Effect of screening for hepatitis C virus antibody and hepatitis B virus core antibody on incidence of post-transfusion hepatitis

JAPANESE RED CROSS NON-A, NON-B HEPATITIS RESEARCH GROUP

Since November 1989, Japanese Red Cross blood centres throughout the country have screened donors for hepatitis C virus (HCV) with an Ortho enzyme-linked immunosorbent assay for antibody to the C100-3 viral peptide. Simultaneously, the centres started to screen for units with high-titre (≥26) antibody to hepatitis B virus core antigen (HBcAb) in the absence of hepatitis B virus surface antigen and antibody. To test the effectiveness of this policy, the incidence of post-transfusion non-A, non-B hepatitis (PTNANBH) and post-transfusion hepatitis B (PTHB) after screening had been introduced (November, 1989, to December, 1990, inclusive) was compared with the incidence before screening (January, 1988, to October, 1989, inclusive). Incidence of PTNANBH in patients who had received 1–10 unit transfusions was 4.9% (58/1189) before screening vs 1.9% (15/784) afterwards. Incidence in those who had 11–20 unit transfusions was 16.3% (64/392) vs 3.3% (4/124). Incidence of PTHB was 0.25% (4/1597) before screening; no cases have been detected subsequently. These results show the effectiveness of the first-generation anti-HCV test and indicate the value of screening for high-titre HBcAb in addition to HBV surface antigen testing in HBV endemic areas.

Introduction

Despite screening donated blood for hepatitis B surface antigen (HBsAg) and for serum alanine aminotransferase (ALT) concentrations higher than 35 Karmen units, post-transfusion non-A, non-B hepatitis (PTNANBH) developed in 621 (18.1%) of 3437 transfused patients studied in Japan over the 11-year period 1976–1987.1 The frequency of post-transfusion hepatitis B was considerably reduced by these measures, but even so 11 cases (0.3%) were reported. Incidence of PTNANBH in patients who had received blood transfusions of 11 units or more, we therefore analysed the effect of the screening carried out since November, 1989, on PTNANBH: before HCVAb and HBcAb screening was introduced, recipients of 11–20 unit transfusions were more than three times as likely to contract PTNANBH as recipients of 1–10 units (16.3% vs 4.9%). To separate the effect of screening from changes in the proportion of recipients of blood transfusions was 163% (64/392) vs 33% (4/124). To screen for HCV we used the Ortho enzyme-linked immunosorbent assay for antibody to the C100-3 peptide of the virus (Ortho Diagnostics). HBcAb was determined by the capacity of the test sera at a 26 dilution to inhibit a limited amount of HBcAg (25 μl, 4 haemagglutination units/ml) in agglutinating erythrocytes fixed with glutaraldehyde and coated with anti-HBc. HBsAg was determined by passive haemagglutination. Standardised kits for testing HBsAg, HBcAb, and HBsAb were prepared by Japanese Red Cross blood centres.

Results

908 cases were followed up after screening began (November, 1989–December, 1990, inclusive). The results were compared with those of 1581 cases detected before HCVAb and HBcAb screening was initiated (January, 1988–October, 1989, inclusive). It was already known that the number of units of blood transfused was an important determinant of the incidence of PTNANBH: before HCVAb and HBcAb screening was introduced, recipients of 11–20 unit transfusions were more than three times as likely to contract PTNANBH as recipients of 1–10 units (16.3% vs 4.9%). To separate the effect of screening from changes in the proportion of transfusions of 11 units or more, we therefore analysed the effect of the screening carried out since November, 1989, according to these two groups. Among patients who

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HCV-related antigens. In Japan, are linked especially to post-transfusion HCV infection. The programme is also effective more complete protection from the risk of post-transfusion hepatitis B, including the fulminant type. Fortunately, the number of such donors tends to be small, so the loss of units would not threaten the blood supply. We recommend that blood banks in HBV endemic areas should add screening for high-titre HBcAb to their existing HBsAg screening method.

With respect to HBcAb screening, Hoofnagle et al. proposed that such screening can identify blood units infectious for HBV, HBCAb screening was adopted as a surrogate test for preventing PTNANBH before the HBcAb screening became available in Australia and the USA. Although our aim in starting high-titre HBcAb screening was to decrease the incidence of post-transfusion hepatitis B, this strategy may also have contributed to the decrease in PTNANBH.

The reduction in the frequency of PTNANBH shows the usefulness of our screening policy; the programme is also important for the prevention of hepatocellular carcinoma, cirrhosis, and chronic hepatitis. These conditions are closely linked to PTNANBH, and, in HCV-endemic areas such as Japan, are linked especially to post-transfusion HCV infection. In the hope of providing more complete protection against post-transfusion hepatitis C, we are now investigating more sensitive screening tests with other HCV-related antigens.

With respect to HBcAb screening, Hoofnagle et al. have proposed that such screening can identify blood units infectious for HBV with undetectable levels of HBsAg. However, this policy is difficult to implement in most Asian countries since HBV infection is endemic and a large proportion of the population is HBcAb-positive. Since HBsAg negative/high-titre HBcAb units that are positive for HBV DNA by polymerase chain reaction were also related to fulminant cases of PTBH, exclusion of units with high-titre HBcAb as the only marker of HBV infection may reflect more complete protection from the risk of post-transfusion hepatitis B, including the fulminant type. Fortunately, the number of such donors tends to be small, so the loss of units would not threaten the blood supply. We recommend that blood banks in HBV endemic areas should add screening for high-titre HBcAb to their existing HBsAg screening method.

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REFERENCES


SHORT REPORTS

Production of parathyroid-hormone-related protein by cholesteatoma cells in culture

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Specimens of cholesteatoma were removed at surgery from five patients who had evidence of bone resorption. Parathyroid-hormone-related protein (PTHrP) was detected, by radioimmunoassay, in conditioned media from keratinocyte cultures derived from all five samples. Concentrations of PTHrP in conditioned media from secondary cultures were higher for the cholesteatoma cells than for normal keratinocytes from controls matched for age and sex. Thus, production of PTHrP by cholesteatoma may be a contributory factor in the bone destruction commonly associated with this disorder.


Cholesteatoma is characterised by the presence of a keratinising epithelium in the middle ear. It is thought to be derived from ingrowth of the migratory keratinocytes of the epidermis covering the tympanic membrane and deep external ear canal. Although the pathogenesis is not fully understood, the disorder is commonly associated with severe localised bone loss, the epithelium being separated from bone by a layer of inflammatory granulation tissue. The factors causing the bone loss remain unknown. Few studies have examined the possibility that the cholesteatoma produces factors which promote bone resorption. Instead, research has concentrated on theories of pressure necrosis and cellular/biochemical reactions associated with the inflammatory tissue.