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Case Report

MRSA septic pulmonary emboli presenting as isolated focal chest pain in an adolescent ☆☆☆★★

Danielle G. Rabinowitz, MD, MM^{a,d,e,*}, Stephen M. Chrzanowski, MD, PhD^{a,d,e},
 Jeffrey I. Campbell, MD^{b,d}, Jaclyn Davis, MD^{c,d}, Robert N. Husson, MD^{b,d},
 Alicia M. Casey, MD^{c,d}, Carolyn H. Marcus, MD^{a,d}

^a Division of General Pediatrics, Boston Children's Hospital, Boston, Massachusetts

^b Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts

^c Division of Pulmonary Medicine, Boston Children's Hospital, Boston, Massachusetts

^d Harvard Medical School, Boston, Massachusetts

^e Department of Pediatrics, Boston Medical Center, Boston, Massachusetts

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ABSTRACT

This case demonstrates the importance of considering septic pulmonary embolism (SPE) on the differential for chest pain in the pediatric population, especially in patients with a history of skin and soft tissue infection. The adolescent patient in this report, with a history of axillary hidradenitis suppurativa complicated by methicillin-resistant *Staphylococcus aureus* (MRSA) superinfection and recent completion of a 3-month course of doxycycline, presented with isolated focal chest pain in the absence of other infectious or respiratory signs or symptoms. Initial pulmonary imaging revealed multiple bilateral wedge-shaped nodules. Three specialty teams were consulted in the patient's evaluation, resulting in biopsy of a suspicious lesion that confirmed the diagnosis of MRSA SPE. Following a course of targeted antibiotic therapy, the patient's chest pain resolved and imaging findings improved. Insights gleaned from the workup of this patient are useful in formulating a framework for recognition of SPE in children presenting with chest pain, and also highlight the importance of considering insidious SPE presentation in the setting of antibiotic pretreatment.

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Abbreviations: CRP, C-reactive protein; CT-PA, computed tomography-pulmonary angiography; DVT, deep vein thrombosis; ED, emergency department; HS, hidradenitis suppurativa; MRSA, methicillin-resistant *Staphylococcus aureus*; SPE, septic pulmonary embolism.

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* Corresponding author.

E-mail address: danielle.rabinowitz@childrens.harvard.edu (D.G. Rabinowitz).

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Introduction

Chest pain is a common complaint in pediatrics, particularly in adolescents, and has numerous and often undetermined etiologies. Multiple studies have corroborated that the largest proportion of chest pain in children is idiopathic in nature, with a high prevalence of cases otherwise secondary to musculoskeletal or respiratory/infectious etiologies [1,2,3,4]. Gastrointestinal, cardiovascular, and hematologic sources are less typical [1,2,3,4]. Acute chest pain leading to evaluation in the emergency department (ED) among adults is predominantly attributable to cardiac causes, with the most common etiology being acute coronary syndrome, although this disproportionately skews toward patients of older ages [5]. Pulmonary embolism is another important consideration for chest pain, with septic phenomena representative of a much rarer variant as compared to venous thromboemboli [6]. In adults, septic pulmonary embolism (SPE) typically presents with the triad of chest pain, fever, and dyspnea [7]. The findings in children are significantly more variable, with limited literature on the topic [8]. Here, we report on an adolescent patient with chest pain notably without associated infectious or respiratory signs or symptoms ultimately found to have methicillin-resistant *Staphylococcus aureus* (MRSA) SPE.

Clinical presentation

A 17-year-old female with a history of mild intermittent asthma and axillary hidradenitis suppurativa (HS) complicated by recent MRSA superinfection for which she received a 3-month course of oral doxycycline therapy completed 3 days prior to presentation, presented to a referring hospital's ED with 1 day of sharp, nonradiating, left-sided pleuritic chest pain worse in the supine position. She was otherwise in her usual state of health, without any recent fevers or additional respiratory complaints. Her only medication was oral contraceptive therapy. She denied personal or family history of venous clots, or other hematologic, cardiac, respiratory, or autoimmune diseases.

At the referring hospital, she was afebrile and had normal vital signs aside from mild tachycardia that did not improve with intravenous fluids. She was nontoxic appearing, and her exam was unremarkable beyond tenderness to deep palpation of the left, midthoracic chest wall. No arrhythmia, friction rub, or murmurs were noted on cardiac exam. The patient had symmetric chest rise, and her lungs were clear to auscultation. There was no swelling or pain appreciable in her lower extremities. Aside from a site of resolved abscess in the right axilla, there was no evidence of active skin or soft tissue infection.

Initial diagnostic workup began with an electrocardiogram that demonstrated sinus tachycardia. A D-dimer returned elevated at 0.65 mcg/mL (normal high <0.50). Computed tomography pulmonary angiography (CT-PA) was performed to evaluate for pulmonary thromboembolism. CT-PA identified 3 wedge-shaped and rounded nodular opacities in both lungs, with the largest measuring 11 mm in diameter in the left up-

per lobe along the anterior pleural surface adjacent to the mediastinum, which prompted transfer to our institution. Our radiologists reviewed the imaging and felt that the lesions were most suspicious for an inflammatory versus infectious process. An echocardiogram was normal. Doppler ultrasound of her lower extremities was negative for deep vein thrombosis (DVT). Additional lab work in the ED demonstrated mild leukocytosis to 11.98 K cells/uL and elevated C-reactive protein (CRP) to 4.63 mg/dL (normal high <0.50). Coagulation studies, a complete metabolic panel, and liver function tests were all within normal limits. The patient was admitted to the general pediatrics unit for further workup and management.

Hospitalization course

Given imaging suggestive of possible pulmonary inflammation or infection, and with the prominent left upper lobe pulmonary nodule likely contributory to her chest pain given its location abutting the pleura, the rheumatology, infectious disease, and pulmonary teams were consulted. The patient was administered nonsteroidal anti-inflammatory drug therapy for pain control and possible anti-inflammatory effect, with minimal improvement in symptoms.

Due to a range of rheumatologic conditions possibly associated with the finding of multiple pulmonary nodules, among them lupus, numerous vasculitides, and sarcoidosis, a broad-based inflammatory workup was pursued. Aside from elevations of CRP that peaked on the fourth day after symptom onset at 12.37 mg/dL and then fell to 2.72 mg/dL in the absence of treatment, and erythrocyte sedimentation rate that was elevated on day 2 to 32 mm/hr (normal <30) and was subsequently normal, all other rheumatologic testing was unrevealing. Procalcitonin was within the normal range.

From an infectious standpoint, the differential considered for pulmonary nodules in our immune-intact patient with mild symptoms included pyogenic bacteria, fungi (particularly aspergillus and endemic mycoses), mycobacteria, and other slow-growing bacteria. Results of testing included negative cultures (blood, respiratory, and sputum acid fast bacilli stain and culture) as well as negative serum aspergillus galactomannan enzyme-linked immunoassay, urine histoplasma capsulatum antigen, and expanded respiratory viral panel testing. No empiric antibiotics were administered.

In light of nonelucidating rheumatologic and infectious testing, the pulmonary team recommended a biopsy to directly obtain a tissue sample of a representative pulmonary lesion. Wedge biopsy of a right upper lobe lesion was performed via thoracoscopy in parallel with bronchoscopy with bronchoalveolar lavage. Gram stain of lung tissue revealed few polymorphonuclear cells and rare gram-positive cocci in pairs. Within 12 hours of collection, aerobic culture of the tissue was positive for an organism that was ultimately identified as MRSA (sensitive to tetracycline), establishing the diagnosis of MRSA SPE. Bronchoalveolar lavage culture remained negative.

In the absence of other localizing infectious symptoms, there was a strong suspicion for hematogenous seeding from the patient's past superinfected axillary HS, despite negative blood culture, and lack of other signs of active infection.



Fig. 1 – Chest CT pre- and postantibiotic therapy with linezolid for MRSA septic pulmonary emboli. Note the prominent anterior left-sided thoracic nodule abutting the pleura that is no longer present on imaging after 4 weeks of linezolid administration.

Abdominal ultrasound was pursued to evaluate for other sites of septic emboli, with one additional 12 mm in diameter lesion detected in the left superior renal pole.

Our patient was consequently initiated on a 4-week course of oral linezolid therapy. After completing treatment, she had no ongoing chest pain, normalized inflammatory markers, resolution of the lesion on renal ultrasound, and improvement of the pulmonary lesions on repeat chest CT (Fig. 1).

Discussion

We describe an adolescent with MRSA SPE presenting with isolated chest pain. She was also found to have an asymptomatic renal lesion. Her only known risk factor was a history of MRSA-superinfected HS with recent completion of a prolonged course of doxycycline therapy.

Chest pain is a common chief complaint in presentations of SPE. In a review of 168 cases of SPE in patients ages 14 and older, nearly half presented with chest pain [7]. The data are sparser in studies specific to pediatrics given the rarity of SPE overall in this demographic; yet, in a retrospective single-center analysis of 10 pediatric patients, 4 presented with chest pain though this may be an underrepresentation of prevalence given that 2 patients were neonates [8].

Most patients presenting with SPE have at least one additional sign or symptom beyond that of focal chest pain. Indicators of infection or respiratory derangements are also prevalent. In the aforementioned review, the vast majority of adult patients were febrile on initial evaluation (86%), as compared with only 2 of the 10 patients in the pediatric study, though all evaluated children were clinically septic and toxic. With regard to respiratory impacts, 48% of adults had dyspnea, 41% cough, and 14% hemoptysis; 6 of the 10 described children had one or more respiratory signs or symptoms (dyspnea, tachypnea, hemoptysis, cyanosis, or hypoxemia) [7,8]. Thus, it was surprising that our patient was not ill appearing and had isolated chest pain in the absence of other sequelae. A

potential explanation for her lack of respiratory or infectious symptoms was her long-term treatment with doxycycline for superinfected HS in the months leading up to presentation. Doxycycline, which is known to inhibit staphylococcal toxin-induced cytokines, likely contributed to her well appearance through playing a critical role in dampening the inflammatory response to presumed disseminated infection [9].

One study in adults identified the highest proportion of SPE etiologies secondary to skin and soft tissue sources (44%), greater than infective endocarditis (27%), and infected peripheral DVT (17%) [7]. This appears to be consistent with the etiologies of SPE in children; in the pediatric cohort previously mentioned, 50% of cases were associated with skin and soft tissue infections [8]. The infectious source in our patient was postulated to be her MRSA-superinfected HS. We believe that this is the first documented case of SPE attributable to superinfected HS, though the mechanism of this type of infection in leading to embolic phenomena by way of hematogenous spread is aligned with that of other localized skin and soft tissue infections such as cellulitis, abscess, and myositis etiologies previously reported [7,10].

Our patient's chest imaging was consistent with the imaging findings of SPE described in the literature. Typically, both chest x-ray and CT-PA identify bilateral abnormalities, discrete nodules, and wedge-shaped lesions. In addition, over half of both children and adults have cavitory lesions [7,10]. Interestingly, our patient did not have cavitory lesions. It is possible that the doxycycline therapy prevented progression to cavitation but was not sufficient to eradicate the infection or that the emboli had occurred coincident with the acute onset of pain and had not yet cavitated.

Conclusion

We discuss the workup of a pediatric patient with isolated chest pain ultimately found to be secondary to MRSA SPE. Our case suggests that antibiotic pretreatment may suppress

typical signs and symptoms of bacterial infection, potentially leading to diagnostic delay, and also highlights the importance of chest imaging in SPE identification. Though biopsy may be necessary in order to determine the causal pathogen—and was further warranted in our patient whose clinical well-appearance raised less initial suspicion for SPE overall—it is our hope that in patients with additional infectious and respiratory signs and symptoms as well as concerning lab work, a care team's ability to identify the constellation of presenting chest pain, associated history of skin and soft tissue infection, and characteristic imaging findings will more readily lead to SPE diagnosis and inform therapy.

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REFERENCES

- [1] Selbst SM, Ruddy RM, Clark BJ, Henretig FM, Santulli T. Pediatric chest pain: a prospective study. *Pediatrics* 1988;82:319–23.
- [2] Leung AK, Robson WL, Cho H. Chest pain in children. *Can Fam Phys* 1996;42:1156–64.
- [3] Drossner DM, Hirsh DA, Sturm JJ, Mahle WT, Goo DJ, Massey R, et al. Cardiac disease in pediatric patients presenting to a pediatric ED with chest pain. *Am J Emerg Med* 2011;29(6):632–8. doi:10.1016/j.ajem.2010.01.011.
- [4] Hambrook JT, Kimball TR, Khoury P, Cnota J. Disparities exist in the emergency department evaluation of pediatric chest pain. *Congenit Heart Dis* 2010;5:285–91. doi:10.1111/j.1747-0803.2010.00414.x.
- [5] Knockaert DC, Buntinx F, Stoens N, Bruyninckx R, Delooz H. Chest pain in the emergency department: the broad spectrum of causes. *Eur J Emerg Med* 2002;9(1):25–30. doi:10.1097/00063110-200203000-00007.
- [6] Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. *Chest* 1995;108(4):978–81. doi:10.1378/chest.108.4.978.
- [7] Ye R, Zhao L, Wang C, Wu X, Yan H. Clinical characteristics of septic pulmonary embolism in adults: a systematic review. *Resp Med* 2014;108(1):1–8. doi:10.1016/j.rmed.2013.10.012.
- [8] Wong KS, Lin TY, Huang YC, Hsia SH, Yang PH, Chu S. Clinical and radiographic spectrum of septic pulmonary embolism. *Arch Dis Childhood* 2002;87(4):312–15. doi:10.1136/adc.87.4.312.
- [9] Krakauer T, Buckley M. Doxycycline is anti-inflammatory and inhibits staphyococcal exotoxin-induced cytokines and chemokines. *Antimicrob Agents Chemother* 2003;47(11):3630–3. doi:10.1128/AAC.47.11.3630-3633.2003.
- [10] Goswami U, Brenes JA, Punjabi GV, Leclaire MM, Williams DN. Associations and outcomes of septic pulmonary embolism. *Open Resp Med J* 2014;8(1):28–33. doi:10.2174/1874306401408010028.