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A rare case of multiple thromboses in a pediatric patient with Mycoplasma pneumoniae infection

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ABSTRACT

Medical literature discusses the immunogenicity of Mycoplasma pneumoniae and the capability of this bacteria to increase the risk of thrombosis-related events. We present the case of a two-year-old female patient, unvaccinated, with a recent measles infection, who is admitted to the hospital for fever and dyspnea. Serological screening discovered a Mycoplasma infection, paired with the imagistic proof of multiple deep vein thromboses. The evolution was favorable after treatment.

Keywords: Mycoplasma pneumoniae, systemic inflammation, thromboses

Introduction

Mycoplasma pneumoniae is one of the smallest pathogens to exist, but it may lead to a high number of community-acquired pneumonia cases in children (10-40% of pneumonia cases) [1].

The course of Mycoplasma pneumoniae infection is mainly mediated by the host's defense response to the bacteria, with a sometimes exaggerated pro-inflammatory status, which may result in lung injury, cardiac manifestations, renal injury, hepatitis, and last, but not least, thrombosis [2-4].

Generally, the course of Mycoplasma pneumoniae infections is self-limited, with a favorable outcome. There are reported cases of ''walking pneumonia'', in which patients accuse only a lingering productive cough and fatigability, which is inconsistent with the radiological aspects [5,6]. The imaging in this atypical pneumonia usually suggests unilateral or bilateral lower pulmonary lobe implication [7].

But the particular immunogenicity of Mycoplasma pneumoniae induces signals that kick-start the conglomeration of inflammatory cytokines, specifically IL-1, IL-8, and TNF-a [8], which overlaps the host defense mechanisms and plays an important role in the development of immunothrombosis (a coagulopathy normally associated with systemic inflammation, sepsis).

Case description

A 2-year-old, female patient presented in the Emergency Room at Brasov Clinical Hospital for fever bouts (a maximal value of 39.6 degree Celsius) that started 7 days before presentation, accompanied by debilitating cough and dyspnea, observed by the mother one day before hospital admission.

The girl is born at term, with no obstetrical details worth mentioning. The immunization scheme is incomplete (the last vaccine she received was at 4 months old, the hexavalent vaccine).

The patient's medical history consists of one hospital admission in October of 2023, for bacterial pneumonia. It is worth mentioning that the patient received 100 mg/kg/day of ceftriaxone IV for three days during that hospital admission. Afterward, she exhibited monthly respiratory manifestations, mainly a debilitating productive cough, that led to visits

to the local general practitioner and repeated antibiotic treatment at home. The patient had measles recently, in November 2023, a disease that was treated at home as well.
The clinical state of the patient at the present hospital admission is critical. She exhibits debilitating bouts of dry, irritative cough, expiratory dyspnea, pulmonary bilateral crackles, sat02-80% without administered oxygen, and tachycardic (HR=170 bpm). She has a normal weight for her age (12.5 kg, P48th).
The thoracic X-ray describes bronchopneumonia (photo no. 1).

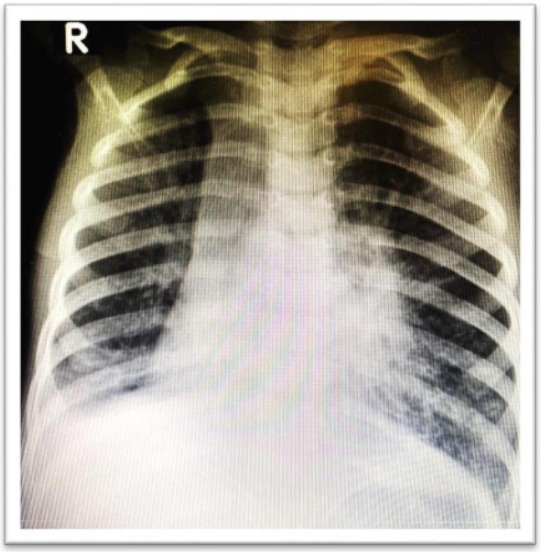


Photo no.1-Thoracic X-ray

Laboratory tests reveal accentuated inflammatory syndrome, with high levels of white blood cell count-29720/mm3 (normal values: 4500-11 000/mL), CRP 8 mg/dl (normal value <1 mg/dL), ESH 65 mm/h, (norma values: 0-10 mm/h) and procalcitonin 1 ng/ml (normal values <0.5 ng/mL) along with elevated levels of D-dimers- 6 ng/ml (normal values <0.5 ng/mL). Treatment was started with ceftriaxone 100 mg/kg/day iv, vancomycin 60 mg/kg/day iv, methylprednisolone 4 mg/kg/day iv, 4 liters of oxygen flow on mask, intravenous drips with glucose and electrolytes.

On the first night of hospitalization, the patient exhibited a tonic seizure, with the sudden installment of a generalized maintained contraction, eyes rolled back and oxygen saturation levels decreased down to 50%, all of which lasted 30-50 seconds. The return to consciousness was not followed by post-ictal sleepiness. Laboratory tests immediately after the neurologic manifestation showed severe metabolic acidosis (pH=6.9, pCO2-71 mmol/L, HCO3 13.5 mmol/L), which normalized in one hour without medication.
Another thoracic x-ray was performed because the respiratory distress did not alleviate after treatment and more pulmonary consolidations are described.
The cerebral CT scan (photo no. 2) reveals right sinus and transversus sinus thrombosis, and the thoracic CT scan describes major bilateral lower lobes bronchiectases, much more accentuated on the right lower lobe (photo no.3)
Serological PCR method screening results came back with positive IgM antibodies titer for Mycoplasma pneumoniae.

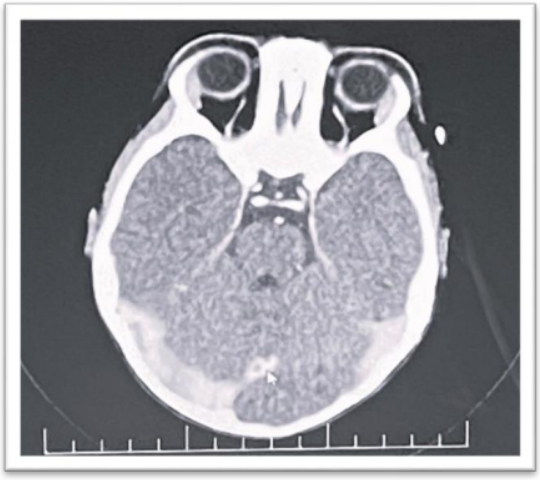
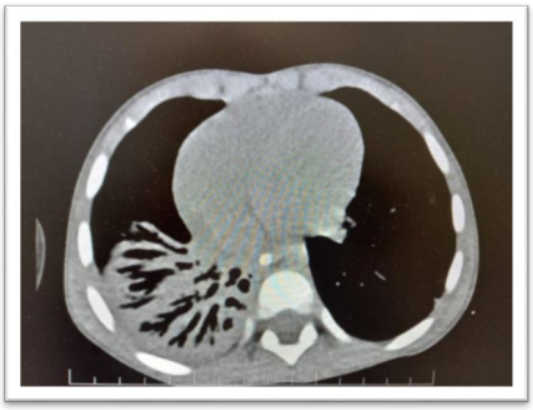


Photo no.2- cerebral CT scan

Photo 3-thoracic CT scan

The patient presented more seizures in the following days, that lasted longer (5 minutes each), with axial contracture, rolled back eyes, and severe desaturations, that did not respond to phenobarbital administration. The association of valproic acid does not prevent neurological manifestations.

She was transferred to the Intensive Care Unit, where she presented cardiopulmonary arrest when she received subsequent doses of adrenaline 0.01 mg/kg iv along with oro-tracheal intubation and careful monitoring until the normalization of heart rate, blood pressure, and oxygen saturation levels. The medication scheme was modified, with the replacement of Ceftriaxone with Meropenem iv (100 mg/kg/day), the association of



Caspofungin iv(50 mg/m^2) and Aciclovir iv(750 mg/day-500 mg/m^2), clarithromycin po (15 mg/kg/day) and the continuation of methylprednisolone (dose was reduced to 2 mg/kg/day for a total of 13 days).

An angio-CT scan (photo no.4) was performed and another thrombosis site was discovered: pulmonary thromboembolism at the right posterior segmental pulmonary artery and the middle lobar artery.

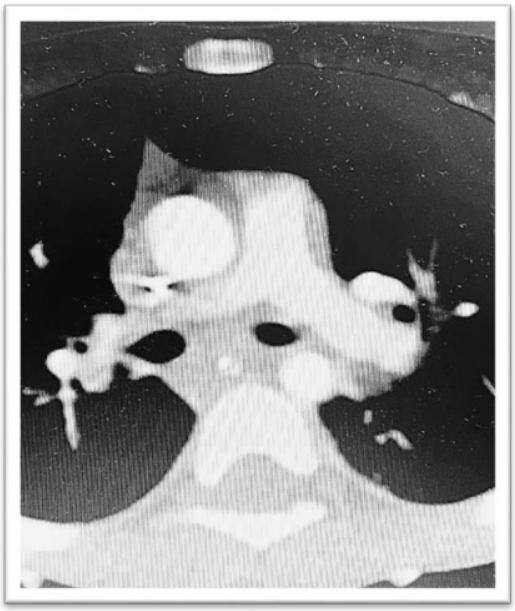


Photo no.4-angio CT scan

A low molecular weight heparin anticoagulant was associated with the treatment and she was successfully extubated after 3 days, with a complete regain of consciousness, no apparent neurological sequelae, and no subsequent seizures.

A race for the search of thrombosis etiology began. Normal values of protein C and S were found, negative antiphospholipid antibodies, and the genetic profile for thrombophilia did not meet the required criteria to diagnose a hereditary thrombophilia.

The patient did not have a positive history of seizures or other thrombosis events pre-hospital admission that could justify a preexisting condition.

She also did not present malnutrition or modified levels of pancreatic elastase levels that could explain the presence of bronchiectasis to cystic fibrosis.

Therefore, the clinical and paraclinical manifestations of this patient were attributed to the systemic inflammation associated with Mycoplasma pneumoniae, in a non-vaccinated host, with depleted resources after a recent measles episode. The high value of procalcitonin, along with the positive Mycoplasma pneumoniae PCR serology, confirmed the septical dissemination. A cerebral RMN and a thoracic angio-CT scan were performed

to reassess the situation of deep thromboses after 3 weeks of treatment. Cerebral vein thromboses visibly decreased, while there were no evident alterations in the size of the pulmonary artery thrombosis.

The patient was successfully discharged, after 24 days of hospitalization, with a good general state, Glasgow Coma Scale of 15, no seizures or neurological sequelae, no residual cough, no dyspnea, normal oxygen saturation levels, no pulmonary crackles, and normal heartbeat rate. Laboratory tests at discharge reveal normochromic normocytic moderate anemia (Hb=8 g/dl-probable in the acute infectious context), normal values of WBC, CRP, ESH, procalcitonin, D dimers value halved than the one at admission (3 pg/ml).

The mother was educated on the necessity of the correct administration of enoxaparin injections and the patient continued with enoxaparin 2000 ui/vial-0.15 mg twice a day subcutaneously. The use of other anticoagulant medications was discussed (factor X inhibitors-dabigatran, or coumarin derivates-acenocoumarol), but because of practical reasons, enoxaparin was elected. After being discharged, the patient came back twice a month for clinical re-evaluation, along with periodical re-assessment of main laboratory tests (complete blood count, inflammatory syndrome markers-CRP, ESH, seric urea, and creatinine, AST, ALT, D-dimers, fibrinogen-all of them with no notable alterations).

Discussion

Inflammation is a natural and necessary response of the host in defending against a pathogen factor. There is an increase in blood flow to facilitate the conglomeration of inflammatory mediators. Activated

neutrophils release pro-inflammatory and pro-thrombotic factors, that, along with the endothelial wall dysregulation, sometimes lead to immunothrombosis [9]

Another key factor in sepsis-related thrombosis is the aggregation of platelets in the regions with endothelial wall injury. They generate signals that kick-start the hemostasis process, with the sole purpose of wound healing, but unfortunately, these processes are amplified in sepsis [10].

Pairing all of the above with the characteristic immunogenicity of Mycoplasma pneumoniae increases even more the risk of thrombosis-related events [11-14].

Although hematological manifestations in Mycoplasma pneumonia are viewed as rather uncommon events, the development of profound venous thrombosis is possible because Mycoplasma is an intracellular pathogen and has direct cytotoxicity, inducing the activation of the inflammatory cascade, as well as a consequence of the hypercoagulability state that derives from systemic inflammations [15]. Medical literature describes one case of profound venous thrombosis in a patient with Mycoplasma pneumoniae infection that did not show any respiratory manifestations [15].

Medical literature describes, as well, the presence of deep venous thrombosis in patients that did not have congenital predisposition for this type of hematological malfunction, but rather only secondary to infection with Mycoplasma pneumonia [16,17].

The particularity of this case stems from the dramatic clinical course of an unvaccinated two-year-old who recently recovered from measles, with probably weakened immunity resources to fight a systemic inflammation caused by Mycoplasma pneumoniae. This resulted in multiple deep vein thromboses in a child without hereditary thrombophilia or any other found hereditary blood coagulation abnormality.

Another important entity that is worth discussing is the hematological sequelae- chronic pulmonary thromboembolism, that requires chronic anticoagulant use. The patient is to receive three months of enoxaparin with bimonthly clinical re-evaluation for active hemorrhages [18].

Conclusions

Mycoplasma pneumoniae-related thrombosis is an individual clinical entity.

Refractory deep vein/artery thrombosis may need prolonged anticoagulation therapy, carefully tailored to the age and weight of the child. We consider there is a stringent need to extend the clinical studies of anticoagulant medications in the pediatric population, especially for children under 5 years old.

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