Stockton-on-Tees symposium: Recent advances in medicine

[1]CG Mountford, [2]AD Dwarakanath
[1]*Specialist Registrar in Gastroenterology;* [2]*Consultant Gastroenterologist, University Hospital of North Tees, Stockton-on-Tees, UK*

ABSTRACT This symposium provided an update on recent advances in medicine relevant to the general physician. The opening session on respiratory medicine session focused on lung cancer and lung transplantation. Everyday practical issues of dealing with abnormal liver function tests were considered in session two as well as the challenges in improving end-of-life care. Clinically orientated presentations in the third session covered case-based discussions on severe metabolic acidosis and the management of Parkinson's disease. The final session on gastroenterology included an update on *Clostridium difficile* and an overview of risk assessment for upper gastrointestinal bleeding and the use of risk assessments as a tool in clinical practice to avoid unnecessary hospital admission.

KEYWORDS Abnormal liver function tests, *Clostridium difficile,* end-of-life care, lung cancer, lung transplantation, metabolic acidosis, Parkinson's disease, upper gastrointestinal bleeding

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Correspondence to ***C Mountford, Department of Gastroenterology, University Hospital of North Tees, Stockton-on-Tees TS19 8PE, UK***

tel. ***+44 (0)1642 617617***
e-mail ***c.mountford@doctors.org.uk***

SESSION 1

Diagnosis and staging of lung cancer

Dr R Harrison (Consultant Physician, University Hospital of North Tees) spoke about advances in the diagnosis and staging of lung cancer. The national lung cancer audit of England and Wales reported 22,628 cases of lung cancer in 2007.[1] An increasing incidence is seen in females and those experiencing social deprivation. Relative one-year survival for lung cancer has increased over time, but there has been no major change in five-year survival. Advanced stage disease at the time of diagnosis is associated with poorer survival. The best survival rates in patients with non-small cell lung cancer are seen within stages of disease where surgical resection is possible.

The key goal in improving survival is achieving earlier diagnosis and hence an improved resection rate. A recent study showed that 50% of patients have symptoms for more than 14 weeks before presenting to a practitioner.[2] Improved referral and investigative pathways once patients have sought help can improve patient processing and ultimately the surgical resection rate.[3] Accurate staging is crucial in determining surgical resectability: the finding of mediastinal lymph nodes at the time of staging renders a case inoperable.

Historically, computed tomography (CT) has been the investigation of choice for staging. However, the use of CT in mediastinal staging relies on the premise that malignant lymph nodes are larger than benign ones. Recent studies have shown this not to be the case, and both the sensitivity and specificity of CT are limited when using size as a surrogate for malignant nodal involvement.[4] Positron emission tomography – computed tomography (PET-CT) fusion scanning is helpful for the detection of extra-thoracic nodal involvement, but there remains scepticism of its accuracy in determining mediastinal nodal involvement. Endobronchial ultrasound (EBUS) is more sensitive, specific and accurate than CT or PET scanning for mediastinal staging.[5] It also has the advantage of allowing transbronchial needle aspiration performed in real-time and is less invasive than mediastinoscopy. A very strong argument for its use in the staging process was made and local experience presented.

Lung transplantation

Dr A Fisher (Senior Lecturer in Respiratory Medicine and Consultant Chest Physician, Freeman Hospital, Newcastle) discussed lung transplantation. The first human lung transplant was carried out in 1963. Since then, more than 25,000 lung transplants have been performed. Median survival is worse overall than for other solid organ transplantation. The challenges of balancing immunosuppression against infection in an organ with exposure to the outside environment are great.

Patients who may be suitable for lung transplantation are those who have advanced lung disease refractory to medical therapy, whose survival without transplantation is estimated at 2–3 years. Over time the average age of recipients has increased.[6] However, there are international guidelines on age limits depending on the type of transplantation being performed. Absolute contra-indications to lung transplantation include current smoking, mechanically ventilated patients, progressive

neuromuscular disorder, active malignancy or untreatable dysfunction of other vital organs. A comprehensive pre-operative work-up by a dedicated multi-disciplinary team is essential. Psychological assessment of the patient is an important part of this work-up. In making a decision, a balance of risks must be made between the existing lung disease and associated quality of life and the operative mortality and postoperative morbidity.

Bronchiolitis obliterans is a major cause of late morbidity in patients who have undergone lung transplantation. A combination of alloimmune and non-alloimmune mechanisms are thought to contribute to this destructive disease process. Current interest exists in the use of macrolide antibiotics to treat or possibly prevent this complication, but further research is needed in this area.

A major problem in clinical lung transplantation is the shortage of donor lungs. One exciting area of development is that of ex vivo lung reconditioning, which may increase the number of viable donor lungs in the future. This technique allows donor lungs that may historically have been unfit for transplantation, for example due to infection or oedema, to be 'serviced' and their quality improved to a level suitable for transplantation.

SESSION 2

Abnormal liver function tests

General practitioners and physicians are often faced with an abnormal finding in liver function tests (LFTs) in a patient's blood results and the question of whether this indicates significant underlying liver disease. A presentation by Dr S Stewart (Consultant Hepatologist, Freeman Hospital, Newcastle) focused on abnormal liver function associated with parenchymal liver disease. It was highlighted that cirrhosis can occur in the context of normal LFTs, but there are usually other clues within the history or examination that point towards this.

The role of liver biopsy in the investigation of abnormal LFTs was explored. In particular, the role of biopsy when LFTs remain persistently elevated with normal liver screen and safe levels of alcohol consumption was discussed. Liver biopsy can be used to diagnose and stage liver disease in this setting. In staging liver disease, use of the non-alcoholic fatty liver disease (NAFLD) fibrosis score can help determine the stage of fibrosis before biopsy and prevent the need for biopsy, which has associated morbidity and mortality in some cases.[7]

The use of liver biopsy to guide treatment in the setting of alcohol-related hepatitis was considered. It was proposed that biopsy should be performed before treating alcoholic hepatitis in order to distinguish it from decompensated cirrhosis. Although the rationale for this approach was presented clearly, its practicality is limited outside of tertiary centres with access to transjugular liver biopsy.

End-of-life care

The importance of holistic care was emphasised by Professor E Pugh (Consultant in Palliative Medicine, University Hospital of North Tees). Approximately half a million people die in England each year, the majority following a period chronic illness either due to cancer, cardiorespiratory disease or dementia. Fifty-eight per cent of deaths occur in hospital, 18% at home, 17% in care homes, 4% in hospices and 3% elsewhere.[8] This contrasts with a century ago when the majority of deaths occurred at home and following more acute illness, often due to infection. This change towards a period of disability before death has generated new challenges in providing quality end-of-life care.

These challenges have been recognised and strategies developed to promote delivery of quality end-of-life care.[8] Challenges to the provision of holistic care within the hospital environment were discussed, in particular the physical environment within wards. The benefits of implementing an end-of-life care pathway in the final stages of life were highlighted as part of holistic care, including spiritual needs.

A significant proportion of patients admitted to hospital could be managed at home and would prefer to die at home, but there is a lack of community support for them to do so. The reasons for this are complex and multifactorial but include a shift in the expectations and culture within society as well as problems with rapid access to community resources. Practice palliative care registers, advanced care plans and end-of-life care pathways applied within the community are all methods by which hospital admissions could be reduced. It is clear, however, that improved funding and provision of 24-hour community palliative care along with a major shift in cultural attitudes will be required.

SESSION 3

Metabolic acidosis

An overview of metabolic acidosis was presented by Professor M Singer (Professor of Intensive Care Medicine, University College London). Arterial base deficit and lactate are useful predictors of poor outcome in the critically unwell patient. They are markers that show good sensitivity but lack specificity and can be used as an early guide to therapeutic response. There is a limited role for bicarbonate as a treatment for metabolic acidosis because if acidosis is secondary to tissue hypoperfusion, bicarbonate therapy may worsen the overall acidosis.

Four cases of patients with profound metabolic acidosis were presented and audience participation sought to

reach the diagnosis. Cocaine overdose, metformin toxicity and sickle cell crisis were all correctly diagnosed. The use of glibenclamide in cases of severe metabolic acidosis induced by drugs was demonstrated in the above cases and its pharmacological effect explained. However, the audience were unable to successfully diagnose the fourth case of beriberi presenting with severe left ventricular failure and were left contemplating how many cases of beriberi they might have missed during their varying years of service. The importance of thiamine supplementation in malnourished patients was also discussed.

Parkinson's disease

Parkinson's disease is a condition characterised by hypokinesis in conjunction with rigidity, tremor and impaired postural reflexes. Important aspects of diagnosis were presented by Dr B Pentland (Consultant Physician, Astley Ainslie Hospital, Edinburgh). Increased tone and rigidity is best demonstrated on slow passive movement and should be examined for proximally as well as distally. Fluctuations in symptoms may be apparent. Emotion aggravates tremor and rigidity, freezing can occur and paradoxic kinesis is recognised. Early non-motor features should be looked for such as depression, constipation and loss of smell as well as cognitive impairment. The diagnosis of Parkinson's disease remains clinical. No diagnostic tests are recommended routinely.

Management of Parkinson's disease was discussed. The importance of patient and carer education and involvement was emphasised. Levodopa remains the mainstay of medical treatment, although motor complications are common, occurring in approximately 70% of patients after nine years. A decision to commence medical treatment should involve informed discussion with patients and be decided on an individual basis, taking into account functional impairment. Treatment remains symptomatic rather than curative. Management dilemmas and treatment side effects were discussed, including the dopamine dysregulation syndromes associated with dopamine agonists.

Finally, candidate neuroprotective drugs were outlined. The case for neuroprotection remains unproven at this stage, but caffeine, co-enzyme Q10, nicotine, creatine, minocycline and oestrogens are some of the potential therapies that are under trial.

SESSION 4

Clostridium difficile

Clostridium difficile (*C. difficile*) is the major cause of antibiotic-associated diarrhoea and causes considerable burden to the NHS. From April 2007 to March 2008, 55,499 cases were identified in England, of which 45,440 were aged 65 years and over.[9] The number of death certificates in England and Wales mentioning *C. difficile* infection has increased each year from 1999 to 2007 and in 2007 there was a 28% increase from 2006 to 8,324 certificates that mentioned *C. difficile* as a contributory factor to or cause of death.[10]

Professor C Probert (Professor of Gastroenterology, Bristol Royal Infirmary) discussed risk factors, in particular the role of quinolone antibiotics. Data were presented suggesting that the role of proton pump inhibitors as a contributory risk factor remains unclear.[11,12] The importance of *C. difficile* testing in patients with an acute flare of inflammatory bowel disease (IBD) was highlighted. The UK IBD audit in 2008 reported that in patients who had IBD and were admitted with diarrhoea, *C. difficile* testing was performed in just 55% of cases (of which 3% were positive).[13]

Some of the problems of diagnosis were highlighted. Enzyme-linked immunosorbent assay (ELISA) techniques are employed for diagnosis in a large number of trusts, but these techniques do lack sensitivity.

An approach to treatment was outlined. In mild disease it was suggested that response to treatment with metronidazole is reviewed on day five and vancomycin 125 mg four times daily be added to or replace metronidazole at that point if necessary. In severe cases, vancomycin 500 mg four times daily was recommended from the outset of treament. Severe cases can be recognised by a raised white cell count greater than 50, low albumin and high lactate. These cases are associated with high mortality, particularly in those patients over the age of 75 years.

C. difficile stools have a characteristic, well-recognised smell. A novel approach to diagnosis based on the extraction of volatile organic compounds was outlined. Data presented on test sensitivity were favourable in comparison to ELISA techniques. The test kit outlined could significantly reduce the time taken to diagnose *C.difficile* infection to a matter of minutes and potentially allow testing and diagnosis to be made on the ward.

Upper gastrointestinal bleeding

Upper gastrointestinal (UGI) bleeding is a common and potentially serious medical emergency. The recent UK audit of UGI bleeding reported that mortality was 7% for new admissions and 26% for inpatients with UGI bleed.[14] Historically, hospital admission is deemed necessary for any patient with UGI bleeding in view of this risk of serious morbidity and mortality.

However, despite these concerns, a substantial proportion of patients with UGI bleeding are low risk and could be discharged if identified early in their admission. An objective method is needed to correctly identify low risk patients who could be discharged early and safely. The UK national audit recommended that a risk assessment

using a validated scoring system should be a standard of care. The two main scoring systems used in the UK are the Rockall and Blatchford scores.[15,16] The Rockall score is used to predict mortality and rebleeding risk and in its original form requires endoscopy in addition to details of patient age, co-morbidity, blood pressure and pulse at the time of presentation.[15] The Blatchford score predicts the need for treatment and does not require endoscopy.[16] It is calculated using the haemodynamic status, haemoglobin and blood urea of the patient at presentation along with presence or absence of melaena and patient co-morbidity.

Dr D Ashley (Consultant Physician, University Hospital of North Tees) argued that the Blatchford score was better placed to identify low-risk patients suitable for early discharge. Results of audit work carried out locally were presented and a management strategy outlined. It was suggested that patients presenting with a Blatchford score of 0 could be discharged early without the need for consultant review. Patients with Blatchford scores less than or equal to 2 could be observed until the next consultant ward round and, if stable at that point, discharged. Only patients with a Blatchford score greater than or equal to 3 required urgent inpatient oesophago-gastroduodenosocopy (OGD). It was recommended that patients over 50 years with a score less than or equal to 2 receive outpatient OGD because of the risk of malignancy. Through implementing this policy it was demonstrated that a reduction in inpatient endoscopy and mean length of stay could be achieved without compromising patient safety.

REFERENCES

1 NHS. *National lung cancer audit. Key findings about the quality of care for people with lung cancer in England and Wales incorporating headline and completeness data form Scotland*. Leeds: Information Centre for Health and Social Care; 2009. Available from: http://www.ic.nhs.uk/services/national-clinical-audit-support-programme-ncasp/audit-reports/lung-cancer

2 Smith SM, Campbell NC, MacLeod U et al. Factors contributing to the time taken to consult with symptoms of lung cancer: a cross-sectional study. *Thorax* 2009; 64:523–31.

3 Laroche C, Wells F, Coulden R et al. Improving surgical resection rate in lung cancer. *Thorax* 1998; 53:445–9.

4 Kerr KM, Lamb D, Wathen CG et al. Pathological assessment of mediastinal lymph nodes in lung cancer: implications for non-invasive mediastinal staging. *Thorax* 1992; 47:337–41.

5 Yasufuku K, Nakajima T, Motoori K et al. Comparison of endobronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer. *Chest* 2006; 130:710–8.

6 Trulock EP, Christie JD, Edwards LB et al. Registry of the International Society for Heart and Lung Transplantation: twenty-fourth official adult lung and heart–lung transplantation report. *J Heart Lung Transplant* 2007; 26:782–95.

7 Angulo P, Hui JM, Marchesini G et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology* 2007; 45:846–54.

8 Department of Health. *End of life care strategy: promoting high quality care for all adults at the end of life*. London: Department of Health; 2008.

9 Health Protection Agency. Results of the mandatory *Clostridium difficile* reporting system. London: Health Protection Agency; 2009. Available from: http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733750761

10 Office for National Statistics. *Clostridium difficile:* number of deaths increase in 2007. London: Office for National Statistics; 2008. Available from: http://www.statistics.gov.uk/cci/nugget.asp?id=1735

11 Dial S, Delaney JA, Schneider V et al. Proton pump inhibitor use and risk of community-acquired *Clostridium difficile*-associated disease defined by prescription for oral vancomycin therapy. *CMAJ* 2006; 157:745–8.

12 Pépin J, Saheb N, Coulombe MA et al. Emergence of fluoroquinolones as the predominant risk factor for *Clostridium difficile*-associated diarrhea: a cohort study during an epidemic in Quebec. *CID* 2005; 41:1254–60.

13 UK IBD audit Steering Group. *UK IBD Audit 2nd round (2008) report*. London: Royal College of Physicians of London; 2009. Available from: http://www.rcplondon.ac.uk/clinical-standards/ceeu/Current-work/Pages/UK-IBD-Audit.aspx#second

14 Project Group for the UK Comparative Audit of Upper Gastrointestinal Bleeding and the Use of Blood. UK comparative audit of upper gastrointestinal bleeding and the use of blood. St Elsewhere's NHS Foundation Trust; 2007. Available from: http://www.bsg.org.uk/pdf_word_docs/blood_audit_report_07.pdf

15 Rockall T, Logan R, Devlin H et al. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut* 1996; 38:316–21.

16 Blatchford O, Murray WR, Blatchford M. A risk score to predict the need for treatment for upper-gastrointestinal haemorrhage. *Lancet* 2000; 356:1318–21.