crease in the risk of intracardiac reoperation (bypass changes remain unexplained. The operative trauma was of reoperation for regrowth of a tumor not adequately artificial transvenous pacemaker would make the more logical one, especially when one considers an in-

The incidence of the regrowth of the left atrial myxoma has not been well established. The fact that only three other cases have been reported does not necessarily preclude the possibility of its recurrence in many other cases. Gerbode and colleagues and Bahl et al suggested resection of not only the tumor itself, but also the portion of the interatrial septum to which the tumor is attached. Obviously, the area of septal resection depends upon the extent of tumor attachment, and in doing this, one must consider the possibility of inducing AV block. Whether the reduction of the possibility for regrowth following septal resection outweighs its risk for complication (eg, AV block) remains to be established. However, the availability and ease of implantation of the artificial transvenous pacemaker would make the more radical approach seem feasible if one considers the risk of reoperation for regrowth of a tumor not adequately removed. Since the previously reported over-all mortality of 26 percent for the initial resection of atrial myxoma (both right and left) is not small, the more definite and radical approach to the treatment of this lesion seems a more logical one, especially when one considers an increase in the risk of intracardiac reoperation (bypass complications, bleeding problems, hematologic and pulmonary complications).

The sequential postoperative electrocardiographic changes remain unexplained. The operative trauma was limited to the atria and the appearance of complete heart block followed by bifascicular block implies a site of conduction block below the AV node.

From a pathologic point of view, an excellent review of a recurrent left atrial myxoma has just been published in the Archives of Pathology by Kelly and Bhagwat. They believe that the different ultrastructural features separate the primary from the regrowth of left atrial myxoma. While in the primary tumor, the absence of the collagen fibers and the presence of external amorphous lamina was clearly demonstrated; in contrast, the regrowth tumor showed a significant abundance of collagen fibers while the external lamina was absent.

ACKNOWLEDGMENT: The technical assistance of Mrs. Virginia R. Lacey in the preparation of this manuscript is acknowledged.

REFERENCES


4 Kelly M, Bhagwat AG: Ultrastructural features of a recurrent endothelial myxoma of the left atrium. Arch Path 93:219, 1972


Coccidioidin Skin Reactivity in Pulmonary Coccidioidomycosis*

James R. Want, M.D.** and Jay W. Smith, M.D.+ 

We examined the records of 27 patients who had confirmed pulmonary coccidioidomycosis to substantiate the number of patients with negative skin tests; it was also our purpose to closely examine those patients with negative skin tests to explain why they were immunologically different. Eleven of 27 patients, (40 percent) with pulmonary coccidioidomycosis were negative to coccidioidin at the time the diagnosis was originally established. Sixteen of the 27 patients were retested with coccidioidin and 14 (88 percent) developed positive skin reactions while only two (12 percent) remained negative. Most of the patients with negative skin tests at the time of original evaluation (75 percent) had positive skin tests on rechallenge. Since the patients with negative skin tests were clinically and immunologically similar to the patients with positive skin tests, we suspect that many of the original negative reactions would have been positive had the skin testing program been more vigorously pursued.

*From St. Joseph’s Hospital and Medical Center, Phoenix.
**Second Year Resident in Internal Medicine.
†Chief of Internal Medicine.
Reprint requests: Dr. Smith, 350 West Thomas Road, Phoenix 85013

CHEST, VOL. 63, NO. 1, JANUARY, 1973
The purpose of this study is to document the percentage of patients with histologically or bacteriologically proved coccidioidomycosis who have negative skin sensitivity to intradermal coccidioidin. The reason for the study was to see if there was validity to the concept held by some physicians that many patients with pulmonary coccidioidomycosis have negative skin tests.

METHODS

We examined the records of 91 patients who entered St. Joseph’s Hospital from 1961 to 1970 who had a diagnosis of coccidioidomycosis. Only those patients who had either histologically or bacteriologically proved disease and who had a skin test done in the hospital were included in the study. Twenty-seven patients met these criteria. Twenty-three of these patients had histologically proved coccidioidomycosis following lung resections and four had Coccidioides immitis grown from either sputum or pleural fluid. None of these patients had evidence of extrapulmonary coccidioidomycosis.

Those patients who could be located were asked to submit to follow-up testing in 1971. Eight of 11 patients who had a negative skin test were retested. The skin tests were done using 0.1 ml of Biocoxx* 1:100. They were applied intradermally in the forearm by one of the authors using disposable tuberculin syringes. The test was read at 48 hours by one of the authors. If this was negative, a 1:10 dilution of Biocoxx was injected intradermally in the other forearm and read by one of us at 48 hours.

RESULTS

Eleven of the 27 patients (40 percent) had a negative skin test and 16 (60 percent) had a positive skin test at the time pulmonary coccidioidomycosis was confirmed (Table 1).

There was no significant difference between the patients with positive and negative skin tests when compared for age, sex and race.

Ninety percent of patients with positive skin tests were symptomatic at the time of hospitalization compared to 50 percent of the patients with positive skin tests. Approximately 25 percent of each group received amphotericin; none was receiving steroids. Two patients in each group had diabetes mellitus. In both groups the disease by x-ray interpretation was usually cavitary or nodular. The number of patients with pulmonary infiltrates was essentially the same in both groups. There was no difference in the length of time that roentgenographic lesions were present prior to hospitalization.

Fifty-five percent of the patients with positive skin tests had complement fixing antibody in the sera, while 9 percent had precipitating antibody. In those patients with negative skin tests, one-third had complement fixing antibody and none had precipitating antibody. The average lymphocyte count was essentially the same in both groups of patients.

Eight of the 11 patients with negative results had skin tests applied again in 1971 and six (75 percent) had positive delayed hypersensitivity on rechallenge (Table 2). The average length of time between skin tests was five years. Four had a positive reaction to 1:100 coccidioidin and two had a positive reaction to 1:10 coccidioidin. Eight of the patients who had originally shown a delayed hypersensitivity skin response to coccidioidin were also rechallenged in 1971 and all of these patients remained sensitive to 1:100 coccidioidin. Of the total number of patients with confirmed coccidioidomycosis who were retested in 1971, 88 percent were positive and 12 percent negative (Table 1).

DISCUSSION

The known reasons for anergy to coccidioidin were not obviously present in the patients with negative skin tests at the time coccidioidomycosis was confirmed.

The coccidioidin skin test frequently becomes negative in disseminated disease. However, there was little evidence for dissemination except in two patients who had complement fixing antibodies with titers of 1:16 and 1:32. Some authorities consider a titer above 1:256 evidence for dissemination. Extrapulmonary coccidioidomycosis was not documented. Although a significant number of patients with negative skin tests were symptomatic, only three patients were sick enough to be treated with amphotericin B. Almost an equal percentage of patients with positive skin tests were treated with amphotericin B. Racial background predisposes to dissemination and the disease is most likely to disseminate in Negroes, Mexicans and Filipinos. However, only one patient with a negative skin test was Mexican; there were no Negroes or Filipinos. None of the patients was pregnant (pregnancy has also been implicated in dissemination).

There was no evidence of immunologic deficiency in these patients. During the follow-up time of from one to ten years, they were not subject to repeated pyogenic or opportunistic infections. There was no evidence of Hodgkin’s disease or sarcoidosis, diseases frequently

---

* Manufactured by BioProducts Research Laboratory, Tempe, Arizona.

Table 1—Coccidioidin Skin Test Results: Original Investigation and Rechallenge

<table>
<thead>
<tr>
<th>Time of Diagnosis</th>
<th>Original No. Patients</th>
<th>Original No. Patients</th>
<th>Rechallenge</th>
<th>Rechallenge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>with Negative Skin Tests</td>
<td>with Positive Skin Tests</td>
<td>1971</td>
<td>88%</td>
</tr>
<tr>
<td>Time of Diagnosis</td>
<td>11/27 (40%)</td>
<td>16/27 (60%)</td>
<td>2/16 (12%)</td>
<td>14/16 (88%)</td>
</tr>
</tbody>
</table>

Table 2—Coccidioidin Skin Test: Status on Rechallenge 1971

<table>
<thead>
<tr>
<th></th>
<th>Eight of 11</th>
<th>Eight of 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Originally</td>
<td>Originally</td>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Were</td>
</tr>
<tr>
<td>Rechallenged</td>
<td>Rechallenged</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>2/8 (25%)</td>
<td>0/8 (0%)</td>
</tr>
<tr>
<td>on Rechallenge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>6/8 (75%)</td>
<td>8/8 (100%)</td>
</tr>
<tr>
<td>on Rechallenge</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
associated with impaired delayed hypersensitivity. The average lymphocyte count in patients with negative skin tests and in patients with positive skin tests was almost identical. None of the patients was taking a steroid preparation at the time of skin testing.

Most of the patients with negative skin tests at the time of diagnosis were probably not anergic since all but two were positive on rechallenge. The reason for the apparent conversion from the original negative skin test to the positive skin sensitivity in 1971 in 75 percent of those rechallenged is not known. It should be noted, however, that 8 of 11 were tested originally with only a 1:100 dilution; in only 3 was a 1:10 cocciidioidin applied. Cripet points out that a pulmonary infection may not be detected unless a 1:10 or stronger skin test is applied.

It does not seem likely that the positive skin sensitivity on rechallenge was due to reinfection since 99 percent of patients who have a primary infection with Cocciidioides immitis develop immunity which is lifelong and complete.1 All of the patients who originally had positive skin tests maintained their positive reactivity when rechallenged.

Another possible explanation for conversion of negative skin test to positive is that the original skin test was done too early in the course of the disease. It is theoretically possible for the clinician to apply the skin test too soon for it may take as long as three weeks of active infection before the test becomes positive.4 This reasoning does not provide an adequate explanation in these patients for the pulmonary lesions were known to be present for an average of 2.5 months before the original skin test. Likewise, most of the pulmonary pathology was manifest on chest roentgenograms by discrete nodules or cavities, lesions which usually take longer than three weeks to develop.2

Although we do not know the exact nature of the antigen used for skin testing in the early 1960’s, it is unlikely that a bad lot of antigen could explain the original negative tests. Skin tests were applied almost every year during 1961-1970 and it is quite unlikely that defective antigen would be in commercial use for such a long time.

Of course another possibility is that the original skin test was applied incorrectly or was misread. It is known that the intradermal skin test cannot be valid if it is given subcutaneously. This can occur easily with carelessness, but may be reported as a properly applied test if the person administering the test is not properly motivated. The reading is also liable to error by the novice.5 Frequently, the erythema produced by the skin test is minimal and careful observation and palpation are required to appreciate the induration of a positive test.5 We have no way of checking on inadequate procedure since the original skin tests were performed by many different laboratory technicians during the ten year period.

In conclusion we found that 11 of 27 patients (40 percent) with pulmonary coccidioidomycosis were negative to cocciidioidin at the time the diagnosis was originally established. Sixteen of the original 27 patients were retested with cocciidioidin and 14 (88 percent) developed positive skin reactions while two (12 percent) remained negative. Most of the patients with negative skin tests at the time of the original evaluation (75 percent) had positive skin tests on rechallenge. Since the patients with negative skin tests were clinically and immunologically similar to the patients with positive skin tests, we suspect that many of the original negatives would have been positive had the skin testing program been more vigorously pursued with the higher concentration of cocciidioidin.

REFERENCES

1 Fiese MJ: Coccidioidomycosis. Springfield, Ill, Charles C Thomas, 1958, p 92
4 Cripet LH: Clinical Immunology and Allergy. New York, Grune and Stratton, 1969, p 729

Focal Mononucleosis Myocarditis Simulating Myocardial Infarction*

Richard Miller, M.D.; Cameron Ward, M.D.; Ezra Amsterdam, M.D.; Dean T. Mason, M.D., F.C.C.P.; and Robert Zelfs, M.D., F.C.C.P.

A 17-year-old boy with documented infectious mononucleosis presented with the clinical, electrocardiographic and enzymatic picture compatible with acute myocardial infarction. He was found to have completely normal findings at cardiac catheterization, including exercise study and coronary arteriography. The diagnosis of focal mononucleosis myocarditis was considered to be the most likely explanation for his unusual clinical course.

The incidence of cardiac involvement in infectious mononucleosis is not great; cardiac symptoms are present in 0.7 percent of patients and electrocardiographic abnormalities are noted in 6 percent.1 The spectrum of cardiac manifestations ascribed to infectious mononucleosis is quite varied and includes pericarditis, myocarditis, various arrhythmias, conduction disturbances, and nonspecific electrocardiographic changes involving the ST and T segments. We are not aware, however, of mononucleosis presenting as an acute myocardial infarction. Thus, the following case is that of a patient who presented with clinical symptoms and lab-

*From the Laboratory of Clinical Physiology, Section of Cardiovascular Medicine, Department of Medicine, University of California at Davis School of Medicine; the Sacramento Medical Center, Sacramento, and Woodland Memorial Hospital, Woodland, California. Reprint requests: Dr. Zelfs, University of California School of Medicine, Davis 95616

CHEST, VOL. 63, NO. 1, JANUARY, 1973