NobleStitch PFO Closure for Recurrent Strokes in a Patient on ECMO with COVID-19

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Abstract

Cryptogenic stroke is a complication commonly associated with patent foramen ovales (PFOs). However, current guidelines do not address PFO management in COVID-19 patients. This report describes a challenging case of an unvaccinated patient with recurrent strokes and refractory hypoxemia secondary to COVID-19 pneumonia who underwent a PFO closure using NobleStitch.

Keywords : Cryptogenic stroke; Patent foramen ovale; NobleStitch; COVID-19; Intracardiac shunt; Echocardiography

Manuscript

Severe hypoxemia secondary to COVID-19 pneumonia is a significant contributor to morbidity and mortality.[1] Patent foramen ovales (PFOs) can exacerbate hypoxemia through an intracardiac shunt, slowing recovery and worsening outcomes.[2-4]Additionally, cryptogenic stroke is a complication commonly associated with PFOs, however, current guidelines do not address PFO management in COVID-19 patients who suffer from recurrent paradoxical emboli, especially in the setting of COVID-19 pneumonia, increased right-sided pressures, and hypercoagulable state.[3, 4] This is significant considering approximately 25% - 34% of the population suffer from a congenital PFO.[3, 5] Interestingly, a recent cross-sectional study (n=75) of patients under mechanical ventilation secondary to COVID-19 pneumonia found a prevalence of PFOs in 15% of their patients.[6] While most patients with a PFO do not require surgical intervention, selected patients may strongly benefit from PFO closure to prevent recurrent cryptogenic strokes.[7] This report describes a challenging case of an unvaccinated patient with recurrent strokes and refractory hypoxemia secondary to COVID-19 pneumonia. The patient was subsequently found to have a PFO and underwent a PFO closure using NobleStitch EL (Heartstitch, Fountain Valley, CA).

FDA approved in 2019, NobleStitch enables a deviceless method of PFO closure [8, 9] Using percutaneous access, NobleStitch approximates the septum primum and the septum secundum using two polypropylene sutures and a single polypropylene knot, thereby avoiding the risks associated with septal occluders, such as infection, anticoagulant use, arrhythmias, device erosion/dislodgment, and hindered left atrial access.[8, 9] Initial registry data (n=192) has demonstrated that NobleStitch is a safe and effective method of PFO closure, revealing complete resolution of the right-to-left shunt in 75% and a grade 1 residual right-to-left shunt in 14%.[9] Although recent studies have begun to refine the inclusion criteria for this procedure to improve postprocedural residual shunting, long term outcomes of this device will be better further understood with the completion of the prospective multicenter clinical trial slated to conclude in 2026.[10-12]

Case Presentation

A previously healthy 42-year-old unvaccinated male presented to the hospital with a two-day history of dyspnea, fever, chills, and was diagnosed with Coronavirus disease-2019 (COVID-19) infection. The patient was admitted for a higher level of care when his dyspnea progressively worsened. His differential diagnosis at the time of presentation included acute hypoxic respiratory failure secondary to COVID-19, severe acute respiratory distress syndrome (ARDS), and pulmonary embolism**.**

Initially, his condition was stable on 40 L/min via a high-flow nasal cannula, intravenous steroids, and antiviral therapy. On inpatient day #4, the patient's oxygenation worsened. Arterial blood gas confirmed hypoxemia with a PaO_2 of 51 mmHg and a $PaCO_2$ of 30 mmHg. Overnight, the patient developed severe respiratory distress with an oxygen saturation of 60%, requiring an escalation of respiratory and pharmacological support. He was subsequently placed on bi-level positive airway pressure ventilation followed by endotracheal intubation. Post-intubation, his PaO_2/FiO_2 ratio was initially 93, which declined to 59 on 100% FiO_2 and positive end-expiratory pressure of 10 cm H_2O. Due to refractory hypoxemia, the patient was transitioned to prone ventilation, inhaled epoprostenol therapy, and eventually placed on veno-venous extracorporeal membrane oxygenation (VV-ECMO) support.

One week later, the patient's hospital course was further complicated by an acute ischemic cerebrovascular accident. He was noted to have left arm and leg weakness with a right facial droop. Computed tomography (CT) of the head showed a hypodensity in the left medial cerebellum consistent with a subacute cerebellar infarct (Figure 1). CT angiography revealed a thrombus occluding the V4 segment of the left vertebral artery, which is associated with the occlusion of the left posterior inferior cerebellar artery. Three days later, a repeat head CT revealed a hypodensity at the parietal-occipital junction raising concern for the evolution of the suspected infarction. Transthoracic echocardiography was performed, and a saline contrast injection revealed right to left shunting through a PFO which was found to be <5mm (Figure 2 and Video 1). Interventional cardiology was subsequently consulted for PFO closure due to repeated paradoxical thromboembolic events.

The patient was taken to the hybrid operating room for transesophageal echocardiography assessment of PFO. After evaluation of the patient's PFO, it was concluded that closure with NobleStitch, a deviceless

PFO closure technique would be the most beneficial method of treatment given this patient's young age, amenability to repair, and hypercoagulable state.[9]

After femoral venous access was obtained, the septum primum and septum secundum were grasped using NobleStitch grasping arms respectively, and later a KwiKnot was applied to close the PFO (Figure 3, Video 1). A postprocedural saline bubble study confirmed no residual intracardiac shunt (Video 1). The patient was weaned off VV-ECMO and pressure support ventilation over the next two weeks. He ambulated shortly thereafter and was subsequently discharged to outpatient rehabilitation where he continued to improve.

Discussion

While the role of PFO in refractory hypoxemia and cryptogenic stroke in patients with COVID-19 may have often been overlooked throughout the pandemic, there is currently no evidence-based recommendation regarding the management of these patients.[1, 3-5, 13] To our knowledge, this report highlights the first case of PFO closure in a COVID-19 patient using NobleStitch.

While COVID-19 can often present with thromboinflammation and a hypercoagulable state, right-to-left shunting through a PFO further increases the risk for paradoxical embolism, possibly due to the increased right atrial pressure.[3, 5, 14] This is a predicament in patients with a PFO in the setting of COVID-19 pneumonia, where increased right-sided pressures induce vascular damage, further activating the coagulation system and exacerbating the risk for paradoxical embolism.[1, 4, 5] Moreover, the increased pulmonary pressures in these patients may be responsible for the refractory hypoxemia that is seen.[3, 4] Surgical correction may not only improve oxygenation and right-to-left shunting in these patients, but it can also help prevent cryptogenic strokes.[1, 4, 13]

The NobleStitch provides a novel way of closing a PFO which represents a significant source of embolic stroke and refractory hypoxemia.[8] Guided by transesophageal echocardiography (Video 1), this technique effectively closes the PFO by applying sutures through the septum primum and septum secundum, subsequently creating a knot between the two sutures and removing excess suture material, thereby avoiding many risks that accompany septal occluders.[8] Hypercoagulable patients such as those with COVID-19 may be at increased risk of thrombotic complications with permanent implants with a large device burden. Additionally, these permanent devices can eventually hinder left-sided heart procedures in younger patients who might benefit from such interventions later on in the future.[9]

Thus far, NobleStitch has shown promising results in terms of effectiveness, safety, and longevity.[9, 10, 15] To improve patient selectivity, a retrospective observational study of 247 patients who underwent PFO closure with NobleStitch suggested new predictors of residual shunting after intervention. This study revealed improved outcomes with a preoperative PFO < 5mm in width and absence of a spontaneous right to left shunt, indicators that were both met in our patient.[10] Another prospective single-center study with a six month follow up period (n=116) investigated factors that may have contributed to residual intracardiac shunting ≥ 2 (20%, $n = 23$), revealing partial stitch detachment (n=12), atrial septal tear (n=3), and KwiKnot embolization (n=2) as the main causes of right-to-left shunting at follow up.[11] Although NobleStitch is not without complications, it has clear advantages over commonly used device PFO closures.[8, 9, 11]

This case highlights how the NobleStitch procedure may be used to close a PFO in a COVID-19 patient on VV-ECMO with refractory hypoxemia and cryptogenic stroke. Particularly useful in younger patients, this deviceless system overcomes many of the complications associated with traditional PFO closure devices.[8] Given the ubiquity of COVID-19 and its complications, early detection and treatment of PFO in patients with severe COVID-19 are critical for timely recovery and prevention of serious sequelae.[4] Furthermore, given the hypercoagulable state with severe COVID-19, choosing a deviceless method to close the PFO may avert clot formation, future strokes, and the need for anticoagulation. This case highlights that the NobleStitch device shows promise in avoiding severe neurologic sequelae of cryptogenic stroke. Notably, PFO closure with NobleStitch is a relatively noninvasive cardiac intervention with a low device burden, allowing for future surgical intervention, especially in younger patients.

Conflicts of Interest

No conflicts of interest to declare. No funding was required for this case study. All clinical information is anonymized within this case report. Permission was also obtained from the patient to report this case; therefore, no ethical approval was required.

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Figure Legends

Figure 1. Head computed tomography demonstrating a wedge-shaped area of low attenuation within the inferomedial aspect of the left cerebellar hemisphere with loss of gray-white differentiation in the axial (Inset A) and sagittal views (Inset B), consistent with subacute infarction.

Figure 2. Transthoracic echocardiography bubble study demonstrating the presence of saline contrast (bubbles) in the left ventricle, diagnostic of a right-to-left intracardiac shunt through a patent foramen ovale.

Figure 3. Transesophageal echocardiography demonstrating V-sign, a V-shaped indent on the septum primum, which reflects tension due to the NobleStitch KwiKnot.

Video Legends:

Transthoracic echocardiography bubble study demonstrating the presence of saline contrast (bubbles) in the left ventricle, diagnostic of a right-to-left intracardiac shunt through a patent foramen ovale (PFO).

Midesophageal (ME) bicaval view with and without color flow Doppler indicating a gap between the septum primum and secundum.

ME bicaval view with and without color flow Doppler showing Noblestitch guidewires through the PFO to access the left atrium (LA).

ME bicaval view with and without color flow Doppler demonstrating guidewires into the superior vena cava (SVC) and LA to grasp the septum secundum.

3D view of the wire crossing the PFO.

ME bicaval view showing the Noblestitch catheter across the PFO into the LA, grasping the septum primum.

ME bicaval views showing the KwiKnot application, joining the septum primum and secundum together.

ME bicaval view showing the V-sign: a V-shaped indent on the septum primum, which reflects tension due to the Noblestitch KwiKnot.

ME bicaval view 2D and 3D views showing the post-procedural bubble studies with absence of bubbles in the LA, indicating a successful closure.