Correspondence

PHILLIP MORICE, ALYN leµl leaves little induced 26,7une produce bronchoconstriction, Ind of calibre.3 Research Council. not to be low bilateral gone proposed 2 Barnes 1985;290:267-9. We thank Miss K Leys for performing the β receptor assay. AHM was supported by the Asthma Research Council.

We thank Professor V Wynne for permission to report on his patient and Miss K Leys for performing the β receptor assay. AHM was supported by the Asthma Research Council.


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Subacute hepatic necrosis induced by piroxicam

Hepatotoxicity is a recognised side effect of most non-steroidal anti-inflammatory drugs1 and may be hepatocellular, cholestatic, or a combination of both. In most cases the prognosis of those patients who survive the acute phase is good, though recognition and withdrawal of the offending drug is important. Piroxicam, a relatively new agent belonging to the oxicam class, appears to be the least hepatotoxic non-steroidal anti-inflammatory drug.2 We, however, describe a patient who presented with features of acute hepatocellular injury that progressed to fatal subacute hepatic necrosis despite withdrawal of the drug.

Case report

A 66 year old woman of previously good health developed jaundice with dark urine and pale stools three days after starting piroxicam for plantar fasciitis (40 mg/day; total dose 120 mg). The drug was immediately stopped. There was no history of blood transfusion, recent injection, contact with jaundice, or ingestion of other drugs or alcohol. Results of investigations were: plasma bilirubin concentration 525 nmol/l (19-0 mg/100 ml), aspartate transaminase activity 430 IU/l, alkaline phosphatase activity 190 IU/l (24 KA units), total protein concentration 74 g/l (albumin 38 g/l), and prothrombin time 16/12 seconds. Tests for hepatitis A and B viruses and antinuclear, smooth muscle, and mitochondrial antibodies gave negative results. Liver biopsy two weeks after the onset of jaundice showed an acute hepatitis with spotty necrosis (figure).

Despite some initial clinical and biochemical improvement she remained severely jaundiced and 12 weeks later developed progressive abdominal and leg swelling with the onset over 24 hours of drowsiness and confusion. She was transferred to the liver failure unit at this hospital. On examination she was in grade II hepatic coma and had gross ascites. Results of investigations were: bilirubin concentration 407 nmol/l (23-8 mg/100 ml), aspartate transaminase activity 730 IU/l, alanine transaminase, activity 258 IU/l, total protein 70 g/l (albumin 21 g/l), and prothrombin time 39/13 seconds. Serum autoantibody screen was positive for antinuclear antibodies (titre 1/160). She began treatment with corticosteroids but shortly afterwards suffered gastrointestinal bleeding. She died 105 days after the onset of jaundice. Liver biopsy immediately after death showed severe confluent centrilobular necrosis with extensive bridging collapse and prominent mixed inflammatory cell infiltration (subacute hepatic necrosis) (figure).

Comment

Mild and transient rises in serum transaminase activities have been described during clinical trials of piroxicam4 and we have found one report of probable piroxicam induced cholestatic jaundice.5 In our patient the temporal sequence together with exclusion of viral hepatitis A and B and the initially normal autoantibody screen all point to a drug induced hepatitis. Despite withdrawing the drug the illness progressed to fatal subacute hepatic failure.

It has been thought that adverse drug reactions including hepatotoxicity due to non-steroidal anti-inflammatory drugs may be more common in patients over 65, and this was shown with benoxaprofen.6 The reason is
unknown, though increased susceptibility to immunological injury in the elderly may be important. Interestingly in this respect, despite immediate withdrawal of piroxicam after the onset of jaundice in our patient evidence of severe liver damage persisted and was subsequently associated with hyperglobulinaemia and the formation of antinuclear antibodies in high titre (1/50) in the patient. The perpetuating autoimmune reaction triggered by piroxicam was responsible for the continued progression of the lesion to subacute hepatic necrosis.

A recent report from France described four patients with chronic active hepatitis due to clometsam (an iodide derived non-steroidal anti-inflammory drug widely used in France) which was associated with the formation of antidiode-stranded deoxyribonucleic acid antibodies. Withdrawal of the drug was followed by biochemical and clinical improvement with reduction in or disappearance of autoantibodies.

We find that corticosteroids are not useful in patients presenting with subacute hepatic failure. If this patient had been younger we would have considered liver transplantation at the time of transfer, when it was apparent that spontaneous recovery was very unlikely to occur.


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Programme for early detection of gastric cancer

The low incidence of gastric cancer in the United Kingdom precludes such screening as is practised in Japan; however, high risk groups are identifiable. Morbidity and mortality statistics for consultations by general practitioners show that one in 50 patients presenting for the first time with dyspepsia will have gastric cancer. In this study a programme for the early detection of gastric cancer has been developed, based on examination of this selected population by endoscopy.

Patients, methods, and results

General practitioners from six practices were invited to refer all patients over the age of 40 presenting with dyspepsia to a dyspepsia clinic held in their health centre by members of the hospital team. After being interviewed and examined patients were informed that endoscopy was required to investigate their symptoms. Endoscopy was performed at the hospital during the next week and thus a diagnosis was established within three weeks of the initial consultation. The referring doctor was informed of the diagnosis so that treatment could be begun. Patients with benign oesophageal and duodenal disease were not seen again. Those with gastric ulcers were re-examined to ensure healing at two morbidity and mortality statistics for consultations by general practitioners show that one in 50 patients presenting for the first time with dyspepsia will have gastric cancer. In this study a programme for the early detection of gastric cancer has been developed, based on examination of this selected population by endoscopy.

Patients with malignancy were referred for appropriate treatment.

Over two years 683 patients were referred. Forty five (7%) failed to attend the dyspepsia clinic or the appointment for endoscopy. We grouped the diagnoses as benign oesophageal disease including hiatus hernia and oesophagitis (198 patients), benign gastric disease including gastric ulceration and superficial gastritis (149 patients), and benign duodenal disease including duodenal ulceration and duodenitis (123 patients). In addition, there were 33 cases of malignancy, and 91 patients yielded normal results at endoscopy.

Fifteen (2%) patients had gastric cancer (two had stage I cancer, five stage II, three stage III, and five stage IV), 10 (67%) of whom were suitable for radical resection. All stage I lesions and two stage II lesions were diagnosed at follow up endoscopy. Three patients originally had gastric ulceration with adjacent intestinal metaplasia and one had atrophic gastritis. The remaining 18 cases of malignancy were either oesophageal tumours detected at endoscopy or cancers diagnosed by further investigation on the basis of clinical suspicion after endoscopy yielded normal results. There were seven oesophageal cancers, three colorectal cancers, four bronchial cancers, three cases of carcinomatosis, and one case of metastatic carcinoid.

A group with potentially precancerous histological changes was also identified. Seventy nine (12%) had atrophic gastritis, intestinal metaplasia, or dysplasia alone or in combination. Twenty two had these changes adjacent to gastric ulcers but, as stated, four had a malignancy diagnosed during the study.

Comment

The rate of detection of gastric cancer in our study is similar to that predicted from mortality statistics for general practitioner consultation. The combination of specialised clinics in familiar surroundings and careful explanation of the examination contributed to the high compliance rate. The high rate of radical resection contrasts favourably with that of 18% from a previous regional survey. Equally encouraging was the proportion of lesions limited to the submucosa, which at 15% exceeds that of about 1% reported previously and is comparable with the 30% detection rate reported from Japan.

It remains to be seen whether follow up of those with premalignant changes will increase the number of patients with early gastric cancer. Further study is necessary to show whether the methods used in this pilot study are suitable for widespread use. The programme has been extended to include the Sandwell district of the West Midlands where the incidence of gastric cancer is higher (West Midlands Cancer Registry, personal communication). This will enable prospective documentation of the true incidence of gastric cancer and evaluation of the financial implications of such a service.

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Prognosis of patients discharged from a coronary care unit

Previous work has shown that patients with and without acute myocardial infarction have a similar risk of death from coronary heart disease in the year after discharge from a coronary care unit. I present a retrospective study of survival of such patients over 10 years.

Patients, methods, and results

A total of 298 patients from 371 consecutive admissions to a coronary care unit who survived to 28 days were divided on discharge into two diagnostic categories (with and without acute myocardial infarction) according to the World Health Organization electrocardiographic classification and serial measurements of serum creatine phosphokinase activity. Acute myocardial infarction was regarded as certain or probable when acute or non-acute ischaemic electrocardio-