Evaluation of Streptozyme and Antistreptolysin O Tests in Streptococcal Pyodermal Nephritis

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Received for publication 19 March 1973

The evaluation of the streptozyme test in sera from 34 patients with streptococcal pyodermal nephritis was studied. Ninety-seven percent of the patients developed high titers of antistreptozyme antibodies on the first bleeding after hospitalization, in contrast to only 40% of patients who developed elevated antistreptolysin O titers. The high antistreptozyme titers declined during convalescence and reached normal levels in the sixth month after onset of the disease. The most significant fall in titers occurred between 1 and 2 months from the onset of disease. The streptozyme test may be particularly helpful as a rapid screening test for antibodies in streptococcal pyodermal nephritis.

The determination of antistreptolysin O (ASO) titers in human sera is most commonly performed as an aid in the diagnosis of streptococcal and poststreptococcal diseases (12). However, elevated serum titers occur in approximately 85% of patients with rheumatic fever and with nephritis after streptococcal upper respiratory infection, whereas only 50% of patients with pyodermal nephritis show such an elevation in titer (4, 10, 14). Studies on serological responses in pyodermal nephritis from Trinidad (11), Red Lake (1, 7), and Alabama (5) indicate that about 85% of the patients with this complication showed elevated titers of anti-deoxyribonuclease (DNase) B antibodies, which is considered the test of choice in the diagnosis of streptococcal pyodermal nephritis. The difference in the immune response to a variety of streptococcal exoproducts in rheumatic fever and pyodermal nephritis has recently been summarized and discussed (4, 13).

The streptozyme antibody test (antistreptozyme [ASTZ]) (Princeton Laboratories, Inc.) is designed to measure antibodies against five streptococcal extracellular products: streptolysin O (SO), DNase B, hyaluronidase nicotinamide adenine dinucleotide glycicydrolase, and streptokinase, in a single test (6, 8).

A good correlation between ASO and ASTZ titers in sera of rheumatic fever patients has been demonstrated (6). However, no such comparison has been made in sera from other poststreptococcal sequelae.

Since only 41% of sera from streptococcal pyodermal nephritis patients obtained in our laboratory during an epidemic of acute glomerulonephritis associated with type 55 group A streptococci (2, 10) showed elevated ASO titers, it was of interest to compare the streptozyme and ASO tests in this group of patients.

MATERIALS AND METHODS

Control group. Sera were collected from a total of 104 children, aged 3 to 13. They were chosen from the same socioeconomic environment and geographic regions where the glomerulonephritis epidemic was dominant and from which regions patients were admitted to the hospital. These children were age matched, as far as possible, to the patients. None had a clinical history of streptococcal disease, streptococcal infections of the throat, or pyodermia during the 2-month period preceding collection of the sera samples.

Patients. The bacteriological and clinical studies and the collection of sera from nephritic patients have been described previously (2, 10). Sera (41%) were collected from 81 patients (ages 3–13), on admission to the hospital and at monthly intervals thereafter. For serological evaluation the patients were divided into two groups. Group I was compiled of all the 81 patients on whom a comparison of ASTZ and ASO tests were done, and group II was comprised of 34 out of the 81 patients on whom serial studies were performed. The 47 patients were omitted because they had a recurrent group A streptococcal infection during the period of the study. This was established by serological and bacteriological tests.

Determination of the streptococcal antibodies.
Sera from each child were analyzed for ASO by methods described previously (9), and for the streptozyme test (ASTZ) they were analyzed by the instructions enclosed with the reagent (see also reference 8) (Wampole Laboratories, Div. of Denver Chemical Mfg Co., Stamford, Conn.).

RESULTS

Upper limits of normal values in control groups. The distribution of ASO and ASTZ titers in the control group is presented in Table 1. Although we were unable to completely age match the experimental and control group, the data are nevertheless of general value in showing the distribution of ASO and ASTZ levels in this group. For establishment of normal values, the arbitrary upper limit of normal for the control group was determined as previously described (14) by separation of the upper 20% from the lower 80%. By this definition, the upper limit of normal for the control group was 170 for ASO and 100 for ASTZ.

Comparison of the streptozyme and ASO tests in nephritic patients. The upper limits of normal, as determined by the controls, were used to divide our patients into those who showed normal antibody titers and those who showed elevated antibody titers. Table 2 compares ASO and ASTZ titers for a total of 416 sera taken from 83 nephritic patients upon admission and at monthly intervals thereafter. Of the 416 sera, 329 (79%) had an elevated ASTZ titer, whereas only 137 (33%) had an elevated ASO titer. Only 7 (5%) of the 137 sera with elevated ASO titers did not show an elevated ASTZ titer.

Table 1. ASTZ and ASO titers of the control group

| Titer | No. of sera | Percent | Titer | No. of sera | Percent |
|-------|-------------|---------|-------|-------------|---------|
| <100  | 50          | 48.1    | <120  | 58          | 55.7    |
| 100   | 36          | 34.6    | 170   | 27          | 26      |
| 150   | 10          | 9.6     | 240   | 9           | 8.7     |
| ≥200  | 8           | 7.7     | >340  | 10          | 9.6     |

Table 2. ASTZ and ASO titers in 416 sera obtained from 83 nephritic patients

| Titer | No. of sera | Percent | Titer | No. of sera | Percent |
|-------|-------------|---------|-------|-------------|---------|
| <100a | 87          | 21      | <170a | 279         | 67      |
| ≥150  | 329         | 79      | ≥240  | 137         | 33      |

*See text.

Serial ASTZ and ASO response. Serial studies were performed on sera from 34 patients. The geometric mean of antibody titers and percentage of sera with elevated titers by months from onset of disease was studied. Figure 1 shows that, although 97% of the patients developed an elevated ASTZ titer (150 or more) upon admission to hospital (first month) with a geometric mean of 278 (Fig. 2), only 40% showed elevation of the ASO titer (240 or more) with a geometric mean of only 132. The percentage of sera with elevated ASTZ and ASO titers decreased gradually, reaching 22 and 13%, respectively, 6 months after the onset of infection.

DISCUSSION

The data presented indicate that the streptozyme test, which was employed to evaluate
the antibody response in streptococcal pyodermal nephritis, detects a much higher incidence of elevated antistreptococcal antibodies as compared with the single ASO test. The reason for these marked differences is probably that at least five different antibodies to streptococcal extracellular products are simultaneously measured. Since no separate measurements of antibodies against DNase B, streptokinase, hyaluronidase, and nicotinamide adenine dinucleotide glycohydrolase (all claimed to be present in the streptozyme reagent) were done by us on these sera, we do not know at present which of these antigens contributed to the marked elevated ASTZ titers found. However, it is likely that, since 85% of the patients with pyodermal nephritis had elevated anti-DNase B antibodies (1, 4, 5, 7, 14) whereas only 40 to 50% of the patient had elevated ASO (4, 10, 14), the major antigen determined in the ASTZ test is probably DNase B. This makes the streptozyme test more sensitive than the ASO test alone. Since the most significant fall in ASTZ titers occurred between the first and second months from the onset of disease (the high ASTZ titers decline during convalescence and reach normal levels in the sixth month), it is indicated that this test is most significant during the acute phase of the disease.

The finding that only 5% of the nephritic sera were negative by the ASTZ test cannot be fully explained at present. The possibility that our ASTZ tests included false positives is feasible; however, since we have not tested other antibodies to antigens present in the streptozyme reagent, we are unable to provide any data on this problem. This point was discussed in more detail by Klein and Jones (8). These authors compared the ASTZ with three antibodies: ASO, anti-DNase B, and anti-hyaluronidase, but no clear decision could be made concerning the possibility of false positives, as the anticarotidimide adenine dinucleotide glycohydrolase and antistreptokinase determinations were not done.

Considering the sensitivity level of the streptozyme test and the fact that it detects multiple antibodies, the test seems to be particularly helpful as a rapid diagnostic screening test in pyodermal nephritis, which is characterized by low ASO titers.

Further studies on this test by using large number of patients from an outbreak of acute pharyngitis in a closed community are underway.

This study was supported by research grants from the Medical Research Fund of the Ministry of Health, Jerusalem, Israel, and no. 06-332-2 from the Center for Disease Control, Atlanta, Ga.

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