Correspondence

Chronic hepatitis C in long term survivors of haematological malignancy treated at a single centre

In their review of 42 long term survivors of haematological malignancy Neilson et al found two patients with hepatitis C virus (HCV) and the remaining eight patients with raised aspartate aminotransferase (AST) activity only two were explained by either hepatitis B virus infection or chronic graft versus host disease (GVHD), leaving six patients with unexplained liver dysfunction.

We are interested in the cause of continuing abnormal liver function in these patients in the light of our own experience of following long term survivors of haematological malignancy.

A review of our patients revealed that 21 were in complete remission more than three years after treatment. Two of these patients were HCV positive. They were diagnosed in 1986 and 1990 and received 41 and 28 units of blood, respectively. Five patients had raised AST activities, including both HCV positive patients. All five patients had serum ferritin concentrations (normal range 20–300 ng/ml) above the normal limit (median 863 ng/ml; range 395–4860 ng/ml). Three patients had hepatic siderosis confirmed on liver biopsy.

Murphy et al reviewed survivors of allogeneic and autologous marrow transplant alive one year after transplantation and found that 38 (43%) of 88 had raised transferrase activities not explained by either viral hepatitis or GVHD; 77% had a raised serum ferritin concentration consistent with iron overload and in 15/17 patients liver function improved after venesection.

Following treatment for haematological malignancy, transfusional iron overload is an important cause of increased transferrase activity and should be considered when viral hepatitis and GVHD have been excluded. The long term outcome of untreated hepatic iron overload in this group of patients is uncertain but return of normal liver function after venesection suggests that this treatment may be beneficial. Maintenance of serum ferritin concentrations below 2000 ng/l has been shown to prevent complications in patients with iron overload.1 The role of venesection in patients with evidence of hepatic iron overload and normal liver function remains unclear.

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Baysian Belief Network in histopathology

I read with interest the recent article by Montironi et al on the Bayesian Belief Network.1 It is an important work because it gives general pathologists an overview of how subjective histological features in a grading system can be analysed mathematically. It is particularly in areas like us a very good proposition.2

In spite of its apparent objectivity and precision, the Bayesian Belief Network depends very much on the conditional probability matrix (CPM) and the relative likelihood vector; the former is predetermined by experts and the latter by the observer. In the paper by Montironi et al the CPM construction was based on the authors’ experience. It is conceivable that different experts may have different CPMs and therefore different experts may arrive at totally different results.

Another source of interobserver inconsistency is the establishment of the relative likelihood vector, which carries with it an inherent element of subjectivity. The idea of using video images stored on computer to minimise this inherent subjectivity is a very valid and thoughtful suggestion. It is theoretically possible to have a perfect match if the number of video images is sufficiently large.

As shown by boxes 1 and 2, Montironi et al suggest that the final probability matrix was determined by multiplying the three internal lambdas (from tubular formation, mitosis and nuclear pleomorphism). In order to justify multiplication as the best mathematical manipulation, it has to be assumed that the three parameters are independent variables. Recent studies,1 however, have shown that nuclear grade alone correlates with histological grade, suggesting that such an assumption may not be entirely correct. Therefore, I wonder whether it would be more reliable and accurate if the three internal lambdas are added together to get the final belief probability matrix. One may also take into consideration the relative importance of each parameter by first multiplying the individual internal lambdas by a scalar, followed by addition of the subsequent scaled internal lambdas. For example, if it is considered that tubular formation, mitosis and nuclear pleomorphism have a relative importance of 1:2:3 in the assessment of overall histological grade, the internal lambda for mitosis is multiplied by 2 and that for nuclear pleomorphism by 3 and then added to the internal lambda for tubular formation to give the final belief probability matrix.