Response to: Dr. Culver, Con rebuttal: The treatment of the granulomatous response is beneficial in acute sarcoidosis

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If sarcoidosis were a granulomatous response to an elusive, poorly degradable, non-virulent antigen(s), entailing an unpredictable risk of lethal pulmonary fibrosis, then corticosteroid (CS) intervention would be intuitively justifiable. Its benefit would be clearly evident in controlled trials of acute disease and among intensively treated individuals in tertiary care centers. If, on the other hand, the systemic granulomas are a default response (tending to spontaneous resolution) to diverse antigens in persons with demonstrable impairment in cellular immune response, withholding CS suppression during the early (Th1) response would be the rational decision, and would be evident in the same circumstances. Experimental evidence and clinical experience, both delineated in the MS, favor the latter view: Treated under the former premise, sarcoidosis mortality has been an order of magnitude higher than under the latter. Confining intervention to individuals with chronic, progressive, pulmonary shadowing conforms to current UK,1 ATS, ERS and WASOG guidelines.2

To conform to scientific criteria and length constraints, my rebuttal will be confined to germane data—information on the long-term outcome in persons with recent-onset pulmonary shadowing treated with systemic CS. It will exclude a priori statements, unattested allegations of efficacy and articles lacking new data (Culver 2,14, 17), uncontrolled studies or those lacking long-term follow-up (C1,6,8,11,22,23,24), stage I data (the majority in C6), other treatments including inhaled CS—which is no longer recommended (C10,18,26), other diseases (C15,16,28,32,33,34,35) and non-treatment aspects of sarcoidosis (C21,29,31,32).

Dr. Culver instances not a single example of long-term benefit of CS in controlled trials of acute pulmonary sarcoidosis, nor a response to the far higher mortality reported in tertiary care centers that more frequently prescribe CS. The majority of germane studies advanced in support of his viewpoint are delineated in précis in a systematic review3:

C4 Zaki: Poor compliance with treatment and follow-up studies invalidates this study.3

C5 Israel: Our interpretations differ. In those with pulmonary shadowing the authors reported definite improvement (in a combined radiographic, FVC and corticosteroid requirement assessment) on long-term evaluation in 48% of treated vs. 44% of controls; progression in 38% of treated vs. 16% of controls; normal CXR attained in 6 treated vs. 10 controls. Allocation was unspecified for the 2 sarcoidosis deaths.3

C7 Selroos: enrolled persons with pulmonary shadowing of ≤5-years duration. There was no long-term evidence of
either benefit or harm in this small, controlled trial, consistent with other trials in persons with disease of intermediate duration.3

C8 Johns: Uncontrolled. Usual policy was to avoid CS within first two years (allowing for spontaneous improvement) in the absence of compelling symptoms.

C9 Eule: Untreated controls fared better than CS recipients. See review.2

C19 Paramothayan: Limitations addressed both in the MS and the review.3

C20 Gibson: Limitations addressed both in the MS and the review.3

To the question “...why wouldn’t you treat a patient with acute sarcoidosis?” I answer: 1) Many improve/resolve spontaneously. 2) Avoidance of CS side effects. 3) Persuasive evidence that CS impairs resolution, leading to much higher mortality vs. conservative management.

Conflict of interest

None.

References

