

CASE REPORT

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A case series of ischemic stroke with coronavirus disease 2019 in two Egyptian centers

Nevine El Nahas, Tamer Roushdy, Eman Hamid, Sherien Farag, Hossam Shokri, Mai Fathy* , Eman Abushady, Ahmed Hazzou and Hany Aref

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that has been reported to have various neurological manifestations. Cerebrovascular disorders have been encountered as a coronavirus disease 2019 (COVID-19) presentation in our center during the pandemic.

Case presentation: We are presenting 10 cases with cerebrovascular manifestations after having COVID-19 few days prior to stroke.

Conclusion: Cerebrovascular manifestations can occur in association with COVID-19 and may have significant implications on prognosis and management.

Keywords: Stroke, Egypt, COVID-19, SARS-CoV-2

Background

COVID-19 has been declared by the WHO as a pandemic in March 2020. Since then, there have been reports of patients with COVID-19 presenting solely with neurological manifestations [1] or in addition to the classic respiratory symptoms [2]. In a recent study, 36.4% of patients had neurological manifestations, such as headache, dizziness, acute cerebrovascular diseases, and impaired consciousness [3].

The first COVID-19 case announced in Egypt was on 15 February. At this point, a modified pathway for dealing with suspected cases presenting to ER with stroke and signs of viremia (fever, malaise, and cough) was implemented, in which a CT brain with or without CT angiography according to clinical suspicion of proximal occlusion and CT chest are ordered beside labs and nasopharyngeal swab. Patient is then managed according to guidelines for acute stroke arriving in window of thrombolysis and/or thrombectomy and is admitted to

isolation unit, and on obtaining PCR swab results (approximately within 48 h), the patient is to be managed at the stroke center or transferred to quarantine hospital with initial stroke management recommendations [4]. In our stroke center, we started seeing COVID patients presenting with acute ischemic stroke (AIS) on 28 April.

In this case series, we are presenting 10 cases with AIS after having COVID-19 few days prior to stroke. They were admitted to Ain Shams University Hospital Stroke Centers. COVID-19 symptoms ranged from fever to dry cough, shortness of breath, and myalgia. All patients were proven to be COVID-19 positive by polymerase chain reaction (PCR) (Table 1).

Cases presentation

Patient 1

A 65-year-old male, ex-smoker, hypertensive, with ischemic heart disease (IHD), atrial fibrillation (AF), and bronchial asthma since childhood, presented 2 days after COVID-19 symptoms. AIS onset-to-door time (ODT) was 1 and a half hour of right hemiparesis and global aphasia (National Institutes of Health Stroke Scale

* Correspondence: maifathy23@gmail.com

Neurology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Table 1 Clinical characteristics of the patients

Patient	Age	Gender	Medical history	Stroke presentation	NIHSS on admission and post-r-TPA	COVID-19 severity	Lab results (all patients are COVID-19 PCR positive)		Imaging (brain and chest)	Treatment received	Outcome and mRS	
							CBC ^a	Acute phase reactants ^b (CRP, ESR, Ferritin, LDH)				
Patient 1	65	Male	<ul style="list-style-type: none"> o Ex-smoker o HTN o AF o ISH o BA 	<ul style="list-style-type: none"> OTD 1.5 h o RT hemiparesis o RT hemihyesthesia o RT UMN facial o Global aphasia 	12 and 9	Moderate	HB 16.9 g/dl, WBC 12.6, Lymph. 1.76, neutrophil 10.27, platelet 340	CRP 315 ↑, ESR 10, ferritin 113	1.62 ↑ D-dimer ^c	CT brain: baseline: free, MRI: MCA with hemorrhagic transformation CT chest: multiple unilateral right lower lung lobe ground glass appearance and small peripheral consolidation patches of intermediate probability for COVID	For stroke: r-TPA DTN 25 min For COVID-19: oseltamivir, azithromycin, LMWH	Transfer to isolation unit Discharged after 20 days mRS 4
Patient 2	57	Male	<ul style="list-style-type: none"> o ISH o HF o DM 	<ul style="list-style-type: none"> OTD 3 h o LT hemiparesis o LT hemihyesthesia o LT UMN facial o Partial gaze o Dysarthria 	11 and 7	Severe	HB 15 g/dl, WBC 7.2, Lymph. 0.91 ↓, neutrophil 5.44, platelet 297	CRP 410 ↑, ESR 45	2.35 ↑	CT brain: baseline: free X-ray chest: bilateral ground glass opacities peripheral and central with high probability of COVID	For stroke: r-TPA For COVID-19: azithromycin, 40 mg steroids	Desaturation and put on oxygen 2 L. ICU admission and ventilated for 1 day then died. mRS 6
Patient 3	56	Male	None	<ul style="list-style-type: none"> OTD 2.5 h o LT hemiparesis o LT hemihyesthesia o Ataxia o Dysarthria 	7 and 4	Moderate	HB 16.1 g/dl, WBC 7.5, Lymph. 0.87 ↓, neutrophil 5.96, platelet 223	CRP 1071 ↑, ESR 40	2.16 ↑	CT brain: baseline: free CT chest: bilateral scattered central and peripheral ground glass opacities with high probability of COVID	For stroke: r-TPA DTN 20 min For COVID-19: LMWH 60 IU, azithromycin, 40 mg steroids	Transfer to ICU isolation unit mRS 2
Patient 4	52	Male	<ul style="list-style-type: none"> o Ex-smoker o ISH, o History of pulmonary edema o DM 	<ul style="list-style-type: none"> OTD 1 h o RT hemiparesis o RT hemihyesthesia o RT UMN facial o Global aphasia 	12 and 5	Moderate	HB 14.5 g/dl, WBC 7.5, Lymph. 1.17, neutrophil 5.52, platelet 228	CRP 306 ↑, ESR 50	1.95 ↑	CT brain: baseline: free Follow-up: MCA territorial infarction CT chest: bilateral central areas of ground glass with mild pulmonary venous congestion with minimal pleural effusion and tiny calcified pleural plaques	For stroke: r-TPA DTN 30 min For COVID-19: azithromycin, LMWH, 40 mg steroids	Transfer to isolation unit, discharged later on mRS 2
Patient 5	74	Female	<ul style="list-style-type: none"> o DM o HTN 	<ul style="list-style-type: none"> OTD 3 h o RT hemiparesis o RT hemihyesthesia o RT UMN facial o Dysarthria o Inattention o Diabetic ketosis (RBG 500 placed on insulin pump) 	12 and 8	Mild	HB 11.5 g/dl, WBC 8.6, Lymph 1.07, neutrophil 6.37, platelet 312	CRP 120 ↑, ESR 70, LDH 234 ↑	2.44 ↑	CT brain: baseline: free CT chest: bilateral diffuse basal ground glass appearance and interseptal thickening—indeterminate for COVID	For stroke: r-TPA DTN 30 min For COVID-19: azithromycin, oseltamivir	Transferred to isolation unit and discharged home after stabilization mRS 2
Patient 6	68	Female	<ul style="list-style-type: none"> o HTN 	<ul style="list-style-type: none"> OTD 3 h o LT hemiparesis o LT 	14 and 6	Mild	HB 12.5 g/dl, WBC 4.3, Lymph. 1.46, neutrophil 2.51,	CRP 164 ↑, ESR 45, ferritin 590.6 ↑	3.36 ↑	CT brain: baseline: free Follow-up: RT parietal and frontal MCA infarction CT chest: bilateral central patchy areas of ground glass opacity—intermediate probability of Covid-	For stroke: r-TPA DTN 35 min For COVID-19: azithromycin,	Transfer to isolation room within department and then to isolation unit—much improved.

Table 1 Clinical characteristics of the patients (Continued)

Patient	Age	Gender	Medical history	Stroke presentation	NIHSS on admission and post-r-TPA	COVID-19 severity	Lab results (all patients are COVID-19 PCR positive)		Imaging (brain and chest)	Treatment received	Outcome and mRS
							CBC ^a	Acute phase reactants ^b (CRP, ESR, Ferritin, LDH)			
						19	platelet 232		oseltamivir, full dose LMWH	mRS 2	
Patient 7	59	Male	o DM	o OTD 3 h o RT hemiparesis o RT hemihypesthesia o RT UMN facial o Global aphasia	17 and 15	Severe	HB 12.5 g/dl, WBC 10.7, Lymph. 0.8↓, neutrophil 11, platelet 238	CRP 302.5↑, ESR 55, ferritin 1300↑	1.91↑	CT brain: baseline: free Follow-up: left MCA infarction CT chest: bilateral basal ground glass	For stroke: r-TPA DTN 35 min Desaturated on room air (So2 66%), intubated and ventilated with ICU admission and died the next day mRS 6
Patient 8	62	Female	o AF o ISH o DM o HTN	o OTD 7 h o LT hemiparesis o LT hemihypesthesia o LT UMN facial	10	Moderate	HB 11 g/dl, WBC 8.7, Lymph. 1.33, neutrophil 6.25, platelet 216	CRP 78↑, ESR 58	1.85↑	MRI brain: right external watershed area CT chest: 2 small areas with ground glass appearance, mild right and minimal left-sided pleural effusion, low to intermediate left-sided pleural effusion	For COVID-19: chloroquine, oseltamivir, azithromycin, full dose anticoagulation Transfer to isolation unit and was stable for 12 days mRS 4 Then sudden deterioration with hemorrhagic transformation GCS 3
Patient 9	37	Male	o Smoking o HTN	o OTD 24 h o LT hemiparesis o LT UMN facial o Dysarthria	10	Moderate	HB 12.1 g/dl, WBC 9.55, Lymph. 2.36, neutrophil 6.26, platelet 255	CRP 70↑, ESR 63	2.41↑	MRI brain: RT basal ganglion large ischemic infarction X-ray chest: free except for increased bronchovascular markings	For stroke and COVID-19: antiplatelet then anticoagulation Discharged and much improved mRS 1
Patient 10	36	Male	None	o OTD 12 h o Expressive dysphasia	4	Mild	HB 13.1 g/dl, WBC 5.92, Lymph. 2.03, neutrophil 2.92, platelet 273	CRP 38.9↑, ESR 55, ferritin 584.1↑		MRI brain: LT insular Fronto-parietal. Left cerebellar subacute infarction CT chest: bilateral multilobar multifocal variable-sized patchy and wedge shape ground glass opacities, bilateral lower lobe consolidations shows pre-dominant peripheral distribution—highly suspicious of COVID	For stroke and COVID-19: antiplatelet then anticoagulant Stable despite suffering acute myocardial infarction after stroke by few days. mRS 0

HTN hypertension, DM diabetes mellitus, ISH ischemic heart, AF atrial fibrillation, BA bronchial asthma, UMN upper motor neuron, HB hemoglobin, WBC white blood cells, Lymph. lymphocytes, CRP C-reactive protein, ESR erythrocyte sedimentation rate, LDH lactate dehydrogenase, mRS modified Rankin Score, MCA middle cerebral artery, RT right, LT left, OTD onset to door, DTN door to needle, NIHSS National Institute of Health Stroke Scale, LMWH low molecular weight heparin, GCS Glasgow coma scale

^aHB = normal value 13–17 g/dl, WBC = normal value 4000–10,000, neutrophils = normal value 2000–7000, lymphocytes = normal value 1000–3000, 20–40%, platelets = normal value 250,000–450,000

^bCRP normal value up to 6 mg/l, ESR normal value up to 20 mm/h, ferritin = normal value 13–150 ng/l, LDH normal value 140–270 IU/l

^cD-dimer = normal value up to (0.55 ug/l)

(NIHSS) 12). Investigations showed elevated D-dimer and CRP; computed tomography (CT) chest showed intermediate probability of COVID-19 and normal CT brain. Intravenous thrombolysis (IV r-tPA) was given with door-to-needle time (DNT) of 25 min. Two hours NIHSS was 9, and follow-up magnetic resonance imaging (MRI) (Philips 1.5 Tesla, Germany) showed middle cerebral artery (MCA) M1 territory recent infarction with hemorrhagic transformation. Patient was admitted to isolation unit, then transferred to quarantine hospital and discharged after 20 days with modified Rankin score (mRS) of 4.

Patient 2

A 57-year-old male, with IHD, heart failure with EF 37%, and diabetes, presented 4 days following COVID-19 symptoms. ODT was 3 h of left hemiparesis and partial gaze palsy (NIHSS 11). Investigations showed grade I lymphopenia and elevated D-dimer, CRP, and ESR; X-ray chest showed high probability of COVID-19, and CT brain was normal. r-tPA was initiated with DNT of 33 min. Two hours NIHSS was 7. Patient showed signs of desaturation and was mechanically ventilated and died 3 days from admission.

Patient 3

A 56-year-old male patient, with irrelevant medical history, presented 2 days following COVID-19 symptoms. ODT was 2 and a half hours of left ataxic hemiparesis and dysarthria (NIHSS 7). Investigations showed grade I lymphopenia and elevated D-dimer, CRP, and ESR; CT chest showed high probability of COVID-19 and normal CT brain. r-tPA was given with DNT of 20 min; 2 h NIHSS was 4. Patient was admitted to isolation ward then to quarantine hospital with mRS 2.

Patient 4

A 52-year-old male, ex-smoker, diabetic, IHD, with history of pulmonary edema, EF 38%, presented 3 days following COVID-19 symptoms. ODT was 1 h of right hemiparesis and global aphasia (NIHSS 12). Investigations showed relative lymphopenia and elevated D-dimer, CRP, and ESR; CT chest showed low probability of COVID, and CT brain was normal. Patient received r-tPA with DNT of 30 min. Two hours NIHSS was 5; follow-up brain imaging showed territorial MCA infarction. Patient was admitted to isolation unit and on obtaining PCR results transferred to quarantine hospital and discharged with mRS 2.

Patient 5

A 74-year-old female, diabetic and hypertensive, presented 3 days following COVID-19 symptoms. ODT was 3 h of right hemiparesis and diabetic ketosis for which

insulin pump was used (NIHSS 12). Investigations showed relative lymphopenia, elevated D-dimer, and inflammatory markers; CT chest was indeterminate for COVID-1, and CT brain was normal. r-tPA was given with DNT of 30 min; 2 h NIHSS was 8. Patient was transferred to isolation unit then to quarantine hospital and discharged home with mRS 2.

Patient 6

A 68-year-old female, hypertensive, presented 2 days following COVID-19 symptoms. ODT was 3 h of left hemiparesis and gaze (NIHSS 14). Investigations showed elevated D-dimer, ferritin, and inflammatory markers; CT chest showed intermediate probability of COVID-19, and CT brain was normal. r-tPA was given with DNT of 35 min; 2 h NIHSS was 6. Follow-up MRI showed right MCA territory infarction; patient was transferred to isolation unit then to quarantine hospital with mRS 2.

Patient 7

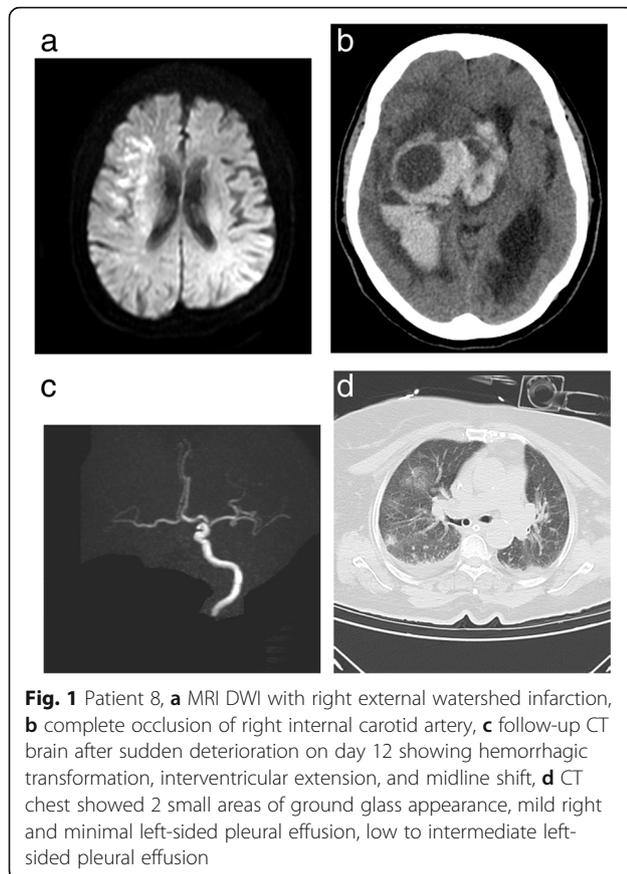
A 59-year-old male, diabetic, presented 2 days following COVID-19 symptoms. ODT was 3 h of right hemiparesis and global aphasia (NIHSS 17). Investigations showed grade I lymphopenia, elevated D-dimer, ferritin, and inflammatory markers; CT chest showed intermediate probability of COVID-19; CT brain was normal. He received r-tPA with DNT of 35 min; 2 h NIHSS was 15. MRI brain showed recent left MCA infarction. Patient developed desaturation on room air, SO_2 66%, intubated and ventilated, and died within 3 days of admission.

Patient 8

A 62-year-old female, diabetic, hypertensive, with IHD and AF, presented 1 day following COVID-19 symptoms with ODT of 7 h of left hemiparesis (NIHSS 10). Investigations showed relative lymphopenia, elevated D-dimer and inflammatory markers, and bilateral basal ground glass imaging on CT chest; MRI brain revealed right external watershed infarction. Patient condition was stable over 12 days with mRS 4, then suddenly deteriorated with Glasgow coma scale 3; CT brain revealed hemorrhagic transformation, interventricular extension, and midline shift (Fig. 1). The patient is still on mechanical ventilator.

Patient 9

A 37-year-old male, hypertensive and smoker, presented 1 day following COVID-19 symptoms with ODT of 1 day with left hemiparesis and dysarthria (NIHSS 10). Investigations showed elevated D-dimer and inflammatory markers, X-ray chest was normal, and brain imaging revealed right basal ganglionic infarction; patient was admitted to isolation unit with initiation of antiplatelet and



anticoagulant, with much improvement and discharged with mRS 1.

Patient 10

A 36-year-old male, with irrelevant medical history, presented 7 days following COVID-19 symptoms with ODT of 12 h of aphasia (NIHSS 4). Investigations showed elevated ferritin and inflammatory markers; chest imaging showed high probability of COVID-19; brain imaging showed left insular and left cerebellar subacute infarction. Patient received antiplatelet and was stable with mRS 0, few days later developed acute myocardial infarction; transthoracic echocardiography (Vivid E9 machine, General Electric, Vingmed Ultrasound, Horten, Norway) revealed fresh apical thrombus with elevated troponin (0.321 ng/ml—normal range < 0.014 ng/ml), and anticoagulation was initiated (Fig. 2). The patient became stable and was discharged.

Discussion

All cases presented with AIS ranging from 1 to 7 days after onset of viremia symptoms which included fever, dyspnea, fatigue, and/or myalgia. CT chest was

suggestive of COVID-19 criteria; D-dimer was mildly elevated, with moderately to markedly increased CRP and ESR. Lymphocytic count ranged from normal to relative or grade I lymphopenia. Similar findings were reported by other groups [5–7]. All cases were confirmed with a positive PCR within 48 h of presentation.

Seven patients received thrombolytic therapy, and the rest either anticoagulant or antiplatelet therapy. Six patients improved as regards stroke with mRS ranging from 0 to 4.

Four out of ten patients (patients 2, 7, 8, and 10) developed complications. Only patient 8 had a neurological cause for deterioration, while patients 2 and 7 had sudden desaturation and eventually died. Patient 10 reached mRS = 0, then had a myocardial infarction, but fortunately, he recovered and was discharged. This agrees with what has been suggested that AIS might be associated with severe form of COVID-19 [8].

The controversy whether COVID-19 can cause thrombosis or hemorrhage still holds, as seen in patient 8 who developed hemorrhagic transformation of her infarction. Although patients with increased D-dimer can suffer from thrombotic events, yet hemorrhage due to prolonged prothrombin time might occur [6].

It is worth mentioning that cases 3 and 10 had no risk factors for stroke; in addition, case 10 was only 36 years old yet developed myocardial infarction few days after AIS. This raises the possibility of occurrence of an inflammatory response termed “immunothrombosis” in such cases [9–11]. However, still one cannot overlook the detrimental effect of hyperthermia, dehydration, and hypoxia in the presence of viral endothelial invasion through ACE receptors that are abundant in endothelial cells [5, 12, 13]. It is also reported that COVID-19 has a role in developing diffuse vasculopathy and vasculitis through inflammatory cell infiltration, endothelial cell damage, and endotheliopathy. All these factors can contribute to platelet aggregation and thrombosis [5].

Out of the current case series, we have the following recommendations: COVID-19 has pulmonary besides extrapulmonary manifestations, and stroke is one of such manifestations, so triaging patients in ER with a proper baseline investigations as CT chest and nasopharyngeal swab can detect hidden COVID-19 cases that ought to be isolated and at the same time managed as stroke guidelines recommend based on onset to door. In our presented cases D-dimer was mildly elevated and lymphocytic count was showing grade I lymphopenia in some but not all cases so it is worth mentioning that other supportive criteria for COVID-19 like symptomatology, CT chest, and PCR are of greater value than labs.

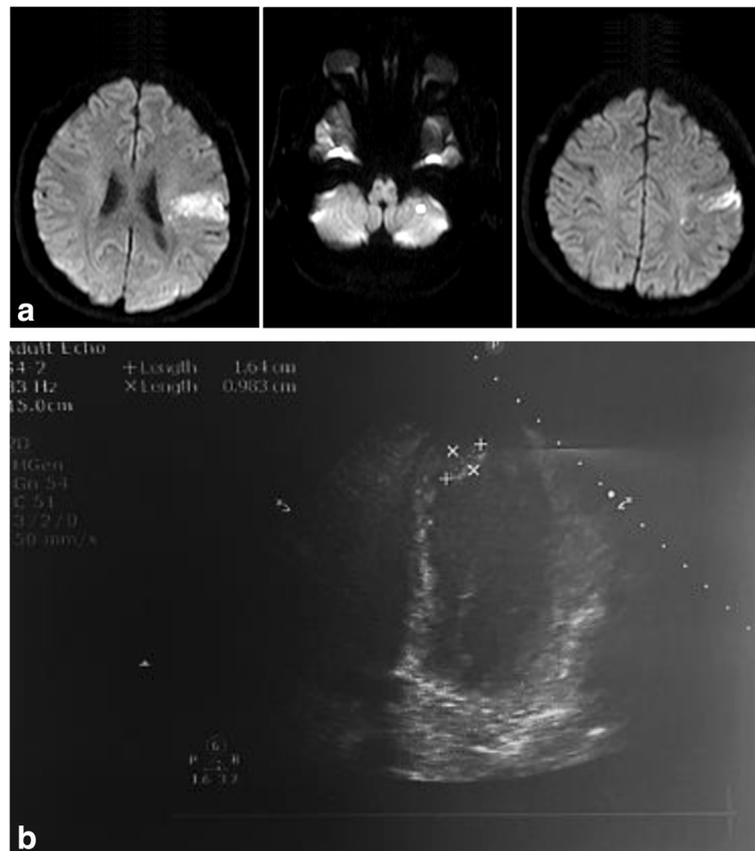


Fig. 2 a MRI DWI of patient 10 with left insular and cerebellar infarction. **b** ECHO of patient 10 with fresh apical thrombus measuring 12 × 16 mm, EF 35%, akinetic all apical segment, mid-anterior wall, mid-anterior septum, and mid-posterior septum

Conclusion

Whether a cause or a coincidence, COVID-19 with stroke has been treated by r-tPA, anticoagulants, and/or antiplatelets. Patient 8 developed intracerebral hemorrhage after receiving anticoagulation, while case 10 developed another thrombotic event despite receiving anticoagulant and antiplatelet. So in order to achieve the best outcome and avoid complications, guidelines for the timing and dosing of medications that guard against immunothrombosis need further elaboration.

Abbreviations

COVID-19: Coronavirus disease 2019; AIS: Acute ischemic stroke; PCR: Polymerase chain reaction; IHD: Ischemic heart disease; AF: Atrial fibrillation; ODT: Onset-to-door time; MRI: Magnetic resonance imaging; MCA: Middle cerebral artery; NIHSS: National Institutes of Health Stroke Scale; CT: Computed tomography; IV r-tPA: Intravenous thrombolysis; DNT: Door-to-needle time; mRS: Modified Rankin score

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Authors' contributions

NE: design and conceptualized the study. TR: conception of the work and drafting the manuscript. EH: acquisition and analysis of data. SF: acquisition and analysis of data. HS: conception of the work and drafting the manuscript. MF: acquisition and analysis of data. EA: data collection and

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The corresponding author takes full responsibility for the data, has full access to all of the data, and has the right to publish any and all data separate and apart from any sponsor.

Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the Faculty of Medicine, Ain Shams University Research and Ethical Committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. We obtained approval from research ethics committee no. FWA 000017585. On 27 August 2020.

Consent for publication

Written informed consent was obtained from participants or next of kin for publication of this case series and accompanying images. We obtained approval from research ethics committee no. FWA 000017585. On 27 August 2020.

Competing interests

None of the authors has any conflict of interest.

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