Treatment of sarcoidosis

Sarcoidosis is an uncommon, poorly understood disorder that most often affects the chest. Its cause is unknown. While the outcome is, in general, favorable, a small number develop scarring of the lungs (fibrosis), which, if extensive, will cause severe shortness of breath or even to death. Treatment is essential when sarcoidosis affects a critical organ such as the heart or brain or causes disabling shortness of breath. Treatment is not required when only the lymph nodes in the chest (stage I) are affected both because there is no risk of lung fibrosis, and because almost all stage I cases clear up (resolve) without treatment. When the lungs are affected (stage II, III), the treatment decision is complicated because not all cases resolve spontaneously or leave only mild scarring (not enough to interfere with usual activities). Stage is a useful guide to outcome. Stage I is the most favorable, with almost all cases resolving spontaneously. Stage II is more likely and stage III even more likely to leave lung fibrosis. We have no way of predicting in an individual whether it will resolve without treatment. The caregiver must weigh the benefit of treatment against its potential harm. Prednisone (a form of cortisone) is very effective in resolving the lung involvement short-term. It has well-known side effects—weight gain, diabetes, high blood pressure, bone thinning—that we would like to avoid. Moreover, it hasn't been shown to benefit persons long-term.

The treating physician faces a dilemma: avoiding treatment with its side effects in the hope that the condition will resolve spontaneously vs. treating in the hope of preventing disabling or fatal lung fibrosis. Small trials comparing treatment vs. no treatment in persons with lung involvement (stage II, III) showed a slightly better long-term outcome in the untreated groups.

Sarcoidosis mortality in referral settings has been far worse than in clinical practice settings. After correcting for the higher proportion of patients with advanced stages, persons in referral settings are both 7-times as likely to receive prednisone therapy and die of sarcoidosis as those in practice settings. Investigators in referral settings have accounted for both the higher proportion treated and mortality by asserting that they reflect the severity of disease in their subjects. An alternative explanation is that prednisone prevents spontaneous resolution by suppressing the immune response. To test these hypotheses would require a direct comparison of disease severity in the two settings. None exists.

Outcomes in two referral settings that used completely different treatment indications provides an alternative means of testing these hypotheses. In one setting, prednisone treatment of lung involvement was limited to four (out of 159) persons whose disease worsened under observation. After 20-years, 141 had resolved, and 18 had local lung fibrosis but no significant impairment. In the other setting, among 335 newly diagnosed persons, prednisone was provided on the basis of "clinical outcome score," which included persistent (not worsening) lung involvement. Of 213 persons evaluated at a 5-year follow-up, 168 had received prednisone. Of those, 144 required continued therapy for chronic disease.

Three forces other than scientific information and belief drive the decision to treat:

1) Patients notified of a potentially serious disease expect to be treated. This expectation may influence the physicians' judgement.

2) Physicians fear that withholding or delaying treatment in persons whose lung involvement is persistent, though not worsening, may result in disabling or fatal lung fibrosis.

3) Guidelines from prestigious professional organizations advise that treatment be withheld in persons whose lung involvement is not worsening over time.

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Publication

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