Azoospermia in testicular sarcoidosis is an indication for corticosteroid therapy

D. Aled Rees, M.D., Alex L. Dodds, M.D., Nia Rathbone, M.D., J. Stephen Davies, M.D., and Maurice F. Scanlon, M.D.

Department of Medicine, University of Wales College of Medicine, Cardiff, United Kingdom

Objective: To report improvement of azoospermia and hypogonadism after high-dose corticosteroid therapy in a patient with testicular sarcoidosis.

Design: Case report.

Setting: University hospital.

Patient(s): A 27-year-old man with testicular sarcoidosis and azoospermia.

Intervention(s): High-dose corticosteroid therapy was commenced in an attempt to improve sperm count and restore gonadal function.

Main Outcome Measure(s): Analysis of sperm count, T, and gonadotropin response to steroid therapy.

Result(s): FSH and LH concentrations decreased and T levels increased in parallel with control of disease activity with steroid therapy. Repeat semen analysis demonstrated a significant increase in sperm count, allowing sperm banking to take place.

Conclusion(s): High-dose corticosteroid therapy may be indicated in testicular sarcoidosis, not only for control of systemic disease activity but also for recovery of gonadal function and spermatogenesis. (Fertil Steril® 2004;82:1672–4. ©2004 by American Society for Reproductive Medicine.)

Key Words: Sarcoidosis, azoospermia, corticosteroids

Sarcoidosis is an uncommon, multisystem disorder of unknown etiology with an estimated prevalence of 1–2 per 10,000 of the population. It is characterized histologically by the presence of epithelioid, noncaseating granulomas and most commonly presents with thoracic involvement, although virtually any organ can be affected. Involvement of the reproductive system is rare with an estimated frequency of genitourinary sarcoidosis in men of <0.2% in clinically diagnosed cases and 5% in autopsy studies (1, 2). Genitourinary manifestations of sarcoidosis include renal disease with nephrocalcinosis, painless testicular masses, and acute epididymo-orchitis with testicular swelling. Despite these presentations, the effects of genitourinary sarcoidosis on fertility and gonadal function have not been examined in detail and no studies have prospectively analyzed changes in these parameters in response to disease therapy. We report a case of bilateral testicular sarcoidosis with azoospermia and hypogonadism in whom high-dose corticosteroid therapy resulted in partial recovery of spermatogenesis and gonadal function.

CASE REPORT

A 27-year-old white man presented to the Ophthalmology department at our hospital with a painful, red eye. He was diagnosed with anterior uveitis and commenced on topical corticosteroid therapy. Serum angiotensin-converting enzyme (ACE) level was elevated at 96 U/L (normal values 20–54 U/L) and a chest X-ray was normal with no evidence of hilar lymphadenopathy. He represented 1 month later complaining of a painless mass in his right testis. Physical examination revealed multiple, small masses in both testes with separately palpable epididymes.

Serum α-fetoprotein and hCG levels were within the normal range, and scrotal ultrasound examination showed multiple hypechoic lesions in both testes. An open testicular biopsy was performed to exclude malignancy. Histological analysis of this sample demonstrated replacement of 90% of the normal testicular tissue with confluent noncaseating granulomas, occasional multinucleated giant cells, and a sparse lymphocytic infiltrate. There was no spermato-
genesis visible in the remaining seminiferous tubules. These features confirmed a diagnosis of testicular sarcoidosis. Biochemical analysis revealed primary hypogonadism with a low serum testosterone (6.1 nmol/L, normal range 8–30 nmol/L) and elevated gonadotropins (FSH 31.5 U/L, normal range 1.4–18.1 U/L; LH 13.8 U/L, normal range 1.5–9.3 U/L), and a semen analysis showed azoospermia.

Although the patient had no immediate plans for paternity, we elected to treat him with high-dose corticosteroid therapy (with weekly bisphosphonates as bone antiresorptive therapy) without concomitant replacement of T in an attempt to improve his sperm count sufficiently to enable sperm banking to take place. As shown in Table 1, there was a gradual decrease in gonadotropin concentrations in parallel with control of systemic disease activity (as indicated by serum ACE levels), returning to the normal range within 7 months of therapy initiation. The T concentration also increased slowly over this time. A repeat semen analysis was performed at month 5 and this sample indicated partial recovery of spermatogenesis with a sperm concentration of 1.2 million/mL, 75% motility, and 75% showing good progression. At this stage sperm banking took place. A repeat testicular ultrasound scan demonstrated a reduction in size of the multiple, hypoechoic lesions.

### DISCUSSION

Testicular involvement in systemic sarcoidosis is unusual but seems to be more frequent in Afro-Caribbean men, in keeping with the higher incidence of sarcoidosis generally in this group (1, 2). Sarcoid granulomas in the genitourinary system most frequently occur in the epididymis with only occasional involvement of the testis, prostate, spermatic cord, scrotum, or penis. Epididymal involvement may be unilateral or bilateral and can present with acute or recurrent epididymitis. Symptomatic epididymal sarcoidosis may respond to corticosteroid therapy, but often requires excisional biopsy for relief of pain. Sarcoid involvement of the epididymis usually demonstrates a periductal distribution and can lead to fibrosis and azoospermia (3, 4), although spontaneous remission is also described.

Few reports exist of sarcoid affecting the body of the testis without epididymal disease and most patients with testicular involvement present between the ages of 20 and 40 years, which coincides with the peak occurrence of testicular malignancy. It is therefore mandatory that all patients with systemic sarcoidosis presenting with a testicular mass undergo exploration and biopsy. In fact, case reports and case series have suggested that sarcoidosis and testicular malignancy often coexist, although whether this association is an etiological one or merely reflects surveillance bias is unclear (5).

The rarity of this condition means that treatment regimes remain somewhat empirical, although anecdotally courses of steroid therapy have been reported to be effective in reducing the size of testicular and epididymal lesions (6, 7). The effect of corticosteroids on fertility in this condition is less clear, although reports have variably shown resolution or progression of epididymal disease on corticosteroid therapy (8). Svetec and colleagues (9) reported a patient with systemic and epididymal sarcoidosis whose sperm counts fluctuated in response to steroid courses administered for control of pulmonary disease activity. The temporal relationship between steroid administration and improvements in sperm count observed in their patient suggested that ductal obstruction could respond to steroid therapy, although spontaneous resolution could not be excluded.

We have shown partial recovery of spermatogenesis and gonadal function in a patient with bilateral testicular sarcoidosis treated with high-dose steroids specifically for this disease presentation. To our knowledge this is the first report where spermatogenesis and gonadal function have been studied prospectively in a patient given steroid therapy for testicular sarcoidosis. In the absence of T replacement, measurement of gonadotropin levels, supplemented with periodic testicular ultrasonography, have enabled us to determine local sarcoid activity in the testes and hence determine response to treatment. These measures can therefore complement serum ACE levels as a marker of overall disease activity. Although it is conceivable that the improvements in

### TABLE 1

<table>
<thead>
<tr>
<th>Month 0</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
<th>Month 4</th>
<th>Month 5</th>
<th>Month 6</th>
<th>Month 7</th>
<th>Month 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH (U/L)</td>
<td>31.5</td>
<td>31.6</td>
<td>29.2</td>
<td>26.3</td>
<td>22</td>
<td>20.8</td>
<td>18.3</td>
<td>17.1</td>
</tr>
<tr>
<td>LH (U/L)</td>
<td>13.8</td>
<td>11.6</td>
<td>11.8</td>
<td>12.6</td>
<td>8.4</td>
<td>10.3</td>
<td>8.6</td>
<td>7.6</td>
</tr>
<tr>
<td>T (nmol/L)</td>
<td>6.1</td>
<td>5.3</td>
<td>6.9</td>
<td>6.3</td>
<td>7.7</td>
<td>8.9</td>
<td>8.1</td>
<td>8.7</td>
</tr>
<tr>
<td>ACE level (U/L)</td>
<td>78</td>
<td>24</td>
<td>14</td>
<td>26</td>
<td>—</td>
<td>34</td>
<td>—</td>
<td>38</td>
</tr>
<tr>
<td>Sperm count</td>
<td>0</td>
<td>1.2×10⁶/mL</td>
<td>40</td>
<td>30</td>
<td>20</td>
<td>15</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Prednisolone dosage (mg)</td>
<td>0</td>
<td>60</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

testicular function might represent spontaneous remission of disease activity, this would seem unlikely given the severity of involvement evident on biopsy at presentation.

Our case illustrates that in addition to restoring ductal patency in epididymal sarcoidosis, corticosteroids may be effective in testicular disease, not only for control of systemic disease activity but also for recovery of gonadal function and spermatogenesis. This treatment modality should therefore be considered in all patients with an interest in paternity presenting with sarcoidosis in the genital tract.

References