

# A Case of Pulmonary Embolism and Stroke in a 16-year-old Girl

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## ABSTRACT

A 16-year-old girl arrived intubated to the emergency department. She had shortness of breath and cough for 2 days with leg pain. On arrival, she was hemodynamically stable with an unremarkable physical exam. Electrocardiogram revealed a prolonged QT interval; laboratory work-up was normal except for an elevated dimerized plasmin fragment D. Acute pulmonary embolism was confirmed by a chest computed tomography scan. A lower extremity duplex scan was negative and echocardiogram revealed a patent foramen ovale with bidirectional shunting. An inferior vena cava filter was placed to prevent acute recurrence and unfractionated heparin was initiated. The next day she was noted to have right hemiparesis. Stroke was confirmed by magnetic resonance imaging. The patient underwent mechanical clot retrieval and was discharged on anticoagulation therapy to a brain rehabilitation unit.

## INTRODUCTION

Patent foramen ovale has been implicated in cryptogenic strokes in adults.<sup>1</sup> There is increasing pediatric data on cryptogenic strokes, where paradoxical emboli are presumed to be the cause of stroke.<sup>2</sup> Although adult cases of pulmonary embolism and stroke in the presence of a patent foramen ovale have been described,<sup>3</sup> our search revealed no such pediatric cases. Here, we present the case of a previously healthy adolescent female with pulmonary embolism and stroke in the presence of a patent foramen ovale.

## CASE DESCRIPTION

A 16-year-old girl was found at home by family members, unresponsive and with labored respirations. Emergency medical service personnel noted spontaneous respirations, stable vital parameters and a Glasgow Coma Scale (GCS) of 6. She arrived intubated to the emergency department in sinus

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tachycardia, with stable blood pressure, adequate perfusion, and normal oxygen saturation on minimal ventilator settings. She had been hiking with family members the preceding week and had arrived home after a long car ride the previous day. She had developed some cough and shortness of breath 2 days before admission. Her past medical and social history was unremarkable. She had been initiated on oral contraceptive pills 4 to 5 months before. Her family history was significant for venous thromboses and pulmonary

embolism in the maternal grandfather. Laboratory work-up was normal except for an elevated dimerized plasmin fragment D (D-dimer) level of 13.42 mcg/ml (normal: <0.5 mcg/ml). Electrocardiogram (ECG) revealed sinus tachycardia with prolonged QTc (500 ms). Head and neck computed tomography (CT) scans were normal. The patient was transferred to the pediatric intensive care unit for further care following a chest CT scan.

Cardiopulmonary, abdominal, and musculoskeletal exams were unremarkable. She was withdrawing all extremities to painful stimuli and no obvious asymmetry was noted on neurological exam. Remifentanyl infusion was used for sedation to allow frequent neurological assessments. ECG continued to show prolonged QTc (480 ms) without any other abnormalities. Chest CT scan revealed massive bilateral pulmonary embolism (Figure 1). Duplex study of the lower extremities was negative for any thromboses. Unfractionated heparin therapy was initiated and appropriate consults were obtained. Given the size of the pulmonary emboli, a retrievable inferior vena cava (IVC) filter was placed to prevent any further pulmonary embolism. The patient was switched to enoxaparin (low molecular weight heparin) for continued anticoagulation after the filter placement. Echocardiogram revealed right ventricular dilatation with normal left ventricular function and a patent foramen ovale with bidirectional shunting. No asymmetry had been noted on the patient's exam until shortly after extubation

when she was noted to have right-sided hemiparesis and aphasia. A head CT scan and magnetic resonance imaging (MRI) obtained thereafter showed a new left striatocapsular and internal capsule infarct in M1 distribution with no acute bleeds (Figure 2). A conventional cerebral arteriogram confirmed occlusion of the left mid-M1 segment and proximal M2 segment of the middle cerebral artery with minimal distal filling suggesting thrombotic occlusion. The thrombus was retrieved with a penumbra device with improvement in hemiparesis and aspirin initiated shortly after mechanical clot retrieval.

The patient was tested for prothrombin and methylenetetrahydrofolate reductase (MTHFR) gene mutation, factor V Leiden and antiphospholipid syndrome. She was noted to be homozygous for MTHFR mutation with homocysteine level in the normal range. Enoxaparin and aspirin were continued at discharge. She underwent brain rehabilitation with marked improvement in function.

Protein C, protein S, and antithrombin III (ATIII) levels obtained at a follow-up visit showed ATIII deficiency. Anticoagulation therapy was switched to warfarin and the patient was counseled against the use of oral contraceptives. She was scheduled for filter retrieval with a plan to close the patent foramen ovale at a later date.

## DISCUSSION

We believe our case to be the first pediatric case report of a documented stroke and pulmonary embolism in the presence of a patent foramen ovale.

Our patient was taking oral contraceptive pills and had recently traveled long distances in a car. Contraceptive pills are a known risk factor for venous thromboembolism, especially for women in the reproductive age group. She had been complaining of leg pain and shortness of breath prior to the sudden syncopal event, suggesting the possibility of venous thromboses and pulmonary embolism. The term “economy class syndrome” was coined in 1988 to describe the association between prolonged travel and thrombosis. The initial articles implicated prolonged air travel; however, recent articles suggest that prolonged bus and car rides also may contribute to the development of thrombosis.<sup>4</sup>

The presence of a prolonged QTc in pulmonary embolism is described, but is infrequent and not specific to this diagnosis.<sup>5</sup> Our patient’s QTc interval normalized on day 2, thus lowering suspicion for prolonged QT syndrome.

A lower extremity Doppler ultrasound test was negative for any thromboses; upper extremity Doppler was not performed. Duplex scanning has a sensitivity of 100% and specificity of 98% for proximal symptomatic deep vein thrombosis, and 94% sensitivity and 75% specificity for distal symptomatic deep vein thrombosis. However, its sensitivity is controversial

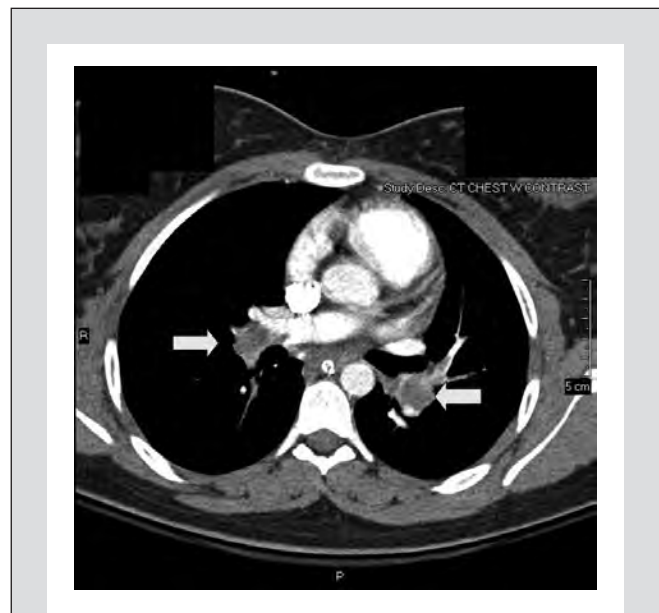


Figure 1: Chest CT Scan Showing Bilateral Pulmonary Embolism

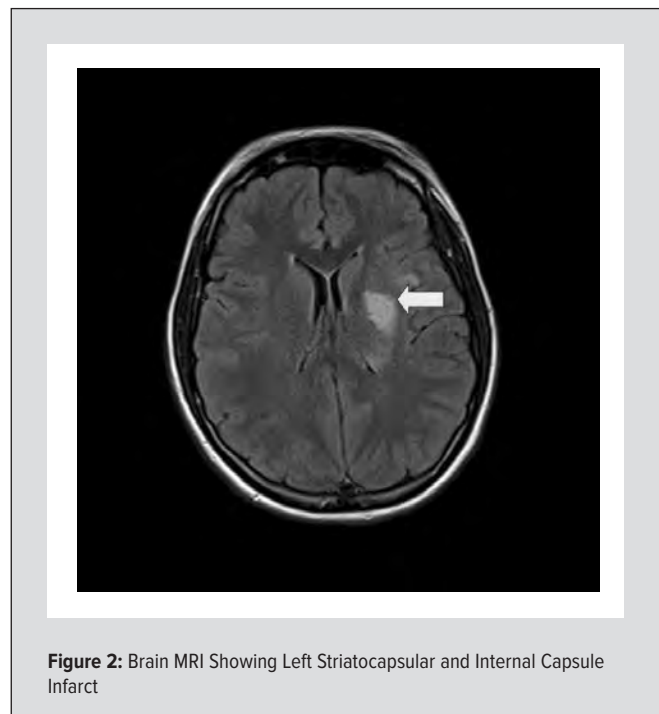


Figure 2: Brain MRI Showing Left Striatocapsular and Internal Capsule Infarct

in asymptomatic patients.<sup>6</sup> Doppler studies tend to be operator dependent and some experts believe that a negative study does not rule out venous thromboses.

An echocardiogram revealed a patent foramen ovale with bidirectional shunting in our patient. Prior to this admission, the patient had never had an echocardiogram. The statistical association of a patent foramen ovale with stroke in children has been shown, but a causal relation has been difficult to establish in pediatric cryptogenic strokes.<sup>2</sup> The prevalence of a patent

foramen ovale in the general population is 10% to 25% and the prevalence in patients with stroke is in the range of 40% to 45%.<sup>7</sup> Currently, there are no FDA-approved indications for foramen closure in the United States. There is evidence for a decrease in recurrent strokes with foramen closure, and current practice consensus in the United States is its closure in these cases.<sup>8</sup> With growing data on safety of the closure devices, a single event might justify placing one in such patients.

The standard of care for venous thromboembolism is systemic anticoagulation alone. IVC filter placement is indicated only in patients who cannot receive anticoagulation. Filter placement may be justified in cases of pulmonary embolism where an acute recurrence can prove life-threatening.<sup>9</sup> There were no known contraindications to anticoagulation in our patient, and unfractionated heparin was initiated as soon as the diagnosis of pulmonary embolism was made. We elected to place the filter to prevent any acute recurrences.

There is early clinical experience with the Penumbra System (Penumbra, Inc USA, Alameda, Calif) for mechanical clot retrieval. It is indicated in large vessel occlusion and has a high recanalization rate. The safety of the procedure increasingly is being established with decreased incidence of symptomatic hemorrhage.<sup>10</sup> Our patient underwent clot retrieval as soon as the diagnosis of stroke was made and the thrombus identified. She tolerated the procedure well and had partial recovery of neurological function immediately after the procedure. It is difficult to comment on the timing of her stroke. Frequent neurochecks had not revealed any obvious asymmetry prior to extubation. Neurological assessment in sedated and mechanically ventilated patients tends to be limited and we may have missed an earlier diagnosis of stroke.

Anticoagulation management was based on American College of Chest Physicians guidelines for management of venous thrombosis and pulmonary embolism. Aspirin was initiated after the stroke was diagnosed. A decision for lifelong anticoagulation treatment was made on follow-up when the patient was noted to be homozygous for the C677T genetic variant of MTHFR and ATIII deficient. This genetic variant of MTHFR is a known risk factor for thrombosis. Patients with hypercoagulability have a higher incidence of pulmonary embolism and paradoxical embolism in the presence of a patent foramen ovale.

## CONCLUSION

Venous thromboembolism is underappreciated in pediatrics, and the diagnosis is not considered very often by pediatric health care providers. Oral contraceptive pills are known to precipitate venous thromboembolism. Other risk factors for thrombosis, such as prolonged travel, smoking, and family history of venous thromboembolism should be explored prior

to prescribing oral contraceptive pills. If a family history for venous thrombosis exists, testing for known hypercoagulable states or a hematology consult should be considered. Families of patients receiving oral contraceptives should be counseled about the possible signs and symptoms of venous thromboembolism so that they can seek timely medical attention if symptoms appear. Differential diagnoses of a syncopal event in an adolescent could include pulmonary embolism in the appropriate setting.

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