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PEDIATRIC PULMONOLOGY WILEY

A complicated presentation of pediatric COVID-19 with necrotizing pneumonia and pulmonary artery pseudoaneurysms

To the Editor,

Children affected by coronavirus disease 19 (COVID-19) typically have milder symptoms and rarely require critical care. Although atypical, evolving literature highlights that children may present with complicated, severe COVID-19 lower respiratory tract infections. Necrotizing pneumonia (NP) is rarely reported as complication of COVID-19 pneumonia.[1] Pulmonary vascular involvements are observed in some patients with severe COVID-19, however, pulmonary artery aneurysm (PAPA) is not reported.[2]

There are several known neurological complications associated with COVID-19, including encephalitis and cerebrovascular disease. Cerebral venous thrombosis (CVT) is a known complication of both subdural empyemas and COVID-19 independently.

This case details a unique presentation of a pediatric COVID-19, complicated with NP with PAPAs, CVT and *Prevotella oris* positive subdural empyema.

1 | CASE SUMMARY

A previously healthy 13-year-old boy presented to an emergency department with 4-day history of fever, headache, and fatigue. SARS-CoV-2 RNA transcription mediated amplification test was positive. Four days later, he developed shortness of breath prompting presentation to the emergency department. He was hypoxic and septic, and physical exam revealed left hemiplegia. Laboratory investigations were notable for platelet count of 30×10^9/L, white cell count of 20.5×10^9/L with neutrophilic predominance, INR 1.5, PT 16.6 s, D-dimer 25,000 ng/dl FEU ($n < 500$), lactate 3.3 mmol/L, and CRP 364 mg/L ($n < 8$ mg/L). Computed tomography (CT) angiogram of the head and neck demonstrated right subdural fluid collections, evidence of right maxillary and left frontal sinusitis, a nonocclusive CVT in the right internal jugular vein extending to the sigmoid sinus. Chest CT scan revealed extensive bilateral pulmonary ground glass opacities with patchy areas of consolidation (Figure 1A). Aerobic and anaerobic blood cultures were obtained (these were ultimately negative) before initiation of antimicrobial therapy with intravenous ceftriaxone, vancomycin, and metronidazole. He was also started on remdesivir, dexamethasone, and heparin.

By hospital Day 7, he improved and no longer required supplemental oxygen. On hospital Day 9, he had a 10-min focal seizure treated with levetiracetam; surgical intervention was deferred at that time.

On hospital Day 11, he experienced recurrence of high fever, tachypnea, and acute chest pain, with an episode of mild hemoptysis and epistaxis, occurring 48 h after discontinuation of dexamethasone. Repeat blood cultures were negative. A cytokine panel on hospital Day 12 showed elevated interleukin-6 of 9.6 pg/ml (normal <5 pg/ml). Chest CT angiogram revealed bilateral new multifocal consolidations with cavitation and a complex right pleural effusion suggestive of NP (Figure 1B). These findings were suspicious for superimposed bacterial infection on COVID-19. Contrast images also revealed multiple bilateral PAPAs, 6 in total and involving all lobes (Figure 1C). Due to the diffuse, multi-lobar distribution of PAPAs and high risk of any invasive procedure, vascular occlusive coiling was not performed, and he was treated with broad spectrum antimicrobial coverage (cefepime, vancomycin, and metronidazole). Heparin was discontinued due to high risk of spontaneous bleeding from the pseudoaneurysms. Intravenous dexamethasone was restarted with subsequent improvement of his fever over the next few days. He remained off supplemental oxygen and had no further hemoptysis. He was transitioned to anakinra for targeted immunomodulation.

Repeat chest CT angiogram on Day 19 revealed persistent PAPAs, enlarged cavitations, and improvement in the pulmonary consolidation and pleural effusion (Figure 1D,E).

On Day 50, he had 2 brief focal seizures, prompting surgical drainage of the subdural empyemas. Intraoperative cultures were negative and antibiotics were later discontinued. Broad-range PCR from the empyema detected *Prevotella oris* and *Porphyromonas endodontalis*. Karius® testing sent on blood samples from hospital Day 12 returned positive for *Prevotella oris*. He recovered and was discharged after a short course of inpatient rehabilitation. Repeat chest CT 6 weeks after discharge showed complete resolution of consolidations, cavities, and PAPAs (Figure 1F,G).

Abbreviations: COVID-19, coronavirus disease 2019; CVT, cerebral venous thrombosis; NP, necrotizing pneumonia; PAPAs, pulmonary artery pseudoaneurysms.

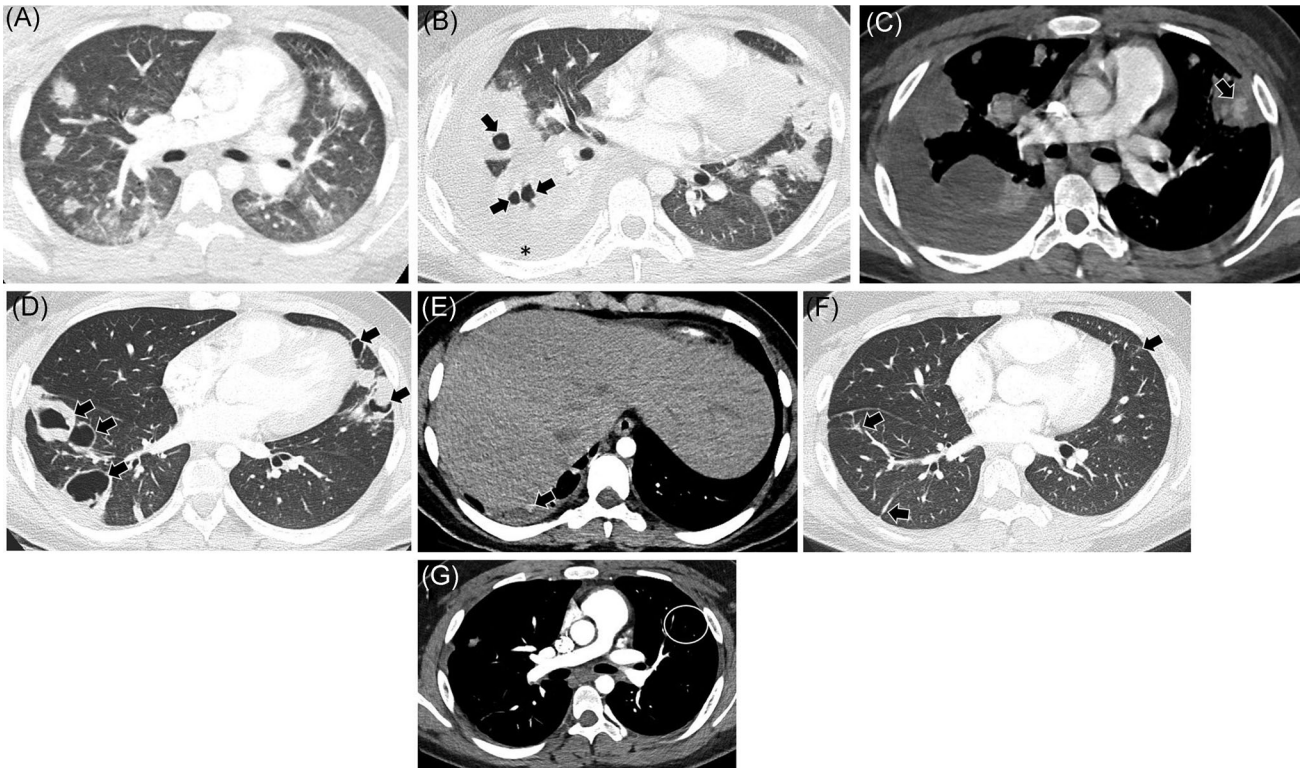

FIGURE 1 (A) Axial, contrast-enhanced, CT of the chest in lung windows and at the level of the left main pulmonary artery demonstrates multiple bilateral patchy areas of consolidation and scattered areas of ground glass. (B) Follow-up, axial contrast-enhanced chest CT in lung windows shows multifocal gas collections (arrows) within an area of consolidated lung in the right lower lobe. In soft tissue windows (not show) this area demonstrated decreased attention. Findings are consistent with necrotizing pneumonia. There is a moderate adjacent pleural effusion (asterisk). Additional areas of patchy areas of consolidation are present in the left base. (C) Axial image obtained at the same time as (B) in soft tissue windows and at the level of the left pulmonary artery demonstrates an irregular blush of contrast within the anterolateral left lung (arrow) with surrounding consolidation, consistent with a pseudoaneurysm. (D, E) Axial, contrast-enhanced CT in lung windows and at the level of the inferior pulmonary veins (D) and axial image at the lung base level and in soft tissue windows (E) show decreased consolidative opacities with evolving areas of cavitation bilaterally (arrows in D). In the right lower lobe, there is a persistent pseudoaneurysm (arrow in E). (F) Axial, contrast-enhanced CT at the level of the inferior pulmonary veins/left atrial junction (same level as D) shows complete resolution of the bilateral cavitary areas and resolution of the consolidation. There is minimal post-infectious scarring in the right lower lobe and lingula (arrows). (G) Axial, contrast-enhanced CT image in soft tissue windows and at the level of the left pulmonary artery (same as CT) demonstrates resolution of the right lung pseudoaneurysm and consolidation (circle indicates prior pseudoaneurysm location). Minimal scarring and pleural thickening are partially visualized on the right. CT, computed tomography

2 | DISCUSSION

In its most severe form, COVID-19 pneumonia causes an acute hypoxemic respiratory failure with development of acute respiratory distress syndrome.[2] There seems to be a strong correlation between illness severity in COVID-19 infection and the presence of bacterial coinfections. In a meta-analysis, the most common bacterial co-infections with COVID-19 were *Mycoplasma pneumonia*, *Pseudomonas aeruginosa*, and *Haemophilus influenza*, in up to 14% of intensive care unit cases.[3] Prevotella has not been described, but it has been demonstrated that overexpression of Prevotella proteins promotes viral infection through multiple interactions with nuclear factor kappa B; this interaction is implicated in increased COVID-19 clinical severity.[4]

Radiologically, the most commonly reported chest CT findings for COVID-19 pneumonia include ground glass opacities, linear consolidations and pleural thickening, and disease severity correlates with the extent of lobar involvement.[2] NP, which presents with thin walled lung cavities, is rarely reported in COVID-19.[1] NP is typically a complication of community acquired pneumonia. Anaerobic bacteria such as Fusobacterium are rarely identified in NP. It is possible that cavitary lung lesions may develop from direct viral cytopathic effect. In our case, the *Prevotella* superinfection is likely responsible for development of NP.

PAPAs may be congenital or acquired with infections being the commonest cause of acquired form; pyogenic bacteria eg. *Staphylococcus aureus*, *Streptococcus pyogenes* are commonly implicated.[5] PAPAs are rarely defined as a complication of NP.[5] Pathophysiologically, PAPAs form due to the pulmonary artery lacks an adventitial wall; therefore, repeated endovascular seeding of the pulmonary artery with septic emboli creates saccular dilations that are more likely to rupture than systemic arterial aneurysms.[5] It is unclear how the COVID-19-associated prothrombotic state affectes development of PAPAs. Cerebral pseudoaneurysms have been associated with COVID-19, however, PAPAs have not.

Massive hemoptysis from ruptured PAPAs is fatal in over 50% of patients.[5] Other life-threatening complications include coronary artery

compression leading to acute coronary syndrome and pulmonary artery dissection. To avoid these complications prompt therapy is required in most cases. Treatment options include transcatheter embolization with coils or endovascular stents, surgical ligation, or even wedge resections and lobectomy.[5] In our case, after multidisciplinary discussion, intravascular occlusion was not pursued in the acute phase. There was no identifiable single PAPA of greatest risk of bleeding, and the extensive multilobar involvement precluded occluding all the PAPAs as this would have left him with insufficient perfusing lung tissue.

3 | CONCLUSION

Our case highlights an atypical and severe pediatric case of COVID-19 infection complicated with NP with PAPAs, CVT, and Prevotella-positive subdural empyema. NP with PAPAs responded to conservative therapy with broad spectrum antibiotics in our case without surgical or vascular intervention. Although COVID-19 has milder course in children, pediatricians should be aware of possibility of severe life-threatening multisystem involvement and secondary bacterial infection in previously healthy children without increased risk factors.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Elizabeth Ristagno: writing review and editing (equal). **Emily Levy**: writing review and editing (equal). **Robert Kahoud**: writing review and editing (equal). **Paul Thacker**: writing review and editing (equal). **Deborah Setter**: writing review and editing (equal). **Nadir Demirel**: writing review and editing (lead).

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