Neurologic Complications of SLE

Key Points:
1. SLE can cause a number of neurologic complications, particularly CVAs, seizures, HA, neuropathies, and cognitive decline.
2. Secondary causes should always be considered.
3. Serologies are generally not helpful in making the diagnosis.
4. It is imperative to evaluate the CSF to rule out infection.
5. High dose steroids should be administered in patients with acute disease.

How commonly does this occur?
CNS effects of SLE are estimated at 40-70%. They may occur at any time during the disease but are rarely the first manifestations of SLE.

What’s the mechanism?
True necrotizing vasculitis is rare. More commonly you see “bland vasculopathy” which is characterized by a small to moderate perivascular accumulation of mononuclear cells of the blood vessel, without destruction. Antiphospholipids antibodies play a role in causing arterial and venous thrombi, leading to ischemic damage to the CNS. Other culprits may be cytokines, neuropeptides, oxidative stress, nitric oxide, and other antibodies.

What about those other antibodies?
- In one report, 45% of pts with CNS lupus had antineuronal antibodies targeted to human neuroblastoma cells in comparison with only 5% of pts with lupus without CNS systems.
- Cognitive dysfunction has been associated with lymphocytotoxic antibodies.
- Ribosomal P protein antibodies have been associated with lupus psychosis and depression.
- Antibodies to a 50-kD antigen in plasma membranes of brain synaptic terminals were shown in one study to be more prevalent in pts with CNS lupus than those without.

What are the more common symptoms?
- **CVA:** Estimated at 7% of lupus pts. First presentation often within 5 yrs of lupus diagnosis and recurrences are common. A strong association exists between APLAS and CVAs and an abnormal MRI may be the first clue to the presence of APLAs. Strokes may be secondary to treatment of SLE, as steroids can cause HTN and atherosclerotic changes.
- **Seizures:** Occur in 15-20% and can be partial or generalized. Can be caused by an acute inflammatory response or scarring in CNS. Secondary causes should also be considered (uremia, infection, drug toxicity, etc…). Seizures are a marker for poor prognosis.
- **Headaches:** migraines and tension HA may occur in up to 40% of pts with SLE. Other causes of HA such as pseudotumor cerebri with papilledema occur more frequently in pts with renal disease and hypercoagulable states so should be considered in lupus pts.
- **Neuropathy:** about 15% frequency in lupus pts and due to vasculopathy of small arteries of affected nerves. Symptoms are usually asymmetric, involving multiple nerves (mononeuritis multiplex) and affect sensory more than motor nerves.
- **Psychiatric manifestations:** Cognitive dysfunction occurs in 40% or more of pts and can be subtle, with obvious deficits seen only on neuropsych testing. Psychosis, anxiety, depression, and dementia are seen at higher rates in lupus pts than in the general population. Steroid psychosis can confuse the picture!

Any other neurologic complications?
- transverse myelitis: consider this in patients with sudden onset of leg weakness or sensory loss and/or bowel or bladder dysfunction.
- optic neuritis and other cranial nerve problems
- meningitis: can also be due to infection, results of therapy (NSAIDs or azathioprine)
How do I diagnose CNS lupus?
Difficult to do, as often there are complicating factors. Serologies usually do not help. Anti-ribosomal P may correlate with SLE psychosis. Important to evaluate CSF to rule out infection. CSF of SLE cerebritis pts can be normal or may have slightly increased protein or pleocytosis. MRI can also help to R/O small CVAs.

So what do I do to treat CNS lupus?
In acute situations, you may need to make empiric treatment decisions. High dose steroids (1 mg/kg/d) should be given in most cases. Response to therapy is indicative that the lupus was cause of symptoms. With APLAS complications, anticoagulation is necessary. For pts with progressive disease unresponsive to steroids, cytoxan (cyclophosphamide), plasmapheresis, or IVIG may be considered...ask for help from your friendly rheumatologist! Usual therapies for HA, seizures, neuropathies, and psych disorders should also be employed. Stem cell therapy is in trial phase now.

References:
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