

Correlation of Australia Antigen With Posttransfusion Hepatitis

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Transfusion of blood containing Australia antigen was associated with development of hepatitis or an antibody response in 74% (31 of 42) recipients. However, hepatitis also occurs in recipients of antigen-negative donor blood. Further study is required to determine precisely how much hepatitis could be prevented by screening donor blood for Australia antigen. At present, it appears that about 25% of transfusion hepatitis could be prevented in this way, and we are optimistic that this figure can be revised upward.

THE AUSTRALIA OR hepatitis antigen is a factor found with high frequency in the serum of patients with viral hepatitis.¹⁻⁵ Current evidence suggests that it is an intimate part or product of one of the etiologic agents of viral hepatitis.⁶⁻⁹ This communication describes a prospective study of patients transfused with blood containing the Australia antigen carried out in an attempt to document a correlation of the antigen with posttransfusion hepatitis and to assess the potential value of testing for this factor as a means of detecting infectious blood donors. The findings indicate that a positive correlation does exist, and that transfusion of blood containing Australia antigen is hazardous. In addition, we find that some cases of posttransfusion hepatitis occur in recipients of antigen-negative donor blood. Further work is essential to determine whether the latter observation reflects a lack of sensitivity in the test system or the existence of other infectious agents. While the implication of these findings may be great, expectations for early, wide-

spread application of this test on a routine basis are premature. Thus, this interim report of an ongoing study is offered to provide perspective on the current status of the problem.

Materials and Methods

All patients and donors whose conditions were studied were from the Columbia-Presbyterian Medical Center in New York city. The specimens of donor blood used for cross-matching were obtained from the blood bank after they had become outdated (usually seven days). Thus, donor specimens were not tested until after the blood had been transfused. The Australia antigen was detected in the two-dimensional immunodiffusion system employed in this laboratory previously.³ The serum of a multiply-transfused hemophiliac was used as the standard Australia antigen antiserum throughout. This antiserum has been shown to have the same specificity as standard antisera used in the laboratories of Baruch S. Blumberg, MD, and Alfred M. Prince, MD. Most positive reactions were visible within 24 hours, but some required three to four days to appear. Complement-fixation reactions were not found suitable for routine use.

All recipients of antigen-positive donor blood were followed up prospectively. In addition, selected recipients of antigen-negative donor blood were followed up as a control group. All patients were kept under surveillance for a minimum of six months after transfusion. While in the hospital, patients were examined and blood specimens obtained for serum glutamic oxaloacetic transaminase (SGOT) determination and the Australia antigen test at least weekly. Following discharge the recipients were seen and blood samples obtained on a 10- to 14-day schedule, either at the medical center or by arrangement with their private physician. Occasionally specimens were not obtained for as long as a three-week interval. In most instances, SGOT determinations were done regardless of whether the patient was symptomatic. About one fourth of the patients were lost to study either because of death from their underlying disease or because of inadequate followup.

Results

Sixty recipients of blood containing Australia antigen have now been followed up a minimum of six months in an ongoing study. Of these 60 recipients, 18 were lost to the study either through early death or our inability to follow them up adequately. Of the 42 recipients who were successfully kept under observation (Table), 22 developed typical signs and symptoms of hepatitis. Most of these patients had marked elevations of bilirubin and SGOT (greater than 250 international units [IU]), but an SGOT level of greater than 100 IU on two occasions was considered significant. Nineteen patients were found to have Australia antigen in their serum while acutely ill, and 14 were sick enough to be hospitalized. The incubation periods of hepatitis in these 22 cases ranged from 4 to 17 weeks. In addition, three patients were observed in which the antigen

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appeared in the serum following the transfusion of antigen-positive blood and was accompanied by evidences of hepatic dysfunction. However, these three patients were known to have other serious disease with hepatic involvement, so that the liver abnormalities could not be clearly attributed to viral hepatitis. Thus, 60% (25 of 42) of recipients of blood containing Australia antigen developed hepatitis and antigenemia, or at least antigenemia.

Six of the recipients of antigen-positive blood were noted to develop antibody to Australia antigen from 2 to 20 weeks after transfusion. None of these individuals exhibited evidence of hepatitis.

During the same period in time that the conditions of the recipients of antigen-positive blood were studied, a control group of 126 recipients of antigen-negative donor blood was surveyed (Table). Eight cases of hepatitis were observed in this group, with incubation periods ranging from 5 to 12 weeks. Only one of these patients was found to have a positive test for Australia antigen while acutely ill. None of the recipients of antigen-negative blood developed antibody to Australia antigen after transfusion. It should be noted that the 126 patients in this control group are only a fraction of the 1,429 recipients of antigen-negative blood transfused during this period of time.

Comment

The observations described here indicate that a positive correlation does indeed exist between Australia antigen and posttransfusion hepatitis. As shown in the Table, 22 of the 42 recipients of antigen-positive blood developed clinical signs of hepatitis, most of them in association with Australia antigen. Three additional recipients developed antigenemia, although they could not be conclusively shown to have viral-induced liver damage rather than hepatic involvement by another dis-

Summary of 168 Patients Who Received Transfusions*					
Blood Infused	No. of Patients	Hepatitis	Antigen Only	Antibody	Well
Positive	42	22	3	6	11
		60%		14%	
Negative	126	8	118
		6%			

*Patients were followed up for a minimum of six months. Total recipients negative for Australia antigen = 1,429; estimate of hepatitis in all recipients negative for Australia antigen = $\frac{1,429}{126} \times 8 = 90$; total hepatitis in both groups: $25 + 90 = 115$.

ease. Thus, 60% (25 to 42) of the antigen-positive blood recipient group developed either hepatitis or antigenemia, or both. In addition, another 14% of this group developed antibody to Australia antigen following transfusion. In total, then, 74% of these recipients exhibited either hepatitis or antibody response following exposure to the Australia antigen. We believe these findings indicate that transfusion of donor blood containing Australia antigen is clearly hazardous.

It should be noted that further development will be required for application of this finding to routine screening of blood donors. As noted in the Table, hepatitis was seen in recipients of antigen-negative blood. Although the incidence (6%) appears much lower than in the antigen-positive recipient group, this comparison may be misleading. It should be noted that the 126 patients followed up in the control group represent only a small fraction of the 1,429 recipients transfused at this institution during the same period of time. It could be estimated that the total number of cases occurring in all negative recipients may have been in the range of 90 cases. If this is an accurate extrapolation, then the total cases of hepatitis in both groups would approximate 115, only 20% to 25% of them attributable to antigen-positive transfusions.

However, the 126 patients in the control group are not really a representative sample of the entire antigen-negative recipient population for several reasons. These patients were all in a cardiac surgery pro-

gram and were initially selected because of their better availability for follow-up. Unfortunately, this selection has biased the study. As cardiac surgery patients, they tend to be sicker than the average recipient, and they received an average of 8 units of blood as compared to an average of 3.2 units per patient in the positive recipient group. Furthermore, almost all of the blood used in the open-heart program is commercial blood, as opposed to the mixture of volunteer and commercial blood given to the average recipient. Finally, it should be mentioned that six of the eight cases of hepatitis in the antigen-negative recipient group occurred in a single two-month period, perhaps suggesting acquisition of the disease from some other source.

Thus, it is essential that a more representative group of patients be followed up in order to assess the true incidence of hepatitis in recipients of antigen-negative blood, and we currently have such a control group under study. It may well be that the incidence of hepatitis in the control group cited is falsely high, so that significantly more than 25% of posttransfusion hepatitis could be prevented by this test. However, this remains to be more precisely defined. In addition, it should be noted that seven of the eight cases of hepatitis in the control group had negative tests for the hepatitis antigen during the acute phase, indicating perhaps that some posttransfusion hepatitis is caused by a different agent or agents.

Finally, the present test system is not ideally suited for routine blood

bank use. The gel diffusion system is lacking both in sensitivity and in speed. An overnight incubation period is usually required to detect most positive reactions. In addition, an adequate supply of antiserum is not available for widespread application of this test at the present time. In our experience to date, complement-fixation reactions, while more sensitive than gel diffusion, have not proved suitable for rapid, large-scale screening purposes because of nonspecific anticomplementary effects. We expect, however, that these technical and supply

problems will be overcome in due time.

John Gorman, MD, assisted in making specimens of donor blood available.

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Severe Muscle Spasms After Visualization of a Subarachnoid Catheter

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Severe muscle spasms followed inadvertent subarachnoid administration of diatrizoate meglumine (Renografin), demonstrating the dangers of using this and similar compounds for visualizing a catheter which may lie in, or communicate with, the subarachnoid space. If radiopaque contrast must be used, as is usually necessary even with catheters sold as radiopaque, it would seem prudent to use an oil-base contrast medium rather than a water-soluble agent.

WE ATTEMPTED to learn more about an unusual response to an epidural anesthetic by visualizing the position of the epidural catheter roentgenographically.

For the radiologist this case emphasizes the different effect a water soluble contrast medium has in the epidural and in the subarachnoid

space. For the anesthesiologist this case emphasizes not only the importance of injecting the test dose of anesthetic through the epidural catheter but also the importance of using an epidural catheter marked at a specific distance from its tip.

Report of a Case

A 54-year-old woman was to undergo a vaginal hysterectomy for intraepithelial carcinoma of the cervix. Her medical history and the results of physical and laboratory examinations were within normal limits. Premedication consisted of hydroxyzine hydrochloride 75 mg intramuscularly, 60

minutes preoperatively.

The patient's blood pressure was 120/60 mm Hg; pulse rate was 70 beats per minute. She was turned to the left lateral position, and, following infiltration of the skin and subcutaneous tissues with a 2% solution of prilocaine, a 16-gauge Tuohy needle was introduced between the spinous processes of L-3 and L-4. The epidural space was identified by loss of resistance to the injection of air. A test dose of 2 cc of a 2.5% prilocaine solution was injected. With the needle bevel directed cephalad, the epidural catheter was threaded into the epidural space. After the epidural catheter was secured with tape, 6 cc of 2.5% solution of prilocaine was injected.

Within minutes, the patient reported numbness and weakness of her left leg and side. She was turned to the supine position and placed in a ten-degree Trendelenburg position, whereupon she reported that the numbness extended to her right leg.

The patient's blood pressure was 130/70 mm Hg; pulse rate was 60 beats per minute. Administration of oxygen with use of a mask was begun. Within minutes, she complained of epigastric pain, and her blood pressure dropped to 70 mm Hg, systolic; pulse rate fell to 40 beats per minute. Ephedrine, 25 mg given intravenously, brought the systolic pressure to 80 mm Hg. A subsequent dose brought the blood pressure to 135/80 mm Hg. The level of analgesia to pinprick extended to T-4, and the patient was able to take a deep breath on command. Her skin was pale, and she continued to complain of epigastric pain. Because of her irrita-

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