old man who developed, 2 weeks after the diagnosis of COVID-19, crescendo transient ischemic attack, complicating a large intraluminal floating thrombus within the right common carotid artery. A carotid thromboendarterectomy under local anesthesia, with patch closure was immediately performed without complications. We conducted a literature review to identify cases of common carotid artery thrombus related to COVID-19. Carotid free-floating thrombus in the common carotid artery is exceptional. However, since the beginning of the COVID-19 pandemic, 15 cases have been published.

INTRODUCTION

In December 2019, the SARS-CoV-2 virus (severe acute respiratory syndrome-coronavirus2) and the resultant Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China. In March was declared by the World Health Organization as pandemic.¹ The most frequent symptoms are fever, cough, dyspnea, and diarrhea, but arterial

thrombotic complications are increasingly been reported.²⁻⁵

Carotid free-floating thrombus (CFFT) is a thrombus attached to the arterial wall, without complete intraluminal occlusion. Its incidence, natural history, and optimal treatment are unknown, and its management is based on case reports and series.⁶⁻⁸

Crescendo transient ischemic attack (cTIA) is characterized by repetitive episodes of transient neurologic ischemia, followed by return to a normal neurologic status. When cTIA is attributable to an ipsilateral carotid artery plaque, the best management is achieved by optimal medical treatment as well as urgent carotid endarterectomy (CEA).⁹⁻¹⁰

CASE DESCRIPTION

We report the case of a 61-year-old man with a medical history of hypertension and moderate asthma. He came to the emergency department on September 16th for the onset of fever and fatigue. The nasopharyngeal swab was positive for SARS-CoV2 on reverse-transcriptase-polymerase-chain-reaction assay, chest X-ray was normal and

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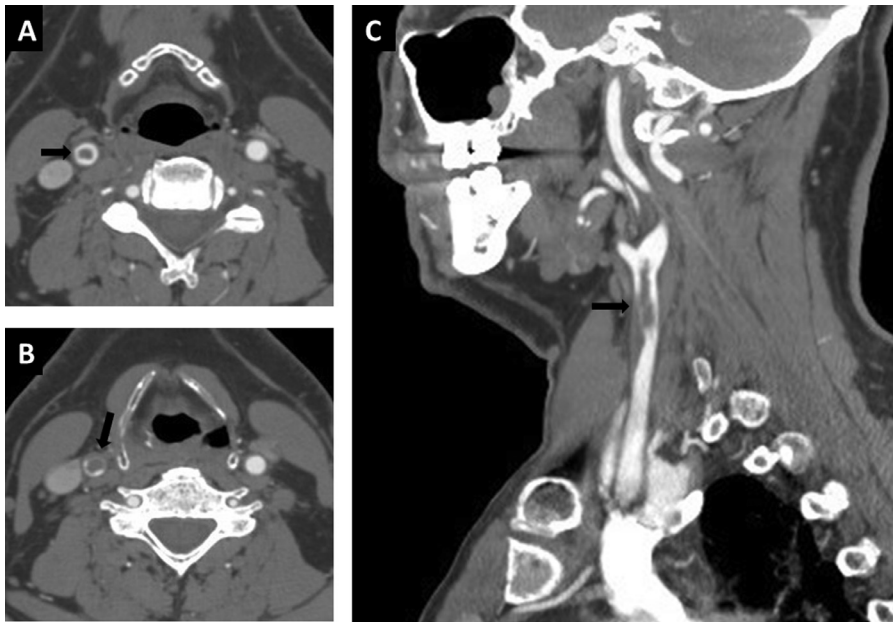


Fig 1. Axial (A and B) and sagittal (C) images of neck computed tomography angiography reveals a thrombus in the right CCA extending into carotid bifurcation. Image A: Thrombus with surrounding blood flow at its distal end. Image B: Thrombus attached to the wall.

he was discharged home. Despite antipyretics and azithromycin, fever persisted for 6 days and he returned to the hospital, but due to normal tests and physical examination, he was discharged.

Three days later, the patient came back to the emergency department with bronchospasm. Complementary tests revealed bilateral infiltrates on chest X-ray, lymphopenia ($0,5 \times 10^9$ cells per L), inflammatory syndrome with elevated C-reactive protein (178 mg/L), ferritin (1189 ng/mL), fibrinogen (798 mg/dL), Il-6 (80,7 pg/mL) and elevated D-dimer (812 ng/mL). Because of persistent dyspnea and low oxygen saturation, the patient was admitted to the hospital. On admission, the patient was tachycardic, tachypneic, and saturating at 86% on room air which improved to 95% on 4 liters nasal cannula.

He received bronchodilators (salbutamol and budesonide) and systemic steroids (methylprednisolone intramuscular first, and dexamethasone 6mg endovenous per day after admission), ceftriaxone and prophylactic anticoagulation with subcutaneous low molecular weight heparin (enoxaparin 80 mg/24h) were also started. The patient continued to desaturate with higher oxygen requirements and started with a dry cough, so a tocilizumab 600mg single dose was administered. After that, clinical (fewer oxygen requirements except when cough attacks) and analytical improvement was evidenced.

On September 30th, concurrent with a cough attack, he suddenly presented with an acute onset of left hand weakness with complete recovery after 1 hr. Urgent computed tomography (CT) head was unremarkable, but computed tomography angiography (CTA) of the head and neck demonstrated a nearly occluding thrombus in the distal right common carotid artery (CCA) extending into the carotid bifurcation (Fig 1). Therapeutic anticoagulation with enoxaparin (80 mg/12h), was started and he was admitted to the intensive care unit for close monitoring. Two hours later, the patient suffered another event of weakness on his left hand. Physical exploration revealed a mild decrease in distal left hand motility (fingers). Four hours afterwards he began with transient numbness on his left hand, without motor deficit associated.

Due to the risk of repeat embolic events, we elected to proceed with an urgent right carotid surgery. A carotid thromboendarterectomy was performed under local anesthesia. First, we dissected internal and external carotid arteries, systemic heparin was administered and, to identify the proximal end of thrombus in CCA, an intraoperative carotid duplex ultrasound was performed (Fig 2). To avoid embolization from thrombus, the internal carotid artery was clamped first, and then the dissection of proximal CCA was completed. Longitudinal arteriotomy of the

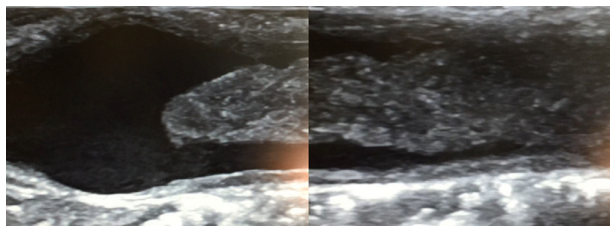


Fig 2. Intraoperative duplex ultrasound shows the mobile distal end of thrombus near carotid bifurcation and nearly occlusion of the right common carotid artery.

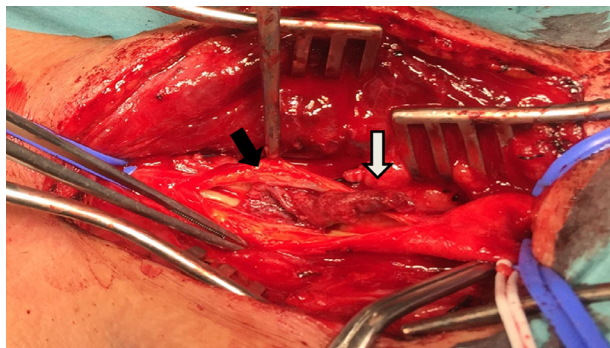


Fig 3. Intraoperative image showing an organized nearly occlusive thrombus (white arrow), which was partially attached to a small atherosclerotic plaque (black arrow).

CCA revealed an intimal flap and an organized nearly occlusive thrombus, which was partially attached to a small atherosclerotic plaque. The free-floating tail of the thrombus extended distally to the level of carotid bifurcation (Fig 3). The thrombus and intimal endothelial flap were easily removed from the plaque. The remaining wall surface of the carotid was soft. A section of the arterial wall was sent to the pathology department. A thin wall knitted polyester (polypatch® Perouse medical) patch closure of arteriotomy was performed. Intraoperative control with carotid duplex ultrasound revealed a proximal intimal flap with flow turbulence associated. The defect was repaired, without residual hemodynamic defect on the duplex. In the course of the surgery, no neurologic complications took place.

Postoperatively, the patient was anticoagulated with enoxaparin 80 mg/12h. He presented neck swelling without need for surgical exploration, the respiratory situation improved and he was discharged on the seventh postoperative day. On examination, he was neurologically intact and with no need for supplementary oxygen. At discharge, the patient's treatment was enoxaparin 60 mg/24h, acetylsalicylic acid 100 mg/24h, and atorvastatin 40

mg/24h (as well as antihypertensive treatment and bronchodilators).

Main pathological findings consisted of a stable atherosclerotic plaque, showing superficial erosion and fresh thrombus adherent to the wall. Endothelial intimal cells were not present. In the muscular layer, some hemorrhage and erythrocytes were seen between the muscular cells, a feature consistent with vessel dissection. The more relevant features were seen at the adventitial vessels: accumulation of inflammatory cells, neutrophils, and lymphocytes. Among endothelial cells of adventitial vasa vasorum, numerous apoptotic bodies, endothelial and inflammatory cells death were present. Fibrinoid necrosis of vessels was not seen. There was also red cell extravasation to the fibro collagenous tissue of the adventitia. We did not find viral particles in the endothelial wall.

A Follow-up carotid ultrasound, 4 weeks after the procedure, showed normal flow and resolution of the neck hematoma, so enoxaparin was changed to rivaroxaban.

LITERATURE REVIEW

An electronic search was conducted of the literature on the Medline (PubMed interface). The electronic search was carried out using the strategy as follows: ("COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR 2019-nCoV[tiab] OR 2019nCoV[tiab] OR COVID-19[tiab] OR covid19[tiab] OR SARS-CoV-2[tiab] OR "severe acute respiratory syndrome coronavirus 2"[tiab] OR (wuhan[All Fields] AND (coronavirus[tiab] OR "coronavirus"[MeSH Terms] OR "coronavirus infections"[Mesh])) AND carotid thrombus. A search included keywords and MeSH terms focus on *carotid*, *thrombus*, and *COVID19*. No language restriction was applied. The PubMed function "related articles" was used to extend the search. All reports were obtained and reviewed, and all references were checked for further literature on this topic. These additional reports were also obtained and reviewed. If multiple cases were presented within a paper, each case was individually reviewed for inclusion or exclusion.

Articles were considered for review if cases of patients with Covid-19 and thrombus in the CCA were described. Inclusion criteria were diagnosis of COVID-19 and a patent common carotid artery with CFFT diagnosed by angiography, carotid duplex ultrasound, CTA, or magnetic resonance angiography. CFFT was defined as a filling defect arising proximally from the carotid wall and with

circumferential blood flow at its distal aspect. We excluded patients with thrombus from embolic sources, complete thrombosis of common carotid artery, small intraplaque thrombus, or perioperative thrombus. The variables considered during data extraction were sex, age, medical history, and neurological symptoms of patients; COVID-19 severity, time from COVID-19 diagnosis to stroke, and antiplatelet or anticoagulant therapy; Location of thrombus and underlying pathology. If carotid surgery was performed, pathological findings were recorded.

DISCUSSION

In non-COVID-19 patients, carotid intraluminal floating thrombi are rare, with a reported prevalence of 1.6% among patients with acute stroke/TIA. Almost all patients (92%) present with neurologic symptoms. The 30-day risk of transient ischemic attack, silent brain ischemia, any stroke or death is 17.1%, and the nature of infarcts associated are mostly atheroembolic (97.7%). Atherosclerosis is the most common cause underlying CFFT; other causes include arterial dissection, hypercoagulable state, or cardioembolism. The internal carotid artery is the segment more frequently affected (75–65%), but the common carotid artery is rarely involved. In a retrospective review of carotid thrombus⁶, CCA was affected in 7% (8/116) of cases, and in a prospective serie⁸ only in 1.6% (1/61) of cases. Regarding the natural history of CFFT, potential outcomes include progression to occlusion, distal embolization, stabilization, or disappearance. Diverse antithrombotic approaches (anticoagulant, antiplatelet and fibrinolytic agents), and carotid interventions (endarterectomy, by-pass, thrombectomy, and stent) early or delayed, have been performed. However, neither medical nor surgical management was clearly superior to the other.^{6–8}

Definition of cTIA includes multiple repetitive TIAs within 24-hr with return to baseline neurological status in between episodes and afterwards. Brain imaging does not reveal a significant area of infarcted brain.⁹ When cTIA is attributable to an ipsilateral carotid artery plaque, symptoms arise from an unstable plaque with recurrent emboli despite antiplatelet therapy, or from unstable cerebral hemodynamics associated with the lesion. With medical therapy alone, a considerable number of these patients, experience a completed stroke within the first months or year and have a poor prognosis. Although urgent CEA in neurologically unstable patients carries a

higher risk than expected after elective cases, it is an accepted indication, considering the natural history of these patients.^{10,11} In patients undergoing CEA for cTIA, systematic reviews of the literature report rates of stroke and death of 6.5% (95% CI, 3.4–10.4%) and stroke, MI, and death of 10.9% (95% CI, 5.5–17.9%)¹². However, in carefully selected patients, CEA performed within 48 hr of initial presentation, is associated with lower rates of death/stroke (0–2%). Strict selection criteria include; patients who experienced an ischemic episode secondary to a high grade, unstable stenosis with structural features at high risk for intracranial embolization, with patent intracranial vessels and no new cerebral infarcts larger than 1.0 to 1.5 cm in diameter on computed tomographic imaging. Absolute contraindications to urgent CEA are coma, intracranial hemorrhage, and infarction in more than one-third of the middle cerebral artery territory.^{10,13}

Several reports highlight the risk for developing symptomatic acute arterial thrombosis on large vessels in patients with SARS-CoV-2, despite using antiplatelet or anticoagulant therapy. A considerable number of cases with thrombus in aorta, common iliac, femoral, and carotid arteries have been published.^{2–4} Indes JE et al³, in a retrospective case control study, reports an odds ratio for arterial thrombosis in COVID-19 patients of 3.37. Among patients with arterial thrombosis, those with COVID-19 tended to be male, were younger, with higher D-dimer and body mass index, and with less cardiovascular risk than patients without COVID-19. In these cases were remarkable, the lack or only mild underlying atherosclerosis, neither cardioembolic source. These data are suggestive of in situ arterial thrombosis out of proportion to the degree of underlying atherosclerotic disease.

We identified 10 articles, reporting 15 COVID-19 patients with free-floating thrombus in the CCA^{2,3,14–21} (Table I). Another 2 COVID-19 patients with CCA totally occluded have been published,^{22,23} these cases were excluded from the review because they did not meet our inclusion criteria. All patients presented with stroke as the chief symptom, and COVID-19 manifestations of mild severity. By adding our case, the time from COVID-19 diagnosis to the onset of neurologic complications was 10,5 days (4–14 days), the majority of patients were men (5 women/11 men), with a mean age of 59 years. Vascular risk factors (VRF) were present in 70% (9/13) of patients with medical history available, hypertension (66%) was the most frequent VRF followed by diabetes mellitus

Table I. Cases published of CFFT in COVID-19 patients

Author	Thrombus location	Sex	age (yo)	Past medical history	Time from COVID19 diagnosis to stroke (days)	COVID19 severity	Treatment	CTA findings	Surgical findings	Pathological findings
Gomez-Arbelaez ²	LCCA	F	76	HTN, HL, psoriasis	15	NE	Anticoagulation	CFFT	NA	NA
Indes JE ³	LCCA	M	56	NE	NE	Mild	CEA	CFFT	Thrombus organized attached to a thickened and inflamed wall	NE
Viguiet A ¹⁴	LCCA	M	73	No PMH	7	Mild	Anticoagulation	Large CFFT appended to non-stenotic plaque	NA	NA
Doo FX ¹⁵	RCCA	M	55	DM	0*	Mild	Chemical thrombolysis	Large CFFT	NA	NA
Fara MG ¹⁶	RCCA	F	33	-No PMH	0*	Mild	-Anticoagulation+dual	Large CFFT	NA	NA
	RCCA	F	77	-HTN, HL,	0*	Mild	Antiplatelet	Large CFFT	NA	NA
	RCCA	M	55	DM, bilateral DVT	0*	Mild	- Anticoagulation	Large CFFT	NA	NA
	RCCA			-No PMH			Anticoagulation+Antiplatelet			
Gulko E ¹⁷	RCCA	F	53	NE	NE	NE	NE	Large CFFT	NA	NA
	LCCA	M	49	NE	0*	NE	NE	Large CFFT	NA	NA
Esenwa C ¹⁸	LCCA	M	56	-HTN, DM	12		-Anticoagulation, CEA	Large CFFT	Organized thrombus	Inflammatory infiltrates into the intima
	RCCA	F	64	-HTN, DM,	12		-	Large CFFT	thrombus moderately adherent to a moderate plaque	
	LCCA	M	75	smoker	4		Anticoagulation+Antiplatelet + CEA	Large CFFT		
				-HL, former smoker			-Anticoagulation+dual Antiplatelet+ CEA			
Mohamud AY ¹⁹	RCCA	M	74	HTN, DM, CKD	14	Mild	Emergent CEA	Thrombus in the carotid bulb	NE	NE
Mowla A ²⁰	RCCA	M	36	No PMH	10	Mild		Large CFFT	NA	NA
							Anticoagulation+Antiplatelet+ Mechanical thrombectomy			
Hosseini M ²¹	RCCA	M	50	Smoker, Laryngectomy, PE after laryngectomy, Hypothyroidism	14	Moderate	Anticoagulation+high dose statin	Large CFFT	NA	NA
Current case	RCCA	M	61	HTN, asthma	14	Mild	Urgent CEA	Large CFFT	Organized thrombus moderately adherent to mild dissected plaque	Vessel dissection. Inflammatory infiltrates in adventitia

Abbreviations M male; F female; yo years old; LCCA left common carotid artery; RCCA right common carotid artery, HTN Hypertension; DM diabetes mellitus; HL hyperlipidemia; DVT deep vein thrombosis; CKD chronic kidney disease; PE Pulmonary embolism; PMH past medical history. NA not applied; NE not specified. 0* COVID and stroke diagnosis at the same time (although some of them, have presented respiratory symptoms previously).

in 44%, hyperlipidemia at 33%, and smoke at 33%. Images on CTA were similar: non-occlusive thrombus adherent to the CCA wall without or with mild atherosclerosis plaque. In 2 patients a thrombus in the aortic arch was also found.^{2,18} In the 5 cases in which a CEA was performed^{3,18,19} the findings were organized thrombus moderately adherent to a soft CCA wall. Esenwa et al¹⁸ analyzed the CCA wall in 3 cases and all of them found intima inflammatory infiltrates in the wall adherent to the thrombus. The authors suggest that, in patients with COVID-19, areas of mild carotid atherosclerosis may be particularly prone to thrombus formation because of the unique combination of endothelitis and COVID-19-associated coagulopathy.

The higher preponderance in males can be explained because in the general population carotid atherosclerosis²⁵ and CFFT affects men more frequently than women.⁶ Furthermore, severe complications of COVID-19, including cerebral ischemia, have been established to be higher in males with cardiovascular risk factors than in females.²⁶

Predisposing risk factors to severe COVID-19 are male sex, underlying cardiovascular disease, or cardiovascular risk factors including non-controlled diabetes mellitus or arterial hypertension, obesity, and advanced age.²⁷ In the present revision, 70% of the patients presented VRF, supporting the current evidence that preexisting cardiovascular risk factors increase the severity and thrombotic complications in COVID-19 patients.

CFFT in CCA is exceptional, however since May 2020 15 cases have been reported in patients with COVID-19. In the general population, a trend for patients with CFFT to be hypercoagulable has been described.⁶ The highly prothrombotic state of some COVID-19 patients could explain the presence of thrombus in vessels of medium and large caliber without or with mild atherosclerotic disease. On the other hand, smaller vessels, like internal carotid or intracranial arteries, are more prone to be totally occluded. Concerning the formation of thrombus over an atheroma plaque without severe stenosis or ulceration, is remarkable the increasing number of cases reported about patients with mild symptoms of COVID-19, whose main complication is cerebral ischemia because of large vessel occlusions.²⁴

In the present case, a 61-year-old man, with hypertension as the only vascular risk factor, the severity of COVID-19 was mild and neurological complications presented at 14 days from diagnosis of COVID-19. Surgical findings were similar to previously reported cases. Because the neurologic symptoms were simultaneous with cough attacks, it

is reasonable that they were due to small embolisms from the thrombus. It is also likely that cough triggered a dissection of the mild atherosclerotic plaque. This small dissection, in addition to the hypercoagulable state of the patient, could have provoked the thrombus formation.

Our study is limited by the small number of included studies, which are mainly case reports or case series, and the inability to prove causality between COVID-19 and CFFT in common carotid artery. Larger well-designed studies are needed to confirm the connection between SARS-CoV-2 and arterial thrombosis, to understand the mechanism underlying arterial thrombotic complications, to identify patients vulnerable for these complications, and finally to reach the optimal management of this new disease.

CONCLUSION

In conclusion, CFFT is an uncommon entity with potentially devastating effects. The location of thrombus in the CCA is exceptional. However, since the beginning of the COVID-19 pandemic, this pathology has increased despite the use of medical treatment, and 15 cases have been published. Carotid endarterectomy of free-floating thrombus in the common carotid artery causing crescendo transient ischemic attacks can be performed safely.

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