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Post-transfusion hepatitis: a problem in Northern Ireland?

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SUMMARY

A retrospective analysis of post-transfusion hepatitis reported to us from 1980 through 1984 revealed 16 patients. We believe that this apparently low incidence is due to lack of notification and make a case for direct notification to us of any suspected cases. Disqualification of implicated blood donors is of prime importance in prevention of transfusion-associated hepatitis.

INTRODUCTION

Reports from different parts of the world suggest a range of incidence of post-transfusion hepatitis from approximately 7% in the USA,[1] 3.4% in one Dutch study[2] to 2% in Sydney, Australia.[3] The only available information for the UK shows an incidence of 2.4% in patients undergoing cardiac surgery in Newcastle-upon-Tyne.[4] Hepatitis in these studies included clinical and sub-clinical episodes (indicated by abnormal liver function tests after blood transfusion).

The aetiology of jaundice in a patient who has previously received blood and/or blood products includes hepatitis B, Epstein-Barr virus and cytomegalovirus. Non-A, non-B hepatitis continues to be associated with blood transfusion, but there is little published evidence of the true incidence of this condition, its clinical importance or long-term consequences.[5, 6] We report on a retrospective analysis of post-transfusion hepatitis notified to us from 1980 through 1984. Prior to this period, notification was anecdotal and follow-up tests on blood donors were minimal.

METHODS

All blood used in the province is collected by the Northern Ireland Blood Transfusion Service from volunteers. Blood donors are routinely tested for hepatitis B surface antigen (HBsAg). Since 1982, the method used is a radio-immunoassay (RIA: Blood Products Laboratory): a sample of each unit of blood is tested within 24 hours of the donation and prior to issue to hospital blood banks. An aliquot of serum from each donation is stored as a reference sample at −20°C for 18-24 months. When an incident of post-transfusion hepatitis is notified, all the units of blood and blood products are traced to individual donors by the date and unique donation number. It is possible to perform additional tests on implicated donors using the relevant stored samples if the notification is within 18-24 months of transfusion.

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When post-transfusion hepatitis is recognised in a patient, the first step is to initiate laboratory tests for hepatitis A and B, cytomegalovirus and Epstein-Barr virus. These tests are performed by the Virus Reference Laboratory, Royal Victoria Hospital. No test is available at present for the detection of non-A, non-B infection which remains a diagnosis of exclusion.[7]

The next step is notification of the patient to the NI Blood Transfusion Service with date(s) of transfusion and donation numbers of all blood and blood products. The investigations and follow-up include:

a) identification of all volunteer blood donors implicated by the unique donation numbers;

b) the relevant stored (−20°C) donor serum is tested for hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface and core antigens (anti HBs, anti HBc), and for liver function tests;

c) recall of donor(s) for a fresh sample of blood to repeat the tests and ensure that implicated donors are excluded from blood donations until all investigations are completed.

RESULTS

Sixteen patients with post-transfusion hepatitis were reported from 1980 to 1984 (see Table). There was a sudden increase in the number of patients reported in 1984 which we attribute to a letter written by one of us (CB) in December 1983, to all haematologists in the province, stressing the importance of notification. Eleven of the 16 patients had no evidence of infection with hepatitis B. Four patients were HBsAg positive and one patient had anti HBc of IgM type indicating response to recent infection with hepatitis B virus. Results of subsequent tests for HBsAg on this patient were not available to us.

The Table shows the correlation between hepatitis B infection in donors and patients. Hepatitis B markers sought included HBsAg, anti-HBc and anti-HBs. There was no evidence of infection in any of 22 donors for three patients positive for HBsAg, indicating that hepatitis B infection in these three patients was not attributable to blood transfusion (1980.1, 1984.5, 1984.7). Two donors out of 20 were implicated in the transmission of hepatitis B to two corresponding patients. One (patient 1980.2) showed a very weak positive reaction when the test for HBsAg was repeated but this had been missed during the initial screening procedure. The other donor (patient 1983.2) was repeatedly HBsAg negative and therefore would not have been identified as infective on routine screening. Anti-HBc was the only marker in this donor and was only detected on further investigation following the report of post-transfusion hepatitis. It is of interest that one further donor out of 14 was anti-HBc positive but no evidence of hepatitis B infection was found in the corresponding patient (1983.3).

DISCUSSION

Sensitive methods are now available for the detection of 'healthy carriers' of hepatitis B virus. The radioimmunoassay currently used in the NI Blood Transfusion Service for screening donors is very sensitive and calibrated to detect very low concentrations of hepatitis B virus (HBsAg) particles. The national minimum requirement is two British Standard Units and we are currently able to detect the lower level of one British Standard Unit. The risk of hepatitis B transmission through blood transfusion has, therefore, been minimised in the

TABLE

Patients with post-transfusion hepatitis notified to the NI Blood Transfusion Service, 1980-1984

Year	*Patients*	*Hepatitis B markers in the patient*	*Number of donors implicated*	*Hepatitis B markers in donors*
1980	1	HBsAg	7	Nil
	2	anti-HBc	6	HBsAg in one donor detected by RIA only*
1981	1	Nil	2	Nil
	2	Nil	15	One donor anti-HBs
1982	1	Nil	3	Nil
1983	1	Nil	2	Nil
	2	HBsAg	14	Anti-HBc in one, but negative six months later.
	3	Nil	14	One donor repeatedly anti-HBc.
1984	**1	Nil	6	Nil
	2	Nil	13	Nil
	3	Nil	6	Nil
	4	Nil	2	Nil
	5	HBsAg	8	Nil
	6	Nil	5	Nil
	7	HBsAg	7	Nil
	8	Nil	26	No follow-up: all donation numbers not available.

HBsAg: hepatitis B surface antigen
Anti-HBc: antibody to hepatitis B core antigen
Anti-HBs: antibody to hepatitis B surface antigen
RIA: radioimmunoassay.
*Original testing by less sensitive method. **Follow-up: drug-induced.

past 5 years, but a few cases of post-transfusion hepatitis B will continue to occur due to very low levels of antigen not detectable by radioimmunoassay.[8] Other transmissible agents such as the non-A, non-B agent, cytomegalovirus and Epstein-Barr virus continue to be important in the aetiology of transfusion-associated hepatitis. There are no simple, reliable and cost-effective screening tests available for the detection of blood donors who are capable of transmitting these infections.

In this report, 11 of 16 patients developed post-transfusion hepatitis which was due to causes other than hepatitis B. If a diagnosis of non-A, non-B hepatitis is suspected it is important to identify the donors implicated, in order to prevent further transmission to other patients through future blood donations. In the absence of a screening test,[7] our present policy is empirical exclusion of any donor implicated in two instances of post-transfusion hepatitis. It is to be noted that, in one patient, the hepatitis was subsequently shown to be drug-induced. Non-transfusion-related causes must be considered early in the differential diagnosis.

One donor who was HBsAg negative but anti-HBc positive transmitted hepatitis B to one patient. This is a rare occurrence but is a known possibility.[8, 9, 10] The value and cost-effectiveness of screening every donation for anti-HBc has been debated.[11, 12, 13] In Northern Ireland, the incidence of chronic asymptomatic carriers of hepatitis B is very low: one in 1500 healthy new donors is HBsAg positive. The risk of hepatitis B transmission from donors who are only anti-HBc positive in our region is estimated to be negligible and does not justify the high cost that such screening would entail.

No hepatitis B markers were detected in one patient although a donor involved was repeatedly positive for anti-HBc. The post-transfusion hepatitis in this patient was attributable to non-A, non-B infection. We have been unable to establish a satisfactory duration of follow-up with regard to hepatitis B markers in this case, although there are other reports of non-A, non-B transmission from donors who are positive only for anti-HBc.[14] Blood products including platelet concentrates, fresh frozen plasma, cryoprecipitate and coagulation factor concentrates are known to transmit hepatitis but none of our present series of patients were exposed to these.

The reported incidence of post-transfusion hepatitis shows great variation, the lowest being 2%.[3] There is little doubt that the apparently negligible incidence in Northern Ireland during the years 1980-1983 must be due to lack of notification. It is still uncertain how many cases are missed, and even among a small population like that of Northern Ireland it is difficult to hazard a guess at the true incidence of the disease. Of the non-B infections, non-A, non-B hepatitis is a significant problem particularly in terms of chronic liver damage, despite the mildness of the initial illness. In the absence of tests capable of detecting an infective donor, we must rely on notification of transfusion-acquired infection and retrospective investigation of blood donors for eventual disqualification of implicated donors.

Lack of notification may be attributed to several factors. A significant proportion of non-A, non-B infection is sub-clinical and serum transaminase levels fluctuate independently of clinical illness.[15] Vague symptoms after surgery or anaesthetic may be ignored by the patient and doctor. The prolonged incubation time of hepatitis B and moderate incubation time of non-A, non-B infection sometimes make the correlation between transfusion and clinical illness difficult. Patients are discharged from hospital and the present system of liaison between general practitioners, hospital doctor and the NI Blood Transfusion Service is unsatisfactory. There is a good case for direct notification to the NI Blood Transfusion Service of any cases of suspected transfusion associated-infection.

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