Correspondence

Preparotomy diagnosis of extrahepatic biliary atresia

Sir,

We were interested in the conclusion of Manolaki and his colleagues on the diagnostic value of gammaglutamyl transpeptidase (GGT) which was in contrast to other reports on this subject. We suggest that the analysis of the data has both methodological and statistical flaws.

In the report of Manolaki et al, the GGT concentrations in both groups were obviously not normally distributed as there was a positive skewing (mean (SD), extrahepatic biliary atresia (EHBA), 975 (518-1) IU/l; intrahepatic disease (IHD), 454 (458) IU/l) and hence the application of Student’s t test was inappropriate. Either the data should have been transformed or a non-parametric statistical method should have been used; otherwise the ‘normal’ range of GGT concentrations for either group could not have been defined confidently.

From a statistical point of view it is more reasonable to take the mean of two medians as a cut off value for the differentiation of EHBA from IHD. Experience from our study of 21 cases of EHBA (median, 1140 IU/l; mean (SD), 1112 (607) IU/l) and 20 cases of IHD (median, 239 IU/l; mean (SD), 275 (195) IU/l) showed that by using the mean (690 IU/l) of the medians of these two groups, the sensitivity and specificity of GGT were 78-9% and 95-2% respectively. This compares favourably with the accuracy of the more invasive procedure of liver biopsy.

We found that the enzyme concentrations at presentation were appreciably lower than the subsequent readings in the EHBA group, and therefore the highest reading available should be taken for statistical analysis. There was a correlation between the enzyme value and the duration of disease in the EHBA group of patients (P=0.05, rank correlation test) and this feature may be utilised for differentiation. Manolaki et al analysed the fractional change in enzyme activity. When there is a low initial and a small subsequent change in GGT activity, its fractional change may be grossly exaggerated and misleading. In their report the time period within which the change in GGT activity was measured was not clear. The absolute rate of rise of GGT should be analysed instead of the fractional change. In our series serial measurement in 9 patients with EHBA exhibited a rapid rise in GGT activity (median=17-1 IU/l/day, range 9-4-246 IU/l/day) but the rate of rise in 11 of 12 patients with IHD was significantly lower (median=1-5 IU/l/day, range −7 to 15-9 IU/l/day, P=0.0021). We therefore suggest that the rate of rise is more diagnostic than a single measurement of the GGT concentration. Repeated measurements during the first two weeks after presentation, which is within the normal duration of diagnostic ‘workup’, could serve as a preparative, non-invasive screening test.

We concur with the authors that the aspartate aminotransferase (AST) titres fluctuated widely and no consistent pattern was detected in either group. The GGT/AST ratio is detrimental therefore to the differential diagnosis unless the AST titres of the IHD group are significantly higher than those of the EHBA group.

S P Lau and K P Fung
Paediatric Department, Queen Mary Hospital, University of Hong Kong, Hong Kong

References


Drs Mowat and Manolaki comment:

Since submitting our paper our experience with serum gammaglutamyl transpeptidase (GGT) values in extrahepatic biliary atresia (EHBA) and intrahepatic diseases causing conjugated hyperbilirubinaemia in infancy (IHD) has emphasised the total unreliability of single GGT value in distinguishing these conditions in the individual patient. Three patients aged less than 16 weeks with surgically and pathologically confirmed EHBA have been seen with GGT values lower than the 162 IU/l which was the lowest value found in the patients studied in paper. One had a GGT concentration in the normal range of 42 IU/l. There is no doubt that the mean concentration of GGT in EHBA is higher than in IHD. We have no wish to argue the relative merits of the statistical methods which may be used to show this. The scatter of GGT values in the patients in our study is very similar to that published for the GGT/aspartate aminotransferase ratio in the Figure in our paper. Irrespective of what cut off value of GGT we derive from statistical methods, we would be depriving some patients with EHBA from the possible benefits of surgery or doing an unacceptably high level of unnecessary laparotomies in patients with IHD.

With respect to serial studies, we apologise for not stating the time period during which preoperative GGT values were studied in patients with biliary atresia. This was determined by the time taken to reach a definitive diagnosis and to submit the patient to surgery. In the vast majority of patients it was less than two weeks, but...
exceptionally may have been three weeks. We observed that GGT values fell in 11 of 22 children with EHBA and rose in 12 of 22 with IHD. We expressed the degree of change in a fractional manner which we agree may be misleading. Nevertheless, while those with IHD may have fallen within the limits defined by Lau and Fung, 11 of 22 with EHBA would not have been considered for laparotomy. On the basis of our experience as reported in our paper, Drs Lau and Fung’s assertion that repeated measurements of GGT could serve as a prelaparotomy, non-invasive screening test is an enticement to malpractice.

Goodpasture’s syndrome

Sir,

I read with interest the paper by Dr Levin et al, and would like to bring to the authors’ attention the fact that this syndrome in children was reported by us and O’Connell et al before Anand et al and Siegler et al. Although the authors correctly begin with the sentence ‘Goodpasture’s syndrome, a term describing the association of glomerulonephritis and lung haemorrhage’, they give no evidence, including that of necropsy examination, that lung involvement occurred in their patients.

Sinasi Ozsoylu
Hacettepe University, Hacettepe, Ankara, Turkey

References


Dr Levin and co-workers comment:

We thank Professor Ozsoylu for his letter, firstly drawing our attention to his earlier report of a child with Goodpasture’s syndrome, and secondly questioning the use of the term Goodpasture’s syndrome in our patients, in whom antiglomerular basement membrane antibody (anti GBM) induced nephritis was present without clinical evidence of lung haemorrhage.

We agree with Professor Ozsoylu’s view that the term Goodpasture’s syndrome was originally used to describe the clinical association of glomerulonephritis and lung haemorrhage. It therefore encompassed a heterogeneous group of patients with a variety of different pathological conditions, including Wegener’s granulomatosis, polyarteritis, and glomerulonephritis with haemorrhagic pulmonary oedema.

The elucidation of the role of anti GBM antibodies in the pathogenesis of most patients with Goodpasture’s syndrome has led to patients with the disorder being defined by immunological and pathophysiological rather than clinical criteria. It has led also to the recognition of patients who have anti GBM antibodies, but without simultaneous lung and kidney involvement. It remains a semantic problem as to whether the term Goodpasture’s syndrome should only be used to describe patients with simultaneously clinically apparent kidney and lung disease, or whether its use should include all patients with anti GBM antibody disease, irrespective of the organ affected. We have followed the precedent set by others in using Goodpasture’s syndrome as a widely accepted abbreviation for the disease which would be more accurately described as anti-basement membrane antibody induced glomerulonephritis and pneumonia.

Recurrent abdominal pain: a psychogenic disorder?

Sir,

In drawing their conclusion that the syndrome of recurrent abdominal pain in childhood does not have a psychological basis, McGrath et al seem to be assuming that only children from emotionally unstable and chaotic backgrounds may suffer psychologically triggered somatic symptoms. In my experience, this is far from the case and the children referred to this paediatric outpatient clinic with recurrent abdominal pain fall into three broad categories:

1 A small group who do come from highly disturbed backgrounds and who often have multiple symptoms suggestive of an emotional trigger. The diagnosis of the psychological causes is almost always made by the family practitioner, who is therefore very unlikely to refer the child to a gastroenterology unit for treatment. The prognosis for the pain is usually linked to the management of the whole family.

2 Children with a strong family history of migraine who suffer episodes of abdominal pain, often with vomiting. They are often labelled as having the periodic syndrome or ‘abdominal migraine’ and it is possible that at least some may have food allergy.

3 The largest group resembles most those children described by McGrath et al. They are usually accompanied to ‘outpatients’ by one or both concerned parents, have no other symptoms, are completely normal on full examination, and their urine is normal on ‘Dip-testing’, microscopy, and culture. A consistent feature of their histories is that the episodes of abdominal pain induce a clear concern in the parents. Often, the first episode of pain has an