The Prevalence of Hepatitis B Surface Antigen and Anti-HCV Antibody in Paediatric Oncology Patients in Hospital Universiti Sains Malaysia

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Summary
This study examined the prevalence of hepatitis B and C markers in 55 paediatric oncology patients who had completed treatment at the Hospital Universiti Sains Malaysia in Kota Baru. All these children had received blood products and had been treated between 1985 - 1996.

Forty seven per cent of patients were positive for hepatitis B or C. Twenty nine per cent were positive for hepatitis C and twenty two per cent were HBsAg positive. Two children were positive for both and none were HIV positive. Four children had an elevated ALT level and one child had jaundice and hepatomegaly. Some children were marker-positive despite immunization and screening of blood.

Key Words: Hepatitis B, Hepatitis C, Transfusion, Paediatric cancer

Introduction
Transfusion acquired hepatitis is a recognised hazard for paediatric cancer patients because they frequently receive blood product support during myelosuppressive therapy¹. Both hepatitis B and C are strongly associated with an increased risk of cirrhosis and hepatocellular carcinoma. It is estimated that by the year 2000, 1 in 1000 adults will be a childhood cancer survivor². The long term consequences of our management of these patients is thus of great importance.

We conducted a study to determine the prevalence of hepatitis B and C markers in paediatric oncology patients who had completed treatment.

Methods
This was a retrospective study of consecutive paediatric oncology patients who had completed chemotherapy and who were attending Hospital Universiti Sains Malaysia in Kota Baru. The records for each patient were reviewed to determine the year of treatment, clinical course and the number and nature of blood products given.

Blood samples were tested for anti-hepatitis C virus (HCV) antibody using a second generation Elisa kit (Abbott Labs). Hepatitis B surface antigen (HBsAg) was tested using Auszyme monoclonal (Abbott Labs.) and antibody to human immunodeficiency virus (HIV-1) using Abbott HIV-1 / HIV-2 (Third generation).

Serum alanine aminotransferase (ALT) levels were also determined. The ALT was considered elevated if it was more than twice the upper limit of normal (>90 IU/l).

Children who were positive for anti-HCV antibody had a confirmatory test using a HCV EIA supplementary assay (Abbott Labs.) one month later. Children who were HBsAg positive were tested again 6 months later, and HBeAg was also tested.
Results
Fifty five children were identified, ranging in age from 1.5 to 16 years. These included 32 cases of leukaemia and 23 solid tumours. The solid tumours consisted of lymphoma (9), Wilms tumour (4), neuroblastoma (3), retinoblastoma (2), germ cell tumour (2) and sarcoma (3). The years of treatment were from 1985 - 1996. Eight children were treated prior to 1989 and 33 children prior to 1994. The interval between completing chemotherapy and testing ranged from 1 month to 10 years.

All children had received blood products, most commonly packed red cells and platelets. Leukaemic patients received an average of 5 units of packed cells and 10 units of platelets while the solid tumour group received 3 and 4 units respectively.

At the end of treatment, 26 of 55 (47%) children were positive for either hepatitis B or C. Sixteen (50%) were leukaemic patients and ten (43%) had solid tumours. The tumours were lymphoma (6), neuroblastoma (2) and sarcomas (2).

Two patients were positive for both hepatitis B and C - 1 from the leukaemia and 1 from the solid tumour group. All the children tested negative for HIV.

Hepatitis C:
Sixteen of 55 patients (29%) were anti-HCV antibody positive. Of these, 12 (38%) were from the leukaemic group and 4 (17%) from the solid tumour group. Two children had elevated ALT levels. Twelve patients had been treated before screening blood for hepatitis C was introduced in 1994. The remaining four patients acquired antibody despite screening. They were anti-HCV antibody negative prior to starting chemotherapy.

Hepatitis B:
Twelve of 55 patients (22%) were HBsAg positive and these included seven (30%) from the solid tumour group and five (16%) from the leukaemic group. Out of 8 children tested for HBeAg, 6 were positive. Three children had raised ALT levels.

Seven of the 12 were treated prior to 1989, when screening of blood for Hepatitis B and immunization was introduced. The five remaining children acquired hepatitis B despite a history of immunization. All five were HBsAg negative prior to starting treatment, thus making perinatal HBV transmission unlikely.

Clinical Course:
Only one child had an acute illness with jaundice, hepatomegaly and elevated liver enzymes. She was anti-HCV positive but subsequently died of her underlying leukaemia.

The leukaemic child who was positive for both hepatitis B and C did not have an acute seroconversion illness. However, the child with a solid tumour who was also doubly infected did have an acute rise in ALT to 1003 IU/L. The ALT has since returned to normal.

Discussion
These results are of concern to us as a high proportion of our childhood cancer survivors acquired hepatitis markers. Our figure of 29% hepatitis C is comparable with that found in leukaemic children in Italy3 (24%) although it is much higher than those with malignancy in the United Kingdom4 (1%). In Saudi Arabia, 11% of oncology patients were HCV positive and only 6% HBsAg positive5. Again, our values for HBsAg are higher.

The most likely route of infection is via blood transfusions as all these children were marker negative at the beginning of their treatment. In this hospital, all donated blood is screened for hepatitis viruses using the test-kits and guidelines as recommended by the Ministry Of Health. Children with leukaemia required more blood product support than children with solid tumours. This may explain why 50% of our leukaemics were marker positive.

Hepatitis C virus is the major cause of post-transfusion hepatitis and this is followed by chronic infection in 70-90% of patients. The incubation period after blood transfusion is usually 7-8 weeks but it can range from 2-26 weeks6. Since the acute infection is subclinical in the majority of cases7, it is not surprising that only
one of our patients had jaundice. The serum transaminases can be normal or may fluctuate widely.

At present, there is no vaccine against hepatitis C. Screening blood donors for anti-HCV antibody reduces but does not eliminate the risk of transmission as evidenced by the two children who were antibody positive despite screening. The best way to confirm infection is to test for HCV ribonucleic acid by polymerase chain reaction, and we are currently in the process of doing this.

Chronic hepatitis B virus infection in children is associated with a 25% lifetime risk of cirrhosis or hepatocellular carcinoma. All the children who were HBsAg positive remained so when tested 6 months later. Hepatitis B immunization of the newborn was introduced in Malaysia in 1989. However, it is well recognised that 5-10% will not develop a protective antibody response. This could explain why some children became HBsAg positive despite being immunised. Alternatively, immunosuppression due to underlying malignancy could have compromised any previously acquired immunity.

Strategies for those who are antibody negative include vaccination. Studies in Turkey suggest that there is impaired response to vaccination with a seroconversion rate of only 41% after 3 doses of vaccine. Another problem with vaccinating children with cancer, is timing. Often these children will already have received blood products before a complete course of vaccine can be given.

Elevated ALT levels may be due to many causes in a child who has had cancer. The underlying disease, drug induced liver damage, viruses other than the hepatitis viruses (eg:CMV) may all cause an increase in ALT. Chronic hepatitis is usually defined by a persistent elevation of serum transaminase levels for more than six months. A liver biopsy would then be indicated - none of our patients have had this yet.

Malone W and Novak R reported that in a series of 31 children with leukaemia and hepatitis, 18 patients developed chronic hepatitis and five died of liver disease. Current recommendations for monitoring disease progression include serum alpha-feto protein levels every 6-12 months and ultrasound of the liver yearly. Interferon alpha is now being used to treat paediatric oncology patients with chronic hepatitis but results are preliminary and the optimal dose and duration of treatment has not been worked out.

Conclusion
In conclusion, we have found that nearly half of the fifty-five paediatric oncology survivors treated between 1985-1996 in Kelantan have acquired a serum marker for hepatitis B or C after transfusion of blood or blood products.

However, this group of patients does include children treated in the 1980’s, prior to the introduction of screening procedures and immunization. Hopefully, future cohorts of children will have lower prevalence rates.

Acknowledgements
We would like to thank Mr. Lau Kwok Leong, Scientific Officer for performing the serological tests.


7. Alter HJ. To C or not to C: these are the questions. Blood 1995;85: 1681-95.


