SYMPTOMS IN PATIENTS WITH SARCOIDOSIS

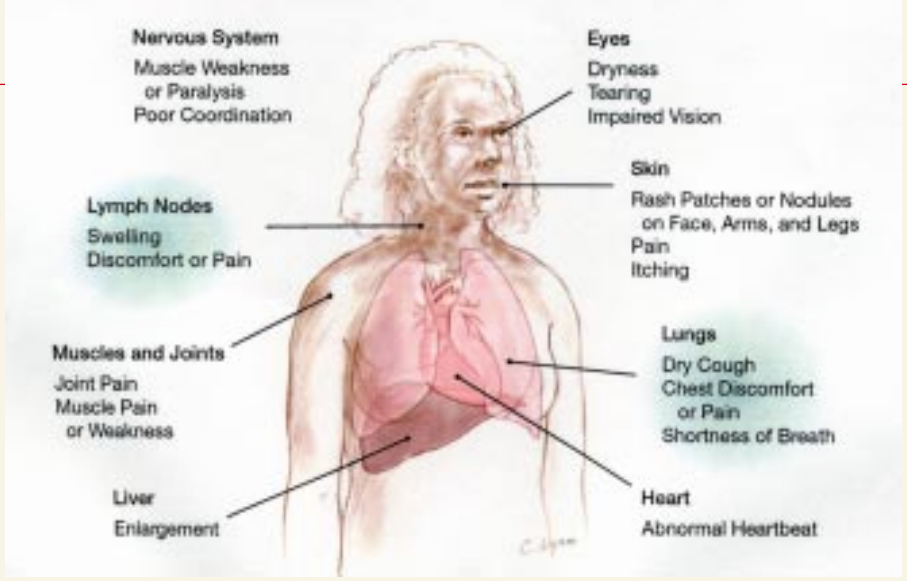

Illustration: Cassio Lynm; courtesy of the American Medical Association.

CAREFUL PATIENT MANAGEMENT IS KEY TO TREATMENT OPTIONS

First line treatments are corticosteroids like prednisone. This has proven extremely effective in most patients, but because of the side effects, it is not desirable for long-term treatment. "Again, you don't know who's going to decline, improve or stay the same, so you have to monitor this carefully," says Dr. Knox.

Certain manifestations must be treated immediately and aggressively. For example with cardiac or neurologic involvement, patients need high doses of steroids and sometimes a second or third agent.

Pulmonary sarcoidosis will often improve without treatment. Physicians typically wait three to six months to see if patients get better on their own if they have mild disease – and this occurs 50 percent of the time. Low oxygen levels, however, would preempt a "wait-and-see" trial period.

The observation period is important for another reason. "There are other diseases which can cause this type of granulomatory inflammation, and if exposed to steroids, can worsen," says Dr. Wilkes. "Therefore, it's important to exclude other diseases such as histoplasmosis or tuberculosis."

When sarcoidosis with lung involvement is clearly indicated, prednisone works well in 70 to 80 percent of patients. With isolated liver disease, the response to prednisone is unpredictable, so it much be watched closely and switched to other agents when necessary. Although pulmonary sarcoid seems to respond well to prednisone, according to Dr. Wilkes, there are no adequately controlled trials of what works well for the central nervous system.

Despite the general effectiveness of prednisone, complications such as cataracts, bone loss, weight gain, glucose intolerance, irritability and mood swings become worrisome after a year of therapy. In patients with these side effects, the dose is sometimes lowered and used in conjunction with a second agent. Hydroxychloroquine is a second line agent used initially for certain lines of cutaneous disease including sarcoid.

With a number of diabetic patients who contract sarcoidosis, therapy must be carefully managed because of the negative response to corticosteroids. Often they have to go sooner to a secondary agent. These work more like chemotherapy and include drugs like azathioprine and methotrexate.

In patients with refractory sarcoidosis, treatment might include a high dose steroid burst or escalation with a second agent. "You tend to fold in more therapies as you go," says Dr. Knox. "People may have life threatening lung disease, but it's usually slow to progress. Over years, continued inflammation and destruction of the lung may require a lung transplant."

Sarcoidosis often is a chronic disease. With granulomatous uveitis, aggressive initial treatment may be followed with symptom-controlling eye drops. With cutaneous sarcoid, the patient may be able to control it with local steroid injections or crèmes and ointments as opposed to systemic steroids. Less intensive therapy may work once the disease is under control.

INVESTIGATIONAL PROTOCOLS FOCUS ON IMMUNE SYSTEM AND GENETICS

These therapies have been available for quite some time, although newer, investigational agents manipulate the immune system more specifically, inhibiting cytokine cascades.

Third line treatments are less traditional and include the use of inflixamab, which is often used to treat other inflammatory diseases such as rheumatoid arthritis and Crohn disease. "When all else fails, we need to consider this," says Dr. Wilkes.

The results look promising but problems may arise with opportunistic infections which appear in patients who are treated with this drug – not for sarcoidosis per se, but in general. These are the very infections that have caused the granulomous inflammation in the first place. "But maybe we'll unmask a common denominator," says Dr. Wilkes. "It's very investigational at this point."

There are several research protocols currently underway at the IU School of Medicine, one of a dozen centers around the country which treats sarcoidosis and one in eight utilizing a multi-disciplinary approach. "Right now we're trying to gather as much information as we can. We currently are seeking patients who are naive to therapy and testing their blood cells in vitro" says Dr. Knox. "In the future, we anticipate having more of an interventional treatment protocol."

There are really no surgeries for sarcoidosis – certainly none that cure the disease. In cases where there has been lung transplantation, there may be a recurrence of the disease, although it's usually mild. Treatments under investigation at the NIH are aimed at manipulating the cytokine cascade, such as pentoxifylline, which is delivered in pill form.

Another area of intense investigation is in the area of genetics. There is some evidence the genes for the ACE enzyme may be different in certain populations, suggesting a more genetic than environmental trigger. "There might be a revealing familial association," says Dr. Knox. "There might be certain genes involved that need to be 'turned off' to stop this inflammation. Much current research is directed toward the genetic basis of sarcoidosis – and I think that's where the future of treatment lies." ■

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