Severe polyneuropathy complicating active Crohn’s disease: rapid response to Infliximab

Treatment with a chimeric antitumour necrosis factor (TNF) antibody (Infliximab) has been shown to be highly efficient for patients with steroid refractory Crohn’s disease (CD). However, the mechanism of action remains largely unknown. Recently, a favourable response to Infliximab treatment was demonstrated in some diseases complicating active CD such as acute idiopathic pancreatitis. We report a case of a middle aged female with CD that developed an aggressive form of polyneuropathy resistant to corticosteroids.

A 55 year old White female, weighting 68 kg, presented with exacerbation of CD (CDAI activity index (CDAI) >450) associated with severe muscle atrophy of the right arm and leg with arthralgias, myalgias, and functional impotence. Neuropathy was characterised by areflexia of the right arm and leg progressively deteriorated and no side effects were recorded. Electromyography performed at week 22 after the start of therapy was normal. CDAI score is <150 at this time. Sign and symptoms of chronic corticosteroid therapy rapidly disappeared.

In conclusion, Infliximab may be a suitable therapeutic option in patients with rare extraintestinal manifestations of CD such as severe polyneuropathy not responding to conventional therapy.

S Rodinò, N Saccà, T D’Amico, A Fragomeni, A Giglio
52 – 452 – 29 – 96

UO Gastroenterology, Azienda Ospedaliero Pugliese-Ciaccio, Catanzano, Italy

Correspondence to: Dr S Rodinò, Via A Brousard, n13, Catanzano 88100, Italy, srodino@tin.it

References

Caution with the use of cyclosporin in pregnancy

We read the article by Alstead and Nelson-Piercy with great interest.

We report a case (submitted for publication) of a woman with fulminant ulcerative colitis in the 29th week of pregnancy. Her disease was refractory to steroids, but she refused to have cyclosporin whilst pregnant. She therefore underwent an emergency Caesarean section and was given intravenous cyclosporin post-operatively. After 48 hours of treatment she developed severe hypertension with hypertensive encephalopathy and seizures. Although cyclosporin has been considered to be safe for both mother and foetus, we would like to highlight concerns that it is associated with potentially life threatening side effects. As a result, patients must be counselled thoroughly about the potential morbidity associated with this treatment and monitored closely. We agree with Dr Alstead in that cyclosporin should be used with extreme caution in pregnancy and the postnatal period.

R Dor, C Blanshard
Academic Unit of Gastroenterology, Homerton University Hospital, Homerton Row, London E9 6SR, UK

Correspondence to Dr Dor; riaz.dor@nhs.net

References

Coeliac disease: is case finding the correct ethical and logistical approach?

I read with interest the debate pertaining to screening for coeliac disease (CD). Although one can argue that CD fulfils the tenets of any screening programme, however, we do not know the natural history of screen detected patients with CD. Logistically when would we decide to screen—at what age and how often thereafter? Serological markers may be highly sensitive and specific but the value of these tests decrease when they are used in the general population.

Although the investigational process for population screening and case finding may be the same, there is an important ethical difference between them. If a patient seeks medical help then the physician is attempting to diagnose the underlying condition (for example: patients with CD who present with symptoms of irritable bowel syndrome). This would be classified as case finding and clearly it is the patient who has initiated the consultation and in some sense is consenting for investigation. Conversely, individuals (who are not patients) found to have CD through screening programmes, may have considered themselves as “well” and it is the physician or healthcare system that is identifying them as potentially ill.

We recently performed a primary care based cross sectional study using immunoglobulins, IgA/IgG antigliadin antibodies and endomysial antibodies to initially recognise CD. 1200 volunteers were recruited from January 1999 to June 2001 from 5 general practices in South Yorkshire, UK. Any patient with a positive IgA antigliadin antibody, positive endomysial antibody or only IgG antigliadin antibody in the presence of IgA deficiency was offered a small bowel biopsy to confirm the diagnosis of CD. Twelve new cases of CD were diagnosed from 1200 samples. The prevalence of CD in this primary care population sample is 1% (95% CI 0.4–1.3%). In this screening study, 9/12 diagnosed cases of CD ultimately had symptoms which could be attributed to CD (for example, anaemia or subtle gastrointestinal symptoms). We, and others have demonstrated a delay in the diagnosis of CD—surely the important change in our clinical practice (both in primary and secondary care) is to have a low threshold for case finding.4 If you look for CD you will find it.

D S Sanders
Gastroenterology and Liver Unit, Room P14, P Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK; d.s.sanders28@btopenworld.com

References

www.gutjnl.com
very large study conducted by an expert team in this field were that mean age at diagnosis was higher in men (p<0.01), mean FNF size smaller (p<0.001), and surgery more often performed (p<0.001) in men (n=18) than in women (n=216). Interestingly, perhaps because of the relatively small number of men (although very large in terms of the rare occurrence of FNF in men), no cases of multiple FNF were noted in the male population. We report here the presence of multiple FNH in a 74 year old patient with a biopsy proven prostatic cancer. This patient had not received any treatment. He was referred to our liver unit in March 2001 for evaluation of multiple liver masses discovered on abdominal ultrasonography during the staging of his cancer. Bone scintigraphy disclosed no metastases. Liver biochemistry was normal except for a mild increase in gamma glutamyl transferase activity. Prothrombin index was 100%. Serological search for hepatitis B or hepatitis C virus infection was negative. Genetic (haemochromatosis, alpha 1 antitrypsin deficiency) and autoimmune liver diseases were carefully excluded, and alcohol consumption was below 10 g/day. Upper gastrointestinal endoscopy and colonoscopy were normal. Tumour markers of malignant primary or secondary liver lesions were within the normal range. Liver Doppler ultrasonography disclosed multiple heterogeneous lesions with a hypochogenic pattern and without an arterial signal. Abdominal tomodensitometry before and after contrast enhancement confirmed multiple lesions with rapid contrast enhancement during the arterial phase. The largest lesion was located between the left liver and segment IV and measured 75 mm.

Because there was no magnetic resonance imaging (MRI) in our centre, ultrasound guided liver biopsy in both tumoral and non-tumoral areas was performed. The diagnosis of typical FNH was made in several of the lesions whereas non-tumoral liver was normal. The patient received hormonal treatment from April 2001. In October 2001, MRI confirmed a diagnosis of FNH with a central stellate area in the largest lesion. In December 2002, he was in good health with unchanged ultrasonography.

This case report is unique in that there were multiple lesions in the male, and that he had not received any previous treatments or portal-caval shunt. Although from a literature search it is difficult to determine the exact number of men with multiple FNH and the numbers are probably very low. In this report, the discrepancy between normal bone scintigraphy and multiple liver lesions strengthens the diagnosis of liver metastasis probable. Nevertheless, histological examination of several hepatic lesions, retrospective MRI, and outcome made the diagnosis of multiple FNH certain. This report, in common with the large series of Luciani et al., indicates that FNH diagnosis may be very difficult in men.

J F Cadranel, K Hadj-Nacer, J C Kikass, O A Cozzer
Services d’Hépato-Gastroentérologie, d’Imagerie Médicale, d’Urologie et d’Anatomie-pathologie, Centre Hospitalier, Lannec, BP72, 60109, Creil, France

Correspondence to: Dr J F Cadranel; francois.cadranel@ch.creil.fr

Guidelines for colonscopic screening in acromegaly are inconsistent with those for other high risk groups

We welcome the joint work of the British Society of Gastroenterology and the Association of Coloproctology of Great Britain and Ireland in commissions guidelines for colorectal cancer screening in high risk groups (gut 2003;50:877–80). In the absence of direct evidence from randomised trials for most of the groups, the various authors have balanced a wealth of recent genetic and epidemiological data with a perception of an individual’s levels of elevated risk against the risks associated with screening. The end result is the recognition that within the label “high risk” there are wide groups of risks such that colonscopic screening and surveillance must be tailored accordingly. This avoids the ineffective, costly, and potentially harmful “blanket-type” approach, which formerly prevailed.

However, within the guideline series, there is one exception—screening and surveillance in patients with acromegaly. We and other researchers1–3 have repeatedly stated that the studies undertaken by the authors of these guidelines have overestimated the risk of colorectal cancer in this patient group. They report a 13–14-fold increase in risk based on colorectal cancer detection rates among acromegalic subjects (see table 3 in Jenkins and Fairclough1). All of these authors have highlighted acute care and colorectal cancer screening in mixed race US populations and lack data to permit age-sex comparisons. This simply does not rank as a well designed controlled study and the recommendations should not receive grade B status.

In the same manner as relative risks for those with relatives with colorectal cancer are estimated from population based data (summarised in Dunlop1), we have argued for a similar approach for patients with acromegaly. Based on three population based studies, we calculated (by fixed effects meta-analysis) a relative risk of 2.0 (95% confidence intervals 1.4–2.9) for colon and rectal cancer combined in acromegaly.1–3 Considered in terms of absolute risk, with an approximate 2% cumulative risk of colorectal cancer by age 70 years in the general UK population, the estimated risk in acromegaly would be 4%. This is far from the incidence in the very high risk groups. In first degree relatives with a strong family history (a high risk group), Dunlop1 recommends early colonoscopic screening and then wait until 53 years for repeat colonoscopy if initial screening is clear (the majority). How can Jenkins and Fairclough justify early screening and colonoscopy five yearly thereafter in all of their acromegalics?

Atkin and Saunders4 have demonstrated that colonoscopic surveillance following initial screening in the non-acromegaly population is determined primarily by clinicopathological findings. These basic guidelines must also be applied to the acromegaly patient population. Jenkins and Fairclough have stated that elevated serum IGF-I levels may predict for recurrent adenomas in acromegalic patients and “should be offered screening at three year intervals”. This is based on data from only eight acromegalic patients with recurrent adenomas and should not replace other well recognised predictors of recurrence.

Looking at the context of (other high risk) groups, the guidelines for colorectal cancer screening in patients with acromegaly are inconsistent. The aggressive approach to
transmural ischaemic colitis following an aeroplane flight

We read with interest the report of Butcher and colleagues (Gut 2002;51:746–7) of two cases of transient ischaemic colitis following an aeroplane flight. This report represents more evidence supporting the suggestion of a possible important role of acquired and hereditary thrombophilia in the pathogenesis of ischaemic colitis. However, the largest study to date concerning these factors in patients with ischaemic colitis was not mentioned in the study. Moreover, the reported patients may also have other acquired or inherited thrombophilic disorders which were not evaluated. Lipoprotein (a), antiphospholipid antibodies, the C677T methylentetrahydrofolate reductase polymorphism, and the G20210A prothrombin gene mutation were not studied in both patients whereas in the second case even the very important factor V Leiden mutation as well as lupus anticoagulant and homocysteine levels were not evaluated. Although the aeroplane flight could be the most important risk factor in these cases, the rather incomplete thrombophilic screening does not permit us to conclude that it was “the only potential risk factor”.

It is known that deep vein thrombosis (mainly symptomless) may occur in up to 10% of long haul airline travellers. In contrast, the hypercoagulable state is more relevant in the role of ischaemic colitis, leading to the development of thrombotic occlusion of the small vessels supplying the colon. In a recent study of comprehensive thrombophilic screening in patients with an established diagnosis of ischaemic colitis, we found the prevalence of acquired and hereditary thrombotic risk factors significantly higher compared with the prevalence of these factors in matched inflammatory and healthy controls. A thrombophilic tendency was demonstrated in the majority of patients and the most significant associations were with antiphospholipid antibodies and with the factor V Leiden mutation. Moreover, we recently found a high frequency of protein Z deficiency mainly with arterial thrombosis, on the recent data of the association of protein Z deficiency in patients with ischaemic colitis (unpublished data). Based on the recent data of the association of protein Z deficiency mainly with arterial thrombosis, protein Z deficiency may be involved in the development of the disease in a subgroup of patients by causing thrombosis in the small mesenteric arteries. Accidental thrombosis is considered the result of localised non-occlusive ischaemia of the small arteries. In contrast, the presence of hypercoagulable states suggests a possible role of...
venous obstruction. It is possible that future identification of subgroups in ischaemic colitis patients with sophisticated imaging techniques could distinguish cases with arterial or venous ischaemia. In conclusion, we suggest that the mechanism of ischaemic colitis is multifactorial. Acquired and genetic factors may interact leading to disease manifestation. Arthralgia and embolic conditions, oral contraceptives, and other medications, as well long haul flights probably play a role in genetically predisposed individuals in the disease pathogenesis.

I E Koutroubakis, A Theodoropoulou, E A Kourounmalis
Department of Gastroenterology University Hospital Heraklion, Greece

Correspondence to: Dr I E Koutroubakis, Department of Gastroenterology, University Hospital Heraklion, PO Box 1352, 71110 Heraklion, Crete, Greece; ikjohn@her.forthnet.gr

References


The Handbook of Clinical Trials and Other Research

Clinicians are notorious for embarking upon research without a full understanding of methodology. Perhaps in the past clinical journals were guilty of publishing papers without being sufficiently critical. No doubt this was a byproduct of well meaning referring by clinicians who were themselves hamstrung methodologically, and lacking insight.

In the new world of publications, the research design has to be explicit, well laid out, and sufficiently robust to support the research reported. Most doctors have had little or no training in research methods, despite having completed an MD. This might be one reason why it is becoming increasingly difficult for even research experienced clinicians to initiate new projects. Indeed, there is a question mark as to whether research can now be done by service based clinicians or whether, because of the newer strictures and disciplines, this should be left to the professional researcher. Perhaps the answer is that clinicians ought to have access to experts who can not only guide them but see them through the entire project. Some have questioned whether clinical research will proceed, the answer, even if only in hope, is yes, but this will require a greater familiarity with research methodology, the patience to plan thoughtfully, and with experienced clinicians.

This handbook provides definitions and contemporary examples. It provides recent references from major journals and is well illustrated. It contains material beyond explanations of research terminology and methodology including the new requirements for the Research Ethics Committees, and the EU Clinical Trials directive. The research rules are fast moving; in the UK there is a single electronic ethics application form now with new rules regarding consent for multicentre

Gastrointestinal Mucosal Repair and Experimental Therapeutics

This book is a worthy addition to the Frontiers of Gastrointestinal Research series that focuses on specialised gastrointestinal research topics. This volume is the 25th of the series and highlights areas of current and emerging interest to investigators in the area of gastrointestinal mucosal injury, repair, and therapeutics.

The book is not a compilation of talks given at a conference but rather an honest attempt to inform and stimulate research areas within that broad field. It has been a number of years since anyone has gathered the information for a reference book for his area, and the editors have intentionally chosen to invite experts to write on their specialised subjects. The emphasis of the book is on the use of experimental cell culture and animal models and, therefore, will be of most use to basic researchers. The book is divided into three broad sections, covering epithelial restitution, mucosal repair and healing, and experimental therapeutics. The chapter authors have taken care to summarise what is known and what remains to be investigated. Several of the chapters provide reviews of a particular area, such as understanding those on angiogenesis, the diacylglycerol/protein kinase C pathway, nitric oxide and its regulation, the roles of cyclooxygenase inhibitors and the involvement of prostaglandin receptors in the gastrointestinal tract. Other chapters contain useful methodology regarding animal models and experimental techniques such as physical stress and strain. The chapters dealing with cytokines and Helicobacter pylori infection are brief, but these subjects are adequately covered elsewhere in numerous reviews. New and potentially useful therapeutic possibilities are examined, including the use of platelets to deliver healing growth factors, the use of polysaccharides such as heparin for gastrointestinal protection, and gene therapy with angiogenic growth factors.

It is not possible for any book to be complete and inclusive of all subjects in such a diverse field as mucosal repair and therapeutics, but this book does a more than reasonable job. It will be a very useful reference for both research newcomers and veterans alike in the field.

E J Dial

Surgery of the Liver, Bile Ducts and Pancreas in Children

This excellent volume builds on the success of the first edition published a decade ago by the senior editor (ERH). Inevitably it is bigger, and, yes, better too. The contributors, drawn from across the world, have been chosen with expertise and this is apparent in their respective chapters. A major beneficial innovation is inclusion of an editor and other contributors from the USA; sadly, for an inherently English book, English spelling has been sacrificed in the process.

All chapters have been rewritten in response to the significant developments in hepatobiliary surgery over the past decade—for example, in the anatomy of the liver and in liver transplantation (now up from 14 to 96 pages). The chapter on “portosystemic shunt surgery” has given way to “surgery for portal hypertension”, reflecting the development of alternative strategies for this condition. As before, detailed and informative chapters on anatomy, physiology, and preoperative management complement the core “surgical” chapters, and there are new chapters on embolization, anaesthesia and perioperative care, nutrition, and the psychosocial aspects of childhood liver disease, which will be of interest to gastroenterologists and surgeons alike. Another innovation is the inclusion of a section on “surgical” paediatric pancreatic disorders, including chapters on embryology and anatomy; this is a logical development that enhances the value of this volume.

The scientific standard is high throughout the book. Each of the topics has been well researched by its author and (with only one exception), chapters are well referenced. Of course one can find omissions but these are minor and very infrequent. The text is easy to read and the editors have ensured that the content is clinically relevant. Each chapter concludes with a useful table of annotated key references, and in some chapters a recommended management strategy is summarised in a box. The book is liberally illustrated with line drawings and both black and white and colour figures, which generally are informative and clearly reproduced. The index is good; I was able, without difficulty, to locate a variety of topics. Overall, the quality of the production is excellent, with very few typographical errors. Although this is a comprehensive book, it is not a large tome, but is comfortable and easy to read.

This book will serve as an invaluable resource for gastroenterologists, paediatricians, surgeons, nurses, and others involved in the surgical care of children with liver, biliary, or pancreatic disorders, whether at a specialist children’s centre or a district hospital, and will appeal to trainees, whose exposure these days to complex hepatobiliary surgery is limited. In addition, gastroenterologists and surgeons treating the increasing number of adults with disorders of childhood will find this book a most helpful companion.

D Lloyd
It is a great pleasure to create a tool that is expected to be appropriate for people with different levels of knowledge and experience. This publication is certainly straightforward to use and is a useful repository of terms and other sources of information. I am glad I have my copy but can you really teach old dogs new tricks?

P Hungin

Hepatology Principles and Practice
E Kunz, H-D Kunz. Berlin: Springer Verlag, colour, pp 825. ISBN 3540 42161 0

“You have a very large parcel”, Zeinab, my secretary said breathlessly as she struggled up from the post room with a copy of this enormous book. It seemed all the heavier as I hugged it around the London bus network from the wilds of East Acton on my way home and then back to work several times. Contained in a reinforced Harrod’s bag, which was the only thing I could find that was strong enough to hold it while I elbowed my way through the myriads of commuters that were forced to travel by bus in lieu of the non-existent Central line, I felt my back pain had returned with a vengeance and did not know whether to take up weight training (where the book would come in handy) or admit defeat and sue the authors for damage. However, sanity soon prevailed and I soon became engrossed in this hefty tome.

At first glance, one could say that another comprehensive book on hepatology is really not needed, given all the other titles on the market. But it turns out that this 2002 English edition of the original German “Praktische Hepatologie”, published in 1998, has been updated and was a labour of love by Erwin Kunz whose son, Hans-Dietel, died before the book could be finished. My schoolboy German is not up to the original edition but this has become a bible in Germany and the current version is welcome, despite the fact that a lot of the English is somewhat awkward with curious turns of phrase. Examples of this include “MRT”, rather than MRI, which is irritating, and “lethality”, rather than mortality, which interrupts one’s reading pattern. However, there are some very nice things also included, for instance the question of who may actually buy this book, or can you really teach old dogs new tricks?

S D Taylor-Robinson

The Association of Coloproctology of Great Britain & Ireland

This annual meeting will be held on 7–10 July 2003 in Edinburgh, UK. Further details: Conference Secretariat, The ACGBI at the Royal College of Surgeons of England, 35–43 Lincoln’s Inn Fields, London WC2A 3PE. Tel: +44 (0)20 7973 0307; fax: +44 (0)20 7430 9233; email: acgbi@acgbi.org.uk; website: www.acgbi.org.uk

European Helicobacter Study Group (EHSG)

This meeting, on Helicobacter infections and gastroduodenal pathology, will be held on 3–6 September 2003 in Stockholm, Sweden. Further details: Professor Torkel Wadstrom, President- EHSG, Lund University, Department of Infectious Diseases & Medical Microbiology, Division of Bacteriology, Solvegatan 25, SE-223 62 Lund, Sweden. Tel: +46 46 173 241; fax: +46 46 152 564; email: torkel.wadstrom@mmb.lu.se; website: www.helicobacter.org

Falk Symposium

135—Immunological Diseases of Liver and Gut

This symposium will be held on 12–13 September 2003 in Prague, Czech Republic. Further details: Falk Foundation e.V., Congress Division, PO Box 6329, Leinwenberstr. 5, 79041 Freiburg/B, Germany. Tel: +49 761 15 14 10; fax: +49 761 15 14 359; email: symposia@falkfoundation.de; website: www.falkfoundation.de

The European Society of Parenteral and Enteral Nutrition (ESPEN)

ESPEN will celebrate its silver anniversary at the time of the annual congress, which is to be held on 20–23 September 2003 in Cannes, France. Further details: www.espen.org

XII Falk Liver Week

The XII Falk Liver Week, in honour of Hans Popper’s 100th birthday, will be held on 15–22 October 2003 in Freiburg, Germany. Further details - see Falk Symposia above.

European Course on Laparoscopic Endoscopy

This course will be held on 18–21 November 2003 in Brussels, Belgium. Further details: Secretary to Professor Cadière, Service de Chirurgie Digestive, Rue Haute 322, Bruxelles 1000, Belgium. Tel: +32 (0) 2 648 07 60; fax: +32 (0) 2 647 86 94; email: straeb.asmb@proximedia.be; website: www.straeb-asmb.com

Hong Kong-Shanghai International Liver Congress 2004

This conference will be held on 14–17 February 2004 in Hong Kong. The topic of the conference is “Liver Diseases in the Post-Genomic Era”. Further details: Ms Kristie Leung, Room 102–105 School of General Nursing, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. Tel: +852 2818 4300/8101 2442; fax: +852 2818 4030; email: kristieleung@hepa2004.org; website: www.hepa2004.org
Transient ischaemic colitis following an aeroplane flight

I E Koutroubakis, A Theodoropoulou and E A Kouroumalis

Gut 2003 52: 1072-1073
doi: 10.1136/gut.52.7.1072-a

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