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) infection. In 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 reviewing survivors of allogeneic and autologous bone marrow transplant alive one year after transplantation and found that 38 (43%) of 88 had raised transarease activity 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 transarease 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.

The role of venesection in patients with evidence of hepatic iron overload and normal liver function remains unclear.

Dr Neilson and Harrison comment:

‘We read Dr Butler’s letter concerning the aetiology of the deranged liver function in our patients with great interest. We agree that iron overload may well be the cause of abnormal liver function in at least some of our patients and we have investigated this further. We have looked at both serum ferritin concentrations and non-transferin bound iron in 38 of our patients, including the six with no obvious cause for liver dysfunction. Our initial results have been published in abstract form’ and the full paper is published in this issue (p853). ‘We feel that it is worth emphasising that serum ferritin alone may not be a reliable indicator that iron overload is the cause of liver dysfunction. Hepatic damage itself leads to raised serum ferritin and non-transferin bound iron, will be assessed. Additional studies looking at putative markers for the haemochromatosis gene will be performed. We feel that this is an important area of research and we would encourage others to respond favourably to requests for information and samples for the iron overload study.’


Bayesian 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 interesting that when applied to nuclear probability matrix (normalised belief) can be reached at the conclusion of the mathematic analysis.

In spite of its apparent objectivity and preciseness, 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 CPM’s and therefore different experts may arrive at totally different normative data even though they may agree on the same relative likelihood vector. With international consensus meetings, it may be feasible to standardise the CPM. However, it may be still better if the CPM is capable of renewing itself based on additional information from new cases.

Another source of interobserver inconsistence 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 valuable 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 suggested that the final nuclear 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, 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 this 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 to 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.

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Standardisation of histopathology reports

I read with interest the paper concerning histopathology reports on primary cutaneous malignant melanoma.1 It is surprising that even six years ago in approximately one in eight cases of malignant melanoma there was no comment on either tumour thickness or on completeness of excision of the tumour in the histopathology report. This is a good argument in favour of standardisation of reports particularly with respect to certain malignant tumours.

In the past pathologists have been reluctant to use standardised reports according to a predetermined protocol. However, the need for reports of this type is rapidly becoming more prominent.

Firstly, and most importantly, failure to mention important prognostic factors in a report on a particular type of tumour could be misleading and negligent in the court of law. This is especially so in light of the fact that a standard textbook now contains prototype standardised reports for most important malignant tumours.2 Secondly, pathologists should provide as much information in their

References


Book reviews


The new eighth edition of Ackerman's Surgical Pathology weighs in at a hefty 18 lb 5 oz compared with the mere 14 lb 1 oz of the now seven year old predecessor. The extra weight has not gone into flab. Much of the text has been expanded and there are many additional high quality illustrations, mainly in colour. The familiar strengths of the still (amazingly) largely single author work in- clude a unity of style, with much of the narrative text with a wealth of relevant clinical and epidemiologi- cal information. Sections on normal anatomy and histology have been greatly expanded and there is much more information on immunohistochemistry, cytogentic and molecular pathology. This must now be the first place to turn to for concise information on the immunohistochemistry of tumours in everyday practice. There is much helpful detail on prognostic factors in tumours. It is difficult and perhaps confusing to read with the new edition. There are some occasional quirks of balance: only one short paragraph on glandular neoplasia in situ of the endocervix with many lesser entities treated in much more detail, the first word on prostatic carcinoma usually succeeds in being both concise and comprehensive. It is an American book and the American nomenclature is used in— for example, germ cell tumours of the testis, although here only the planum classifica- tions are outlined. Although the layout of the two volumes is very similar to that of the pre- vious edition and some of the text is unchanged, this is a substantially better book and a must for all Pathology Departments. It is a false economy to stick to the old edition. My review copy lies solidly on my study desk at home. I consult it so often that I am loathe to move it from there.

RACHEL OOMMAN


This book is a collection of papers from a conference on the application of electron spin resonance (ESR) spectroscopy to the detection of biodearials (active oxygen radicals and transition metal ions), which was held in Tokyo in 1994. Following the introduction, there is a useful overview of the chemistry of oxygen radicals and three chapters which outline the physics and technological basis of ESR. There follows a section which describes the potential of ESR imaging and later chaps- ters consider its application to the imaging of the rat brain. The technique of spin trapping the capture of radicals by stable molecules for future analysis is discussed at length. Two chapters outline the application of ESR to the study of biradical metabolites in vivo and two are devoted to the application of probing active site structures of metalloproteins. The penultimate section considers antioxidants and foods, one chapter being devoted to vita- min E and its interactions in biological systems, while another describes research on antioxidant vitamin activities in micelles and liposomes. The theme of in vivo measure- ments is returned to in the concluding chap- ters, this section including an interesting review of the application of the technology to the investigation of drug delivery. The book is not primarily concerned with the biomedical effects of free radicals. It describes the technol- ogy of ESR in great detail and its application to the measurement of biradicals. As such, it will be of interest to those who wish to learn more about the capabilities of this technique.

M F LAKER


Popular novels have perpetuated the myth to the effect that the estimation of time of death is an exact science. It would certainly make our job a lot easier if it was! Unfortunately, this is far from the case, as some of us find from time to time to our embarrassed chagrin. One well-known pathologist was so disillusioned with the inaccuracy of time of death estimation, that when asked his opinion, he enquired as to the time when the deceased was last seen alive and when the body was discovered and took the midpoint between the two! Despite all the short comings of time of death estimation, it may well be an important issue in a criminal investigation. It is therefore incumbent on the pathologist to give some reasoned guidance, based on scientific principles, and not on the light of his/her experience. Bernard Knight's book is therefore long overdue. Many papers have been published on the subject, testimony to the difficulty of the problem, but it is the first time in the English language literature that the collective knowl- edge on the subject has been brought together in one text. The contributors are all experts in different aspects of the area and have pooled their research findings and wide experience to assist the pathologist. It is both a scholarly, and at the same time, a practical approach to a difficult subject. The various