Angiotensin-converting enzyme in sarcoid


The diagnosis of ocular sarcoid is presumptive in the absence of systemic disease. The association of elevated serum angiotensin-converting enzyme (ACE) levels with active systemic sarcoid has been well described. With a sensitive fluorimetric assay for ACE, we found that five of ten chronic granulomatous uveitis patients without systemic sarcoid had elevated serum ACE levels. None of ten patients with uveitis of known etiology had elevated serum ACE levels. We believe that the association of an elevated serum ACE level with chronic granulomatous uveitis suggests the diagnosis of ocular sarcoid.

Sarcoidosis is a diffuse, noncaseating, granulomatous disease with varied clinical manifestations. Uveitis is a common ophthalmologic manifestation; almost all ocular and adnexal tissues may be involved.1 Sarcoid uveitis is diagnosed when a chronic granulomatous uveitis occurs in conjunction with systemic sarcoidosis. In the absence of systemic disease, the diagnosis of ocular sarcoid is presumptive unless there is histologic confirmation on conjunctival or iris biopsy.2 A chemical marker for sarcoidosis would be an important diagnostic adjuvant in the management of patients presenting with a chronic granulomatous uveitis without systemic sarcoidosis.

Serum angiotensin converting enzyme (ACE) is elevated in some patients with sarcoidosis.3-4 This investigation tests the diagnostic efficacy of serum ACE determinations in patients with chronic granulomatous uveitis but with no evidence of systemic disease.

Materials and methods. Serum ACE was assayed in a masked manner. Duplicate samples were measured by the fluorimetric method of Friedland and Silverstein* with hippuryl-L-histidyl-L-leucine as substrate. The following subjects were tested in this study: 10 consecutive patients with chronic granulomatous uveitis without systemic sarcoidosis, 10 patients with other forms of uveitis (four patients with toxoplasmic, two with chronic cyclitis, and one with each of the following: juvenile rheumatoid arthritis, ankylosing spondylitis, bird-shot chorioidopathy, and Behçet's disease), 10 patients with active sarcoidosis with or without ocular involvement, and 25 normal subjects. All patients were examined in the Uveitis Survey Clinic of the University of California, San Francisco, during 1977. After informed consent was obtained, peripheral venous blood was drawn and allowed to clot for approximately 1 hr at room temperature. The serum was removed and stored at −20° C. ACE activity was stable in frozen samples. The serum ACE levels in normal subjects was 37.2 ± 7.9 nmol/min/ml. This is in close agreement with other studies.4

Results. ACE levels in the 10 patients with chronic granulomatous uveitis are presented in Table I. Systemic evaluation for sarcoidosis was negative in all 10 patients. Complete blood counts, luetic serology, SMA-12, and chest x-rays were normal in all cases. Except for Patient 1, who had a nonreactive P.P.D., Candida, histoplasmin, and coccidioidin skin tests, all other patients had positive cutaneous delayed hypersensitivity and nonreactive P.P.D.'s. Skin testing with Kveim-Siltzbach antigen was not done due to the unavailability of the antigen.

In five out of 10 patients, serum ACE was greater than 2 S.D. above the mean; four exceeded the mean by 3 S.D.

None of the five patients with significantly elevated serum ACE levels was on systemic steroids. One of the five patients with serum ACE levels within the normal range was using systemic steroids. Two of the patients with elevated levels and three of the patients with normal ACE levels were using topical steroid preparations.

Serum ACE values were measured in patients with other forms of uveitis. A comparison of the ACE values in this group and those with chronic granulomatous uveitis is shown in Table II. Only one patient with other types of uveitis had an elevated ACE level, and this was within 1 S.D. of the mean (40.1 nmol/min/ml). This patient was on systemic steroids.

Mean serum ACE from patients with active systemic sarcoidosis was demonstrated to be significantly elevated (57.1 ± 10.5 nmol/min/ml). This is similar to the results of other investigations.3-5

Discussion. The association of elevated serum ACE levels with active systemic sarcoidosis has been well described.3-4 In this study, five of 10
Table I. Angiotensin-converting enzyme in chronic granulomatous uveitis

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Race</th>
<th>Sex</th>
<th>Best corrected visual acuity</th>
<th>Anterior uveitis, iris nodules</th>
<th>Vitreous cells (snowballs)</th>
<th>Posterior uveitis</th>
<th>Candle wax drippings or vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>W</td>
<td>M</td>
<td>20/25</td>
<td>+</td>
<td>1+</td>
<td>Transient papilledema recurrent macular edema</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>B</td>
<td>F</td>
<td>20/40 +2</td>
<td>None</td>
<td>2+</td>
<td>Atrophic pigment peripapillary scars</td>
<td>Perivenous sheathing and candle wax drippings</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>B</td>
<td>F</td>
<td>20/30</td>
<td>None</td>
<td>1+</td>
<td>WNL</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>B</td>
<td>M</td>
<td>20/200</td>
<td>None</td>
<td>3+</td>
<td>WNL</td>
<td>Perivascular sheathing (venules and arterioles)</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>W</td>
<td>F</td>
<td>20/60 -2 CF - 6 inches</td>
<td>+</td>
<td>1+</td>
<td>Macular edema</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>42</td>
<td>W</td>
<td>M</td>
<td>20/25 -2</td>
<td>(Rare)</td>
<td>WNL</td>
<td>Perivascular sheathing and candle wax drippings</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>B</td>
<td>F</td>
<td>20/200</td>
<td>+</td>
<td>2+</td>
<td>WNL</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>W</td>
<td>F</td>
<td>20/35</td>
<td>+</td>
<td>1+</td>
<td>Pigment clumping</td>
<td>Perivenular sheathing</td>
</tr>
<tr>
<td>9</td>
<td>52</td>
<td>B</td>
<td>F</td>
<td>20/20</td>
<td>+</td>
<td>Trace</td>
<td>WNL</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>W</td>
<td>F</td>
<td>20/30</td>
<td>+</td>
<td>2†</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

* T, topical; S, systemic.
† Posterior pole not visualized at time of evaluation.

Table II. Comparison of ACE values in uveitis

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ACE values (±S.D.) (nmol/min/ml)</th>
<th>Number with elevated ACE values</th>
</tr>
</thead>
<tbody>
<tr>
<td>I*</td>
<td>50.7 ± 16.2</td>
<td>5/10</td>
</tr>
<tr>
<td>II†</td>
<td>28.5 ± 8.4</td>
<td>0/10</td>
</tr>
</tbody>
</table>

* Group I, 10 patients with chronic granulomatous uveitis.
† Group II, 10 patients with uveitis of known etiology (not sarcoid).

No patient with other forms of uveitis tested had a serum ACE level 2 S.D. above the normal mean. In contrast, patients with systemic sarcoidosis studied had significant elevations in serum ACE.

Elevation of serum ACE is probably more specific than an elevation of the serum lysozyme in sarcoidosis. Lysozyme is elevated in tuberculosis, uremia, megaloblastic anemia, various types of leukemia, Crohn's disease, osteoarthritis, and collagen vascular disease. In contrast, elevations of serum ACE have been described in less than 10% of patients with other granulomatous diseases.

The source of increased serum ACE in these patients with chronic granulomatous uveitis is not known. Possibly the ocular disease had sufficient associated inflammation to produce elevated serum ACE in the absence of systemic sarcoidosis. More likely these patients had occult systemic sarcoid in a clinically quiescent phase.

It is not unusual for a patient with sarcoidosis to initially seek medical consultation because of ocular disease. Only hilar adenopathy and pulmonary abnormalities are more common than ocular manifestations when clinically detectable lesions are considered. In addition to serum ACE, gallium scans may possibly be a reasonable diagnostic ad-
juvant in this group. Our results indicate that ocular involvement in sarcoidosis may be more common than generally recognized.

In conclusion, we believe the association of an elevated serum ACE with a chronic granulomatous uveitis suggests the diagnosis of ocular sarcoidosis. Serum ACE is a useful ancillary test for diagnosing ocular sarcoidosis and other granulomatous disorders.

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Key words: sarcoidosis, uveitis, granulomatous uveitis, angiotensin converting enzyme (ACE), sarcoid uveitis

### REFERENCES


### Peripheral stimulation and human cyclofusional response. Mark J. Sullivan and Andrew E. Kertesz.

Cyclofusional responses consisting of both motor and nonmotor components were measured during stimulation in the peripheral visual field. A 5.75° torsional disparity presented in 10°, 30°, and 50° diameter visual stimulus fields induced binocular, torsional eye movements averaging 2.8° to 3.4°. When torsional disparity was excluded from regions up to 30° diameter in the center of the visual field, binocular torsional eye movements of 3.3° to 4.4° were observed. A presentation of simultaneous, conflicting torsional disparities in center and annular surround regions of the stimulus field also induced torsional eye movements which reduced the disparity in only one of the two regions while increasing it in the other. The directions of eye movement changed when the surround stimulus area was enlarged at the expense of the area of the conflicting central stimulus. Based on an objective method of monitoring eye position, the findings in this report suggest that peripheral stimulation exercises a strong influence on the cyclofusional motor response component and that under suitable conditions such stimulation may have a greater influence on the cyclofusional motor response than central stimulation. The response to fusional stimulation within the central visual field (foveal and near foveal regions within 10° diameter) has received considerable study, especially in the case of horizontal disparity stimulation and the associated response mecha-