

CASE DISCUSSION: Approach to SLE Patient with Sagittal Sinus Thrombosis

A 13 year old African-American female previously diagnosed with SLE is brought to the pediatric hospital in a comatose state. She had been well until 2 days before admission when she developed a runny nose, low grade fever, and a headache. She worsened 8 hours before admission when her headache became severe and she became lethargic 2 hours before admission. Upon admission, she was noted to respond to pain but not to commands. She had decreased strength and movement of the left arm and leg.

Her past history is noteworthy for the diagnosis of SLE at age 12 based upon finger arthritis, palatal ulcers, + ANA 1:640, + anti-DS DNA, C3 45 and C4 7, and hematuria and proteinuria. Her anticardiolipin IgG was 4 times normal and her lupus anticoagulant was positive. A renal biopsy revealed WHO Class III nephritis with an activity index of 6/24 and chronicity index of 0/12. She was begun on prednisone after 3 Solumedrol pulses, hydroxychloroquine, and a baby aspirin. After 8 months, mycophenolate was added as a steroid-sparing drug. Her medication compliance became erratic.

Physical exam also revealed a B/P of 150/90, HR 110, RR 20. She is noted to have a 2+ malar rash, swollen PIP joints, and enlarged axillary lymph nodes. No other abnormal physical findings were present other than the neurologic findings noted above. A brain CT scan revealed a large right sagittal sinus thrombosis. MRI with contrast detected increased right cerebral signal. Preliminary laboratory testing revealed a WBC of 7,000/mm³ with 75% segs, Hgb. 10.6 g%, platelets 70,000/mm³, ESR 55 mm/hr, CRP 3.0 (<0.8), C3 65, C4 8, and a urinalysis with 1+ protein, 1+ blood, 6-10 RBC/hpf.

The ICU attending consults neurology and rheumatology and initiates steroid therapy, but no anti-coagulation due to the risk of conversion to a bleed. What are your recommendations and justifications for your plan?

DISCUSSANT

Robin Brey, MD

Pediatric Neurologist

University of Texas-San Antonio

The patient is a 13 year-old African American girl with the diagnosis of SLE since age 12, who is brought to the hospital in a comatose state, with the focal findings of left sided weakness. Symptoms began 2 days prior to admission with the symptoms of headache, runny nose and low-grade fever. Her past history is significant for renal involvement related to SLE, arthritis and palatal ulcers. She also has high positive levels of anticardiolipin IgG and a positive lupus anticoagulant. Brain CT and MRI scans revealed the cause of her neurological manifestations, a right sagittal sinus thrombosis. Laboratory analysis provided evidence for non-nervous system SLE disease activity, as well.

This young woman has symptoms and laboratory findings of an SLE flare. In addition she has a right sagittal sinus thrombosis. This could be related to a prothrombotic state associated with antiphospholipid antibodies, but could also be related to SLE disease activity. We are not told whether the “increased signal on the right” seen on brain MRI is related to clot in the sagittal sinus, or brain infarction. This information is important for prognostic reasons, as children with sinus thrombosis who also have brain infarction (either ischemic or hemorrhagic) may have a worse outcome (with or without treatment) (1). Other further work-up that may be helpful in this patient includes the search for other prothrombotic states such as Factor V Leiden, sickle cell disease and deficiencies of proteins C, S and Antithrombin III, although a study of 160 consecutive children with sinovenous thrombosis found that the most frequent prothrombotic abnormality seen was anticardiolipin antibody of the IgG isotype (1). This study also found that another important risk factor for the development of sinovenous thrombosis in children is chronic systemic disease of a variety of types.

Regardless of what we consider the cause of the sagittal sinus thrombosis to be, I would treat this patient with IV heparin acutely, and continue her on oral

anticoagulants for 3-6 months thereafter. Although we do not have results from large, randomized controlled trials, empiric treatment for this condition for the past decade has been to use anticoagulation. A recent small study of 17 children with venous sinus thrombosis showed that anticoagulation in 15 of them did not result in bleeding complications or worsening of their neurological condition (2). Only 2 of the 17 children did not undergo anticoagulation, and all children improved clinically. While the results from this study seem to suggest that cerebral venous sinus thrombosis has a good prognosis in children, in fact, death or significant neurologic deficits are seen in about 50% of children with cerebral sinus thrombosis (2). In studies in adults with cerebral venous thrombosis anticoagulation, *even in the presence of hemorrhagic strokes*, did not lead to bleeding complications and lead to improved outcomes (3). A recent Cochrane Database of Systematic Reviews concluded that based on the limited evidence available, anticoagulant treatment for cerebral sinus thrombosis appeared safe and was associated with potentially important reductions in death and dependency that did not reach statistical significance (4).

Perhaps a more difficult question is related to how long the warfarin treatment should be continued if we attribute the thrombosis to anticardiolipin antibodies. There are no studies in children or adults to help guide us in answering this question. Observational studies in adults with deep venous thrombosis associated with antiphospholipid antibodies suggest that longer term anticoagulation may be needed. It is not at all clear that these results can be generalized to children with deep venous thrombosis or anyone with cerebral venous sinus thrombosis. Given 1) the difficulty and morbidity associated with warfarin treatment in children and 2) the fact that we cannot say that the sagittal sinus thrombosis in this patient was not due, at least in part, to a SLE flare, I would treat her with warfarin for six months and then resume her baby aspirin treatment.

I would treat this patient with three methylprednisolone pulses followed by oral prednisone for her non-nervous system SLE manifestations. We are told that she has been erratic in her medication compliance of late. This may be the

trigger for her current disease flare. For this reason, I would resume the rest of her prior medications (hydroxychloroquine and mycophenolate) as well, except for the baby aspirin until she is taken off warfarin. When she recovers neurologically, I would also discuss the reasons for the noncompliance with the patient and her family. This would help me identify issues that to be addressed in order to increase compliance, e.g. psychological counseling, changing medications to reduce side-effects.

References

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