TREATMENT OF BOVINE TUBERCULOSIS IN
AN ARABIAN ORYX (ORYX LEUCORYX)

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Abstract: In September 1988, treatment of an adult male Arabian oryx (Oryx leucoryx) for bovine tuberculosis was initiated after the animal had reacted positively to an intradermal injection of bovine purified protein derivative. Infection with Mycobacterium bovis had been suspected because of the animal’s rapid weight loss and a history of tuberculosis in the herd to which it belonged. The administration of ethambutol, isoniazid, and rifampicin through the drinking water resulted in a dramatic improvement of the animal’s condition. During the 1-yr treatment period, blood samples were collected on three occasions. Enzyme-linked immunosorbent assays on blood samples were performed by the University of Otago, New Zealand, by the Central Veterinary Institute in Lelystad, the Netherlands, and by the Central Veterinary Laboratory in Weybridge, United Kingdom. Additionally, a lymphocyte transformation test was performed on two different occasions at the University of Otago. All tests showed an unusually high reactivity to M. bovis. Because the animal was well represented genetically in the herd and was precluded from further breeding because of the disease risk to its mates, it was culled at the end of January 1990, more than a year after the inception of treatment. Necropsy was performed in order to establish the effectiveness of the treatment. It was found that there had been remarkable resolution of a very severe tuberculosis infection, but M. bovis was still cultured from a dry, caseous lung lesion and an enlarged mediastinal lymph node.

Key words: Tuberculosis, Mycobacterium bovis, Arabian oryx, Oryx leucoryx, tuberculosis treatment, tuberculosis testing.

INTRODUCTION

The Arabian oryx (Oryx leucoryx) is an endangered antelope, native to the Arabian peninsula. Because of the rarity of the species and the genetic value of the large herd of oryx in Saudi Arabia, conservation authorities in the country responded to an outbreak of bovine tuberculosis in 1987 by treating infected animals with appropriate management and medication, rather than following the common practice of slaughter.

The case of one of the infected animals was particularly interesting. On serologic testing for tuberculosis it showed extraordinarily high levels of reactivity to Mycobacterium bovis and responded very favorably to treatment. Because the animal, a male, was already genetically well represented in the group, it was felt that the risk of transmitting the disease during further matings was too great. It was culled 4 mo after drug therapy had ended, with the specific aim to establish definitively how effective the treatment had been.

CASE REPORT

A mature male (hereafter referred to by its reference number AO9) in a small herd of Arabian oryx at the King Khalid Wildlife Research Centre (KKWRC) showed progressive weight loss during September 1988. Infection with M. bovis was suspected because the herd had a history of bovine tuberculosis. On 22 September 1988 the animal was chemically immobilized with etorphine (M99, C-Vet Ltd., Bury St. Edmunds, Suffolk IP33 3SU, United Kingdom) and xylazine (Rompun 2%, Bayer AG, Leverkusen, Germany), and was transported to a stable for testing and treatment. A standard dose of 0.1 ml bovine purified protein derivative (PPD) (CDI, Edelhertweg 15, Lelystad, The Netherlands) was injected in-
tradermally on the right side of the neck. Three days later it was again immobilized to read the skin test. The PPD injection site showed a distinct swelling. No complications occurred during the immobilizations and both times the animal recovered smoothly after reversal with diprenorphine (M50-50, C-Vet Ltd., Bury St. Edmunds, Suffolk IP33 3SU, United Kingdom).

From 25 September 1988 onwards, AO9 was treated daily with 600 mg ethambutol (Myambutol, Lederle Laboratories Division, American Cyanamid Co., Pearl River, New York 10965, USA), 250 mg isoniazid (Rimifon, F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland), and 600 mg rifampicin (Rimactane, Ciba-Geigy Ltd., Basle, Switzerland). The dosages were originally based on those advised for humans, and were believed to be sufficient for an animal with an estimated weight of 60 kg. However, dosages were recalculated in December 1988, after AO9 had been moved to a new accommodation, and again after AO9 was moved a second time in March 1989. Recalculation was done because the animal was rapidly gaining weight. Furthermore, research at the National Wildlife Research Centre in Taif had demonstrated that daily dosages of 15 mg/kg ethambutol, 5 mg/kg isoniazid, and 12.25 mg/kg rifampicin produced satisfactory serum drug levels in oryx if administered orally in an aqueous solution. By late January 1989, AO9's weight was estimated to be 90 kg. From then on, it was given 1,200 mg ethambutol, 450 mg isoniazid, and 1,200 mg rifampicin daily. Because of erratic local supplies of these antituberculous drugs, various combinations of brands had to be used, but the total dosages of the active ingredients were as listed above.

Each morning the drugs were pulverized and mixed into a bowl of drinking water until suspended. Initially the animal did not always drink all its water, and with a certain amount of water evaporating, it was difficult to assess whether it was ingesting the full dose of drugs each day. First the amount of water given was decreased until AO9 usu-
ally drank it all. After the animal's second move, intake could be more precisely manipulated. Each morning, a small bowl with medicated drinking water was given, which the animal usually drank within a few hours. It was then supplied with water adlibitum until late afternoon, when all water was removed from the pen. Ingestion of most of the drugs was therefore virtually assured. Because of possible underdosage during the first 6 mo of treatment, it was decided to continue treatment until 1 October 1989 (i.e., for a full calendar year).

When the animal arrived in the stable, it was emaciated, lethargic, and anorectic. Within a few days after the beginning of treatment, AO9's food and water intake improved. It gained weight rapidly, and by late November 1988 its condition was close to normal. By March 1989 it was excellent.

Blood for tuberculosis testing was collected on four occasions: in January 1989, March 1989, September 1989, and January 1990 (shortly before the animal was culled). Four laboratories (Table 1) performed enzyme-linked immunosorbent assay (ELISA) tests1,4,5 on samples from AO9, and lymphocyte transformation tests (LTT)1,4 were done in New Zealand (Table 1).

The hematologic profile of the animal, based on several blood samples, showed no abnormal values, except for a consistently high erythrocyte sedimentation rate.

Tuberculosis test results

The intradermal skin test read positive on 25 September 1988. It was not repeated because of the need to chemically immobilize the animal twice in 4 days, and because darting activity in the oryx pens caused great disturbance among the other oryx. Although serum reactivity was still high in September 1989, it was considerably lower than in January 1989 (Table 1). ELISA and LTT results of the other oryx at KKWRC showed much lower levels of reactivity (Table 1). Table 2 gives oryx reference group mean values. The decline in reactivity and the pronounced improvement in the phys-
Table 1. Tuberculosis blood test results of seven Arabian oryx (Oryx leucoryx) at King Khalid Wildlife Research Centre, Saudi Arabia.

<table>
<thead>
<tr>
<th>Date</th>
<th>Mycobacterium bovis titer (ELISA)</th>
<th>Lymphocyte transformation test (LTT)</th>
<th>Mycobacterium avium titer (ELISA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AO 9, adult male, culled 27 January 1990, M. bovis isolated</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:204,800 Bovine ++ +&lt;sup&gt;†&lt;/sup&gt; 1:6,400</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; ND &gt;1:640 ND</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; ND Positive ND</td>
</tr>
<tr>
<td>AO 6, adult female, alive on 27 January 1990</td>
<td>Sep 1989&lt;sup&gt;a&lt;/sup&gt; 1:25,600 Bovine += 1:1,000</td>
<td>Sep 1989&lt;sup&gt;a&lt;/sup&gt; ND Positive Weak</td>
<td>Jan 1990&lt;sup&gt;a&lt;/sup&gt; Negative Negative</td>
</tr>
<tr>
<td>AO 14, adult female, alive on 27 January 1990</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:20 Negative 1:40</td>
<td>Sep 1989&lt;sup&gt;a&lt;/sup&gt; &lt;1:10 Avian 1:10</td>
<td></td>
</tr>
<tr>
<td>AO 15, adult male, alive on 27 January 1990</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:40 Bovine 1:80</td>
<td>Mar 1989&lt;sup&gt;a&lt;/sup&gt; ND Negative ND</td>
<td>Sep 1989&lt;sup&gt;a&lt;/sup&gt; &lt;1:10 ND 1:10</td>
</tr>
<tr>
<td>AO 16, adult female, died March 1989, severe M. bovis infection</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:40 Bovine? 1:80</td>
<td>Mar 1989&lt;sup&gt;a&lt;/sup&gt; 1:1,600 ND 1:10</td>
<td></td>
</tr>
<tr>
<td>AO 17, adult female, died January 1989, no M. bovis isolated</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:40 Avian/bovine 1:80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AO 18, adult female, alive on 27 January 1990</td>
<td>Jan 1989&lt;sup&gt;a&lt;/sup&gt; 1:20 Avian 1:40</td>
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</table>

<sup>a</sup> ND = not determined.
<sup>b</sup> Deer Research Laboratory, University of Otago, Dunedin, New Zealand.
<sup>c</sup> Central Veterinary Institute, Lelystad, the Netherlands.
<sup>d</sup> Central Veterinary Laboratory, Weybridge, U.K.
<sup>e</sup> King Khalid Wildlife Research Centre, Thumamah, Saudi Arabia.
<sup>†</sup> Actual LTT values of AO 9 28.688 (Jan 1989), 3.218 (Sep 1989), >1.000 (Jan 1990).

Table 2. Oryx reference group mean values.

<table>
<thead>
<tr>
<th>Animal (n)</th>
<th>ELISA&lt;sup&gt;a&lt;/sup&gt;</th>
<th>LTT (B-A)&lt;sup&gt;a&lt;/sup&gt; (cpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tb contacts (8)</td>
<td>200 800 3,995</td>
<td>&lt;100 &lt;100 &lt;1,000</td>
</tr>
<tr>
<td>Negative controls (16)</td>
<td>&lt;100 &lt;100 &lt;1,000</td>
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<sup>a</sup> ELISA values are expressed as serum antibody titers, using twofold dilutions from a baseline of 1/100, to obtain an endpoint.
<sup>b</sup> Results from the lymphocyte transformation test (LTT) are expressed as a differential response between PPD-B and PPD-A antigen reactivity. The LTT, measured as counts per minute (cpm) of 3H-thymidine, incorporates the subtraction of PPD-A values from PPD-B levels to obtain M. bovis-specific lymphocyte reactivity. Values less than 1,000 cpm fall within the negative background range.

The organism proved to be resistant to isoniazid.

Pathology

General: The animal’s weight was 115 kg. No external lesions were found. Large fat deposits were found in the subcutis, around the kidneys, in the mesocolon, and in both omenta.

Respiratory system: Nose, pharynx, and trachea showed no lesions, although there were some adhesions between trachea and surrounding lung tissue within the thoracic cavity. Both lungs were voluminous and grayish pink. Multiple fibrinous adhesions were present between pulmonary and parietal pleura and between pulmonary and diaphragmatic pleura. Some of the adhesions were hard and sausage-shaped; others appeared as fibrous plaques. All these lesions were dry and calcified, with resolution of the caseation. Throughout the lungs, nodular to oblong tubercles were found, most of which appeared calcified and inactive. Some of the tubercles were several centimeters in length. The right lung was more severely affected than the left. One fairly large lesion in the right lung contained some rather dry, white, caseous material, which...
was taken for culture. Massive amounts of scar tissue were found throughout the lungs, leaving very little lung tissue unaffected. Loose "pebbles" of calcified material were found along the dorsal ribcage and in the diaphragmatic recesses. A large, sausage-shaped piece of calcified tissue was attached to the diaphragm.

Cardiovascular system: Heart and major vessels appeared normal.

Lymphoreticular system: The left retropharyngeal lymph node was of normal shape and size, but had a hemorrhagic apex. The right retropharyngeal lymph node was circular in shape with a necrotic, calcified center. The prescapular lymph nodes showed mild hyperemia.

The mediastinal lymph nodes were enlarged with calcified lesions, and the bronchial lymph nodes were hyperemic. An unusually long, thin mesenteric lymph node with a bulbous apex was found in the jejunal mesentery. No abnormalities were found in any of the other lymph nodes.

The spleen was large (probably due to the barbiturates used for euthanasia) and had one small, white superficial lesion from which material was taken for culture.

Alimentary system: Adhesions between the visceral and parietal peritoneum were found throughout the abdominal cavity, particularly between the rumen and the abdominal wall, between the large omentum and the abdominal wall, and between the omentum and the liver. A small number of Cysticercus tenuicollis cysts was encountered in the omentum. Otherwise, the alimentary tract showed no irregularities.

Liver: The liver was large with a dark, friable parenchyma and a rather tough capsule. The caudal edge of the left lobe was rounded. Some minor lesions, which appeared as pale foci with surface adhesions, were found on the lateral edges of both lobes.

Urinary system: Minor adhesions were found between the left kidney and surrounding tissue and between the capsula and parenchyma of the left kidney.

Endocrine system: Both adrenals were slightly enlarged, with a hyperemic cortex and petechial hemorrhages in the medulla.

DISCUSSION

AO9 suffered from a classic case of pleuro-pulmonary tuberculosis, in which inhalation of bacilli was almost certainly the cause of infection. Despite the massive destruction of lung tissue during the earlier stages of the disease, treatment resulted in a striking improvement in the animal's condition. There was good resolution of the original tuberculous lesions, leaving extensive scar tissue and large foci of necrotic, calcified material. The isolation of M. bovis from lung and mediastinal lymph node cultures showed that the disease was not totally resolved, although the negative ELISA and lymphocyte transformation test results of the last blood sample suggested that the number of viable mycobacteria left inside the old lesions was too low to maintain immunoreactivity in the animal. The disappearance of reactivity could not be attributed to the immunosuppressive effect of isoniazid, as therapy of AO9 was stopped almost 4 mo prior to the last blood test. Treatment of other ungulates with streptomycin and isoniazid turned positive (skin) reactors into nonreactors, but the animals often converted back to being positive reactors after treatment was discontinued.

Although no histopathology was done, it was thought possible that the macroscopically visible liver degeneration had been due to hepatotoxic effects of isoniazid and rifampicin.

This case history shows that even in an animal severely infected by M. bovis, appropriate therapy can lead to a dramatic recovery. However, therapy should only be considered for valuable animals, because it is expensive, time-consuming, and may not eliminate the organism completely. It does open the possibility of retaining infected animals for artificial propagation programs, when the survival of the species or the genetic value of the individual warrants the risks.
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LITERATURE CITED


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