Tularemic Pericarditis

Report of Two Cases and Review of Literature

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Pericarditis is a rare complication of tularemia. A review of the literature reveals 28 cases of tularemia involving the pericardium. Eleven of these are referred to by Drobinskij in the Russian literature. Twenty-five of the cases were associated with pneumonia, pleurisy, or both of these complications. A report of pericarditis due to ulcero-glandular tularemia by Ljung in 1955, and one of the cases under discussion are the only instances of "isolated pericarditis" due to tularemia without pneumonia or pleurisy reported in the literature. Drobinskij refers to three similar cases in 1947 without further description.

Report of Cases

Case 1: A 37 year old white married salesman was seen on January 9, 1957, with the chief complaint of "severe crushing chest pain" of one to two hours duration. He was in excellent health until two weeks prior to admission when he went rabbit hunting. While dressing one of the rabbits, he noticed the liver was covered with "white spots" and he discarded the animal. Five days later, a small lesion developed on the dorsal aspect of the right hand. On the following day, he developed pain, swelling,

FIGURE 1: Note the small maculo-papular incrustcd lesion 1 x 1 cm. on the dorsal aspect of the right hand.

From the Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee.
and tenderness in the right axilla. These symptoms were associated with fever, malaise, headache, and generalized muscular aching. The next day, he consulted his physician and was told he had "rabbit fever," and was treated with chloramphenicol, penicillin and streptomycin. He remained ambulatory and felt fairly well until two days later.

FIGURE 2: Serial electrocardiograms taken between January 9, 1957 and February 28, 1957 reveal the characteristic T-wave changes found in acute pericarditis. There is slight ST-segment depression in Lead 2, AVF, V-4, and V-5 on January 29, 1957. A premature ventricular beat is present in Lead 3 on February 14, 1957. On February 28, 1957 the electrocardiogram returns to normal.

FIGURE 3: January 10, 1957. There is no cardiac enlargement. The lung fields are clear with the exception of a small calcified nodule in the right upper lobe measuring 1 cm. in diameter which is characteristic of a tuberculoma.
when he developed severe "crushing" substernal pain, associated with "shortness of breath." The pain lasted for one hour. On the following night the pain was more severe and lasted approximately two hours. In the morning because of severe, "crushing" substernal pain radiating to both arms, associated with dyspnea, shock, and cyanosis, the patient was admitted to St. Thomas hospital. After administration of 100 mg. of Demerol, the patient's condition improved and signs of shock disappeared.

Physical examination revealed a temperature of 97.6°F. Respiration 20 per minute and the blood pressure 100/70. There was a small maculo-papular incrusted lesion 1 x 1 cm. on the dorsal aspect of the right hand overlying the first metacarpal-phalangeal joint (Fig. 1). There was a tender, firm 1 x 2 cm. freely movable lymph node palpable in the right axilla. Chest was symmetrical with bilateral, equal expansion. Lung fields revealed no abnormal findings. Heart was not enlarged. There was a normal sinus rhythm with frequent premature ventricular contractions at a rate of approximately 70 per minute. Sounds were of poor quality and there was no friction rub. The remainder of the physical examination revealed no other abnormal findings.

Serial electrocardiograms taken between January 9, and February 28, 1957 revealed electrocardiographic findings of acute pericarditis (Fig. 2). Chest roentgenogram January 10 showed no cardiac enlargement. There was a calcified nodule in the right upper lobe measuring 1 cm. in diameter, which was characteristic of a tuberculoma, otherwise the lung fields were clear (Fig. 3).

Laboratory: White blood cell count was 6,500 with a normal differential. The corrected sedimentation rate was 35 mm. Hemoglobin was 15.9 grams and the VDRL test was negative. Liver function tests were within normal limits and the C-reactive protein was not increased. The serum glutamic oxalacetic transaminase was 80 units. Urinalysis was negative.

The agglutination test for tularemia was negative on January 9, 1957, positive in a titer of 1:160 on January 28, 1:320 on January 30, and negative on February 14.

Course in hospital: On January 9, the patient was started on 0.5 Gm. each of chloramphenicol and streptomycin every six hours. On the following day, a pericardial systolic friction rub was audible and remained audible for one day. After three days in the hospital, he had no substernal pain but occasionally experienced a "dull ache" over the precordium. Frequent premature atrial and ventricular contractions were present throughout the hospital course. Axillary lymphadenopathy disappeared in seven days, and the temperature, pulse and respiration remained normal. On January 19, the doses of chloramphenicol and streptomycin were reduced to 12 hour intervals. The lesion on the right hand disappeared in three weeks. He was discharged in excellent condition on January 26, 1957.

Case 2: A 59 year old highway maintenance worker was seen in the medical clinic at Vanderbilt University Hospital with the chief complaint of "infected finger and

8-16-49  10-11-49

FIGURE 4: Note the marked enlargement of the cardiac silhouette with a small amount of pleural effusion, prominent lung markings, and pneumonitis at the left base on August 16, 1949 compared to the normal cardiac silhouette and clear lung fields on October 11, 1949.
pneumonia.” Six weeks before admission he had “scratched” the fourth finger of the left hand on a nail. Two weeks later he developed fever, chills, weakness, with lymphangitis of the left arm and lymphadenitis in the left axilla. His local physician, treated him with sulfadiazine and penicillin without improvement. Weakness, anorexia, fever, and chills continued and he was given chlorotetracycline for two days, which made him feel better. Two weeks later he developed a hacking non-productive cough, and the chest roentgenogram showed “pneumonia.” Cough and weakness persisted, and the patient lost 28 pounds in weight. He became “short of breath” and developed “sharp pain” in the left upper chest region which was aggravated by coughing and deep breathing. There was no recollection of exposure to rodents, rabbits or other possible sources of infection.

On physical examination he appeared chronically ill with dyspnea and orthopnea. He was thin and apathetic with evidence of recent weight loss. Temperature 102°F, pulse 194, respirations 28 per minute, and the blood pressure 110/68. There was an indurated, crusty lesion with circumscribed erythema on the fourth finger of the left hand. There was a tender, firm lymph node 3 cm. in diameter in the left axilla. Lung fields revealed absent tactile fremitus at the left base anteriorly and posteriorly. There were diminished breath sounds with moist rales extending from the left base to the inferior margin of the scapula, and crepitant rales were audible at the right base. Heart was enlarged 2 cm. to the left of the mid-clavicular line and to right 2 cm. beyond the lateral sternal margin. Heart sounds were distant and of poor quality with a normal sinus rhythm. Over the base, there was a to and tfe friction rub. Radial pulses were paradoxical. No other physical abnormality was found.

Chest roentgenogram on August 16, 1949 demonstrated enlargement of the cardiac silhouette with a C-T ratio of 18 to 29 cm. There was a slight amount of fluid at the left base. Lung markings were prominent with pneumonitis present in the left base. A chest roentgenogram on October 11, revealed a marked decrease in the size of the heart. The C-T ratio was 11 to 28.5 cm., and the heart was long and linear. Lung fields were clear (Fig. 4). Serial electrocardiograms from August 11, showed changes characteristic of pericarditis (Fig. 5). Laboratory examination revealed normal urinalysis, white blood cell count 6,400 with normal differential, hemotocrit 34 mm., and sedimentation rate (corrected) 32 mm. The VDRL test was negative. Agglutinations for tularemia; August 10, 1:320; August 16, 1:20,480; and on August 24, 1:320. Venous pressure and circulation time were normal.

Course in hospital: The patient improved promptly with 0.5 Gm. streptomycin every 12 hours but because of continued fever the dose of streptomycin was increased by

**FIGURE 5**: Serial electrocardiograms taken between August 11, 1949 and August 24, 1949 reveal T-wave inversion in all leads characteristic of acute pericarditis.
<table>
<thead>
<tr>
<th>Case Number and Author</th>
<th>Age</th>
<th>Sex</th>
<th>External Lesion</th>
<th>Pneumonia</th>
<th>Pleural Effusion</th>
<th>Pericardial Rub</th>
<th>Other Signs of Pericarditis</th>
<th>Pericardial Tap</th>
<th>EKG Evidence of Pericarditis</th>
<th>Agglut.</th>
<th>Subsequent Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Simpson 1929</td>
<td>37</td>
<td>Male</td>
<td>Yes (?), Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Precordial pain, dyspnea, x-ray and pericardial tap</td>
<td>Yes</td>
<td>No</td>
<td>1:60</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>2. Pessin 1936</td>
<td>55</td>
<td>Female</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Weak, irregular heart sounds ascites, upper abdominal pain</td>
<td>No</td>
<td>No</td>
<td>1:320</td>
<td>Died 64th day—Postmortem, fibrinous pericarditis with effusion (1,650 cc.)</td>
</tr>
<tr>
<td>3. Stofay 1938</td>
<td>29</td>
<td>Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Chest pain, enlarged heart, distant heart sounds, tachycardia, dyspnea, x-ray</td>
<td>No</td>
<td>Yes</td>
<td>1:1,280</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>4. Foshay 1940</td>
<td>42</td>
<td>Male</td>
<td>None</td>
<td>Yes</td>
<td>(?), Yes</td>
<td>Yes</td>
<td>Precordial pain, dyspnea thready pulse, weak heart sounds, cyanosis</td>
<td>No</td>
<td>Yes</td>
<td>1:5,120</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>5. Stump and Quinn 1940</td>
<td>47</td>
<td>Female</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>Died 19th day, small area of fibrinous pericarditis, aortic stenosis. Myocardial Aschoff bodies, bilateral pneumonia with pleural effusion, focal necrosis of lungs, liver and spleen</td>
</tr>
<tr>
<td>6. Kavanaugh 1941</td>
<td>37</td>
<td>Male</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Dyspnea, cardiac enlargement, edema of legs</td>
<td>No</td>
<td>Yes</td>
<td>1:80</td>
<td>(?) Recovered</td>
</tr>
<tr>
<td>7. Jager and Ranameler 1943</td>
<td>27</td>
<td>Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Tachycardia</td>
<td>No</td>
<td>No</td>
<td>1:1,280</td>
<td>Died 13th day. Lobar pneumonia with cavitation of right middle lobe, left lobar pneumonia fibrinous pleural pericarditis, pulmonary edema</td>
</tr>
<tr>
<td>8. Jager and Ranameler 1943</td>
<td>69</td>
<td>Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>1:20</td>
<td>(?) Recovered, no follow-up</td>
</tr>
<tr>
<td>9. Jager and Ranameler 1943</td>
<td>Yes</td>
<td>Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Distended cervical veins, paradoxical pulse, orthopnea, dyspnea, cyanosis, ascites</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>Died 9th day. No postmortem examination</td>
</tr>
<tr>
<td>10. Jager and Ranameler 1943</td>
<td>Yes</td>
<td>Male</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Dyspnea, cardiac enlargement, distant heart sounds paradoxical pulse, tachycardia, ascites, edema, elevated venous pressure</td>
<td>Yes</td>
<td>Yes</td>
<td>1:1,280</td>
<td>Developed constrictive pericarditis with persistent cardiac embarrassment</td>
</tr>
<tr>
<td>Case Number and Author</td>
<td>Age Sex</td>
<td>External Lesion</td>
<td>Pneumonia</td>
<td>Pleural Effusion</td>
<td>Pericardial Effusion</td>
<td>Initial Rhythm</td>
<td>Other Signs of Pericarditis</td>
<td>Pericardial Tap</td>
<td>ERG Evidence of Pericarditis</td>
<td>Agent</td>
<td>Subsequent Course</td>
</tr>
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</tr>
<tr>
<td>11. Aagaard 1944</td>
<td>23 Male</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Tachycardia</td>
<td>No (?)</td>
<td>1:320</td>
<td>Recovered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Aagaard 1944</td>
<td>37 Male</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Edema, orthopnea, dyspnea</td>
<td>No Yes</td>
<td>1:2,560</td>
<td>Recovered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Morgan 1947</td>
<td>28 Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Dyspnea</td>
<td>No No</td>
<td>1:40,960</td>
<td>Complete recovery after treatment with streptomycin</td>
<td></td>
<td>Died 6th day, Postmortem-pneumonia, sepsis, fibrinous pericarditis, bilateral pleural effusion. Myocarditis, necrosis of liver, spleen, kidneys. Abscess of 3rd finger, right hand</td>
</tr>
<tr>
<td>14-24. (11 cases)</td>
<td>23 Male</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Severe substernal pain, tachycardia, low pulse pressure, dyspnea, x-ray, pericardial effusion, cyanosis, paradoxic pulse</td>
<td>No (?)</td>
<td>1:200</td>
<td>Complete recovery after treatment with streptomycin and pericardiectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. Meredith 1948</td>
<td>30 Male</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Weak heart sounds, dyspnea, edema, distended cervical veins, enlarged liver</td>
<td>Dry tap Yes</td>
<td>1:2,560</td>
<td>Complete recovery after treatment with streptomycin and pericardiectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26. Meredith 1948</td>
<td>13 Male</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
<td>Chest pain, substernal</td>
<td>No Yes</td>
<td>1:960</td>
<td>Recovery after treatment with streptomycin and chloramphenicol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27. Ljunng, et al. 1957</td>
<td>51 Male</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Diminished apical impulse</td>
<td>No Yes</td>
<td>1:1,280</td>
<td>Recovery after treatment with streptomycin and chloramphenicol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29. Author 1957</td>
<td>59 Male</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Subternal chest pain, Tachycardia, dyspnea, paradoxic pulse, cardiac enlargement</td>
<td>No Yes</td>
<td>1:20,480</td>
<td>Recovery after treatment with streptomycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30. Author 1957</td>
<td>37 Male</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
<td>Severe substernal chest pain, dyspnea, cyanosis</td>
<td>No Yes</td>
<td>1:320</td>
<td>Complete recovery after treatment with chloramphenicol and streptomycin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*7. Reported by Jager and Ransmeier, case from Cincinnati General Hospital.
*8. Reported by Jager and Ransmeier, case of Dr. Beers, Gallipolis, Ohio.
*9. Reported by Jager and Ransmeier, case of Dr. Swenson, Grand Rapids, Michigan.
giving 0.5 Gm. every 6 hours. It was noted that the friction rub lasted nine days. The
toxins became afebrile and asymptomatic on the 12th hospital day. On the 16th
hospital day, a temperature of 104.2°F. was considered to be a reaction to streptomycin
and the drug was discontinued. The temperature returned to normal and he was
discharged on August 26, in good condition.

Review of the Literature

A summary of the pulmonary and cardiovascular manifestations of pericarditis caused by tularemia is presented in Table I. In 1929, Simpson3 reported the first case of pericarditis due to tularemia. In
1943 Jager and Ransmier4 in an excellent review of this subject, reported the cardiovascular manifestations in ten cases of tularemic pericarditis. In 1947, in the Russian literature, Drobinskij1 describes one case of pericarditis due to tularemia and refers to 10 others he had seen without further description of these cases. In 1950, Meredith12 describes two cases of tularemic pericarditis, one of which developed chronic constrictive pericarditis. In 1955, Ljung2 describes one case of ulcer-glandular tularemia in which the only complication was pericarditis. In 1957, Marshall et al13 reports a well-documented case of tularemic pericarditis associated with pleuro-pulmonary lesions.

Discussion

It has been postulated that tularemic pericarditis develops by direct extension from adjacent pleural involvement or from areas of pneumonitis. While this is a likely explanation, the finding of cases without apparent pleurisy or pneumonitis suggests either direct infection of the pericardium from the original inoculation site, or the presence of inconspicuous intermediary pulmonary lesions. Whatever the pathogenesis, a diagnostic problem is presented by cases of pericarditis clinically unassociated with pulmonary disease, and on some occasions without a history of exposure to rabbits. The second case in this report is an example of the latter problem and a similar case is described in the report of Marshall and Zimmerman.13 Although pericarditis is a rare complication of tularemia the possibility of prompt, life-saving treatment emphasizes the importance of diagnosing these otherwise serious illnesses.

As emphasized by Morgan11 in 1947, the treatment of choice is streptomycin, but Ljung's case in 1955, apparently did not respond to this drug alone, although it did respond to chlortetracycline. Meredith12 felt that streptomycin was beneficial even when started as late as the fourth month of the disease. It has often been our practice to employ both streptomycin and a tetracycline derivative, or chloramphenicol, in patients with tularemia when they are severely ill, although proof that this is superior to one drug is not yet available.

SUMMARY

Two cases of pericarditis due to tularemia are reported. A total of 28 other cases of tularemic pericarditis were found in the world literature.

Tularemic pericarditis may occur as the only apparent complication of tularemia, a fact of importance in diagnosing certain cases of this serious illness. If treated with streptomycin, tetracycline derivatives or chloramphenicol, the prognosis is similar to benign sero-fibrinous pericarditis.
RESUMEN

Se relatan dos casos de pericarditis debidos a tularemia.

Se han encontrado en la literatura mundial un total de 28 casos más. La pericarditis tularémica puede acontecer como la única complicación aparente de esa enfermedad lo que es un hecho importante para el diagnóstico de ciertos casos de esta grave enfermedad. Si se trata con estreptomicina, derivados de tetraciclincla o cloramfenicol, el pronóstico es como el de la pericarditis serofibrinosa benigna.

RESUME

L’auteur rapporte deux cas de péricardite due à la tularémie. Il a trouvé un total de 28 autres observations de péricardite tularémique dans la littérature mondiale.

La péricardite tularémique peut réaliser l’unique complication apparente de la tularémie, fait d’importance dans le diagnostic de certains cas de cette affection grave. Si elle est traitée par la streptomycine, les dérivés de la tétracycline ou du chloramphénicol, le pronostic est analogue à celui de la péricardite séro-fibrineuse bénigne.

ZUSAMMENFASSUNG

Bericht über 2 Fälle von Pericarditis infolge Tularaemie. In der Weltliteratur fanden sich im ganezne 28 weitere Fälle von tularemischer Pericarditis.


REFERENCES

7 Foshay, L.: “Tularemia: A Summary of Certain Aspects of the Disease Including Methods for Early Diagnosis and the Results of Serum Treatment in 600 Patients,” Medicine, 19:1, 1940.