Case Report

Mycoplasma associated stroke in a 4 year old child- A multifactorial etiology

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Abstract

Mycoplasma pneumonia is a common cause of community-acquired pneumonia in India. Stroke due to infection-induced thrombosis is a rare complication of this infection and etiology can be multifactorial. We report a four-year-old girl with a mycoplasma infection associated stroke with thrombosis of the internal carotid artery and presence of lupus anticoagulant. She also had other risk factors for thrombosis like iron deficiency anemia and dehydration due to diarrhea which probably exacerbated an infection-induced procoagulant state. Lupus anticoagulants may be detected in many asymptomatic children with infections. The presence of other risk factors may precipitate a serious thrombotic event leading to significant morbidity and mortality. Recognising atypical pneumonia in the community and prompt treatment may reduce the serious extrapulmonary complications like stroke in children.

Keywords: Antiphospholipid antibodies, etiology, lupus anticoagulant, mycoplasma, stroke, thrombosis

Introduction

Mycoplasma infection may predispose to a hypercoagulable state due to the production of various inflammatory mediators, platelet activation, endothelial damage, autoantibody production, and direct bacterial invasion. Other infections like Helicobacter pylori, Chlamydia pneumonia, Haemophilus influenzae, Streptococcus pneumonia, Staphylococcus aureus, Escherichia coli, Epstein-Bar virus, Herpesvirus, Cytomegalovirus, HIV, and more recently, SARS COV2 too have been found to be associated with venous and arterial thrombotic events. Mycoplasma infection, along with pre-existing and/or concurrent risk factors for thrombosis, may produce stroke in children.

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Case Report

A four-year-old girl presented with high grade fever and dry cough for six days; watery diarrhea for five days; and lethargy and breathing difficulty of one day.

On admission to PICU, she was febrile and lethargic with a GCS of 11/15. She was pale, tachypneic, tachycardic with prolonged Capillary Refill Time, And crackles were noted over the left chest. Initial laboratory studies showed a microcytic, hypochromic anemia with a hemoglobin of 7.5 g/dL, TC-7,400 cells/uL, platelets-2,46,000/mm.[1] C-reactive protein was 78.5 mg/L. Chest x-ray was suggestive of left-sided consolidation with minimal pleural effusion.

Twelve hours later, she was noted to have right upper motor neuron facial paralysis and right hemiparesis. MRI brain [Figure 1] showed extensive acute infarction of the left cerebral hemisphere with a 5 mm midline shift to the right side. On MR angiogram [Figure 2], non-visualisation of the left

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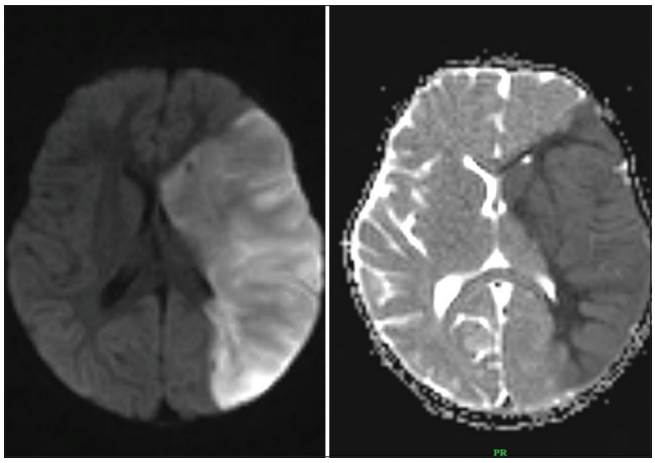

Figure 1: DWI and ADC images showing restricted diffusion in the left MCA territory

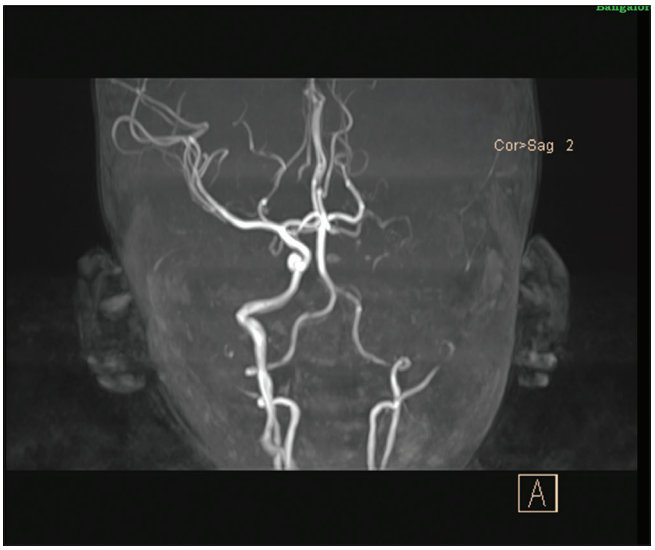

Figure 2: MR angiogram showing non-visualisation of the left internal cerebral and left middle cerebral arteries

internal carotid artery and left middle cerebral artery was noted.

Blood and urine cultures were sterile. Serum samples screened for HIV, HCV, HbsAg, and RPR were non-reactive. Due to a local outbreak of mycoplasma pneumonia prevalent at that time, mycoplasma IgM immunoglobulin was sent and was positive at 58.53 units/ml.

There was no evidence of microangiopathy on the peripheral blood picture. Prothrombin time was normal with an international normalized ratio (INR) of 1.3. Activated partial thromboplastin time was prolonged (55.3 seconds). Homocysteine, C3, and C4 levels were within normal limits; ANA was negative. Haemoglobin electrophoresis did not show a sickle window. Electrocardiogram and echocardiogram were normal. Dilute Russel Viper Venom Time test showed the presence of LA. Anti-cardiolipin and anti-beta-2-glycoprotein antibodies were negative. Mycoplasma infection-induced antiphospholipid antibody syndrome (APS) was considered.

The child was treated with Ceftriaxone and Azithromycin, IV fluids, Aspirin, and hypertonic saline. She became afebrile after 48 hours and showed gradual clinical improvement. She was discharged on oral Aspirin after ten days. LA repeated at eight weeks was positive. Repeat test at six months was negative, after which Aspirin was stopped. At follow-up after one year, she had minimal residual weakness and was able to walk with minimal to no support and minor impediments in speech and learning.

Discussion

Mycoplasma pneumonia is a common cause of community-acquired pneumonia in school-aged children and adolescents during autumn and winter in India, accounting for up to 20% of cases. Onset is usually gradual with mild upper respiratory symptoms, headache, malaise, and low grade fever, which is usually self-limiting but progresses to severe pneumonia and persistent cough in some.

Although it is difficult to differentiate mycoplasma infection from other viral or bacterial infections clinically, a high index of suspicion is needed for this infection when a child with respiratory symptoms who doesn't appear toxic but has tachypnea, dyspnea and hypoxia on examination. Perihilar and perivascular infiltrates are the most common chest x-ray findings. Less commonly, other patterns like lobar pneumonia, airspace consolidation, reticulonodular opacities, pleural effusion, cavitary disease, and hilar lymphadenopathy can occur.[2,3]

M pneumonia can also affect other extrapulmonary organs like skin, digestive system, central nervous system (CNS), cardiovascular system, musculoskeletal system, hematological and urogenital tract.[1] Different neurological manifestations like encephalitis, meningoencephalitis, transverse myelitis, stroke, acute demyelinating encephalomyelitis, Guillain-Barre syndrome, and polyradiculitis have been observed in 1–10% of those hospitalized with mycoplasma infections. These can be due to direct invasion by the organism, vasculopathy, or auto-immune phenomenon.[4]

Stroke in children with mycoplasma infection is a rare para-infectious presentation seen in the age group of 3 to 13 years. Middle cerebral artery is most commonly involved. Occasionally, posterior cerebral artery, lenticulostriate artery, and internal carotid artery involvement has also been reported.[5] Surface proteins and chemical mediator cytokines like tumor necrosis factor-α and interleukin-8 drive an inflammatory milieu.[6] These combined with endothelial damage, platelet activation, and aggregation contribute to hemostatic imbalances. This procoagulant state usually resolves over a period of four weeks.

APS is the presence of a prothrombotic state with a positivity of any one of the antibodies like LA, anti-cardiolipin, or anti-beta-2-glycoprotein antibodies on two occasions done

12 weeks apart. Antiphospholipid antibodies may be produced in viral or bacterial infections due to autoimmunity against the phospholipid-bound plasma proteins, which may result in thrombosis or occasionally be asymptomatic.[7]

For thrombosis to occur, the classic Virchow Triad of hypercoagulability, endothelial dysfunction, and stasis needs to be completed. In some individuals who have had a stroke triggered by infections, other factors such as sickle cell disease, MTHFR gene mutation, Factor V Leiden mutation, deficiency of protein C and S, hyperhomocysteinemia, etc., have possibly contributed to a prothrombotic state.[8] Although we know that iron deficiency anemia is an independent risk factor for stroke in children,[9] its association with infection-induced stroke is yet to be described. In our child, mycoplasma infection-induced hypercoagulable state indicated by the presence of LA complicated by concurrent dehydration and pre-existing iron deficiency anemia could be the cause for ischemic stroke.

The overall outcomes in mycoplasma-associated stroke are good, with no recurrence being reported. Various treatment modalities like Aspirin, IVIG, and plasmapheresis have been tried in mycoplasma-associated stroke, but have no proven efficacy in improved outcomes.

Conclusion

Mycoplasma infections are often under-diagnosed, resulting in several serious extra-pulmonary manifestations like infection-associated thrombosis and stroke in children. Primary care physicians should be aware of various presentations of mycoplasma infection, and treatment should be instituted whenever indicated. Presence of other risk factors in some children and the development of thrombosis only in a few with this infection points to a multifactorial etiology that has not been studied so far. Iron deficiency as a risk factor in infection-associated thrombosis too needs to be studied.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Key Message: Mycoplasma pneumonia infection can induce a transient hypercoagulable state. This, along with the presence of other risk factors, can lead to thrombosis, causing stroke. Early recognition and treatment of community-acquired mycoplasma infection can prevent these life-threatening complications.

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