Pneumonitis in an elderly Bangladeshi man

The incidence of primary varicella zoster virus infection (VZV) in young adults and pregnant women has risen in recent years and is accompanied by a greater risk of serious complications. VZV disease in the elderly usually presents as shingles, as a result of secondary reactivation of latent infection, and can be treated successfully with early antiviral therapy. We report a case of fatal primary infection in an elderly man.

A 66 year old Bangladeshi man with fibrosing alveolitis and non-insulin dependent diabetes mellitus was admitted to hospital with increasing shortness of breath for one week. He was a smoker and had been well controlled on 25 mg of prednisolone daily for the previous two months.

On admission he was febrile (38.5°C), tachypnoeic (50 breaths/minute), and hypertensive (blood pressure, 85/60 mm Hg), with severe mucosal candidiasis. An extensive maculopapular rash, present for three days, was noted and thought to be consistent with amoxicillin treatment, which had been started before admission. Coarse crepitations were heard throughout the chest, oxygen saturation was 80% on air, and blood gases showed type I respiratory failure (pH 7.3; partial CO₂ pressure, 4.8 kPa; partial O₂ pressure, 8.39 kPa; HCO₃, 19.4 mmol/litre). Haemoglobin was 180 g/litre, white blood cell count was 8.5 × 10⁹/litre, serum creatinine was 180 mmol/litre, and blood glucose was 22.2 mmol/litre. Chest x ray showed right mid zone confluent consolidation (fig 1).

Broncho pneumonia was diagnosed; intravenous ceftriaxone, clarithromycin, and fluconazole were commenced. After consultation with the virologists the patient also had a pneumococcal titre taken. The rash was noted to be vesicular and previous treatment with steroids have been withdrawn. Subsequent enquiry did not reveal a chickenpox vaccination history. Skin scrapings and respiratory secretions were then examined for herpes simplex virus (HSV) and VZV by immunofluorescence (Dako, Ely, UK) and were positive for VZV. Subsequent enquiry did not reveal a chickenpox contact. VZV serology (Dade Behring, Deerfield, Illinois, USA) was positive for VZV IgM and negative for VZV IgG antibodies and a diagnosis of chickenpox was made. He received a single dose of normal immunoglobulin (Sandoglobulin; Novartis, Camberley, Surrey, UK; 200 mg/kg) and the aciclovir was continued for 14 days. Respiratory function gradually deteriorated despite 16 hours of prone ventilation each day and he died 23 days after admission.

VZV pneumonitis after primary infection is a severe disease with high mortality, especially in non-immune pregnant women, neonates, and the immunosuppressed. Smoking and previous treatment with steroids have been identified as independent risk factors. In the UK, primary varicella disease in the elderly is a very unusual occurrence because there is almost universal seroconversion by early adulthood. In the tropics, seroconversion occurs at a later age, with seronegativity as high as 42% being found in rural Bangladeshi adults. It is interesting that although this patient had been resident in the UK for over 20 years he remained susceptible. Intensive therapy unit (ITU) management of respiratory failure with ventilatory support is essential in varicella pneumonitis. Retrospective analysis of patients treated with aciclovir has shown some benefit of treatment, especially when instigated early, but there has been no placebo controlled trial to date. High doses (10 mg/kg) are essential to obtain serum titres that are inhibitory to VZV (0.08–1.2 mg/litre). The use of steroids in varicella pneumonia has been controversial, with one small trial showing a reduction in ITU and hospital stay, but no effect on overall mortality. Normal immunoglobulin (100–300 mg/kg) has also been given, with variable results. Prophylactic varicella zoster immunoglobulin (VZIG) has been successful in preventing or attenuating disease in non-immune contacts of primary cases after exposure. A live attenuated vaccine (Oka strain) has been available in some countries, but is available on a named patient basis only in the UK.

This is the fourth fatal case of adult varicella pneumonitis. There have been six deaths in the UK, the second in an elderly Bangladeshi man taking steroids for lung disease. This is the fourth fatal case of adult varicella pneumonitis. Although a characteristic chickenpox rash can precede the onset of pneumonitis by three to five days, our experience in these patients is that it may not be present or may be atypical. Diagnosis is often delayed and initial treatment may sometimes be inappropriate. Varicella is a preventable disease and consideration should now be given to the identification and vaccination of seronegative individuals at risk of severe infection.

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Anaplastic large cell lymphoma: what's in a name?

We have read with interest the editorial by De Wolf-Peeters and Achten, which recently appeared in your journal. As the authors state in this editorial, the lymphoproliferative disease designated anaplastic large cell lymphoma (ALCL) is probably more heterogeneous than currently recognised in the REAL/WHO classification.

Recent studies have shown the existence of a true clinicopathological entity among the CD30 positive anaplastic lymphomas; namely, an ALCL subtype characterised by a specific chromosomal aberration, involving the anaplastic lymphoma kinase (ALK) gene on 2p23, and by excellent prognosis. ALK expression is found in 30–60% (depending on the age of the population studied) of systemic ALCLs with (primary) nodal involvement. It is not found in primary cutaneous and other extranodal ALCLs. ALCL

The remaining controversy concerns ALK negative systemic nodal ALCL, which may be morphologically indistinguishable from primary cutaneous ALCL, but which runs an aggressive clinical course compared with primary cutaneous ALCL. Furthermore, the distinction between ALK negative systemic ALCL and peripheral T-cell lymphoma not otherwise specified (T-NOS) is drawn into question because the formerly acknowledged difference in prognosis between ALCL and peripheral T-NOS might result from the favourable prognosis of ALK positive disease. Thus, as the authors correctly state, criteria for proper distinction between (ALK negative) systemic ALCL and extranodal ALCL, as well as peripheral T-NOS, are needed to determine therapeutic strategies.

Recently, we identified a biological prognostic marker for ALK negative systemic ALCL. We found that a high percentage (> 15%) of activated cytotoxic T lymphocytes (CTLs), present in the reactive infiltrate, is related to poor overall and progression free survival. This biological prognostic marker remained independent of, and seemed more sensitive than, established clinical parameters (such as the international prognostic index) in determining clinical outcome. The same relation between high numbers of activated CTLs and poor prognosis was found by our group for Hodgkin’s disease. These studies suggest that the interaction between tumour cells and reactive immune competent lymphocytes might be more important to clinical outcome than the morphology and immunophenotype of the lymphoma cells. As such, studies intending to clarify the distinction between the above

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Figure 1 Plain chest x ray taken on admission.
When should a coroner’s inquest be held? The Manchester guidelines for pathologists

I am grateful to Dr Roberts and colleagues for their important paper and argument to formulate guidelines on when to report a death to the coroner and decisions thereaf-

ter. The important implications for practitioners in primary and secondary care. One particular dilemma is when to discuss with the coroner what appears to be a natural death, where the cause is unknown or when the practitioner incorporates a double check into the process. This check is supplemented by a third practitioner acting as the crematoria

medical referee.

It is well known that most medical diagnoses are made through clinical history, examination, and investigations, so that unnecessary necropsies and inquests could be avoided, although they may be required given the existing regulations.

Guidelines should be aimed at improving the specificity of the postmortem service as a research tool to be of benefit in three ways when the cause of death is unclear, namely: (1) educating the profession, (2) ascertaining where death is unnatural, and (3) most importantly, facilitating the grieving process of relatives. The latter could be facilitated by next of kin clinics being discussed in this journal, and which target the needs of families attempting to come to terms with the implications of a coronial investigation at a time of crisis, particularly in the situation of sudden death. Such changes should not only improve the quality of the service and its clinical effectiveness, but also be an aid to clinical governance in this area.

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The authors reply

Some years ago, and on the basis of no evidence whatsoever, we suspected that general practitioners were not interested in the outcomes of necropsies. However, and to our great satisfaction, a questionnaire study demonstrated that this view was clearly wrong. Dr Charlton provides further support for the necropsy from primary care, and our pleasure knows no bounds.

We fully support Dr Charlton’s suggestion that pathologists should talk to relatives, and we often do so, on an ad hoc basis, after inquests, etc. However, in most hospitals, including ours, there are not enough his-topathologists to make routine interviews with relatives a realistic proposition. At the moment, we would prefer this task to remain with general practitioners.

Necropsies and inquests have many functions beyond simple confirmation or refu-

tation of clinical diagnoses. We agree that they might be used aimed at different targets, but we would take issue with Dr Charlton’s assertions that many necropsies could be avoided because the diagnosis can be made before death. Clinicians can make correct diagnoses in most cases, but discrepancy rates between clinical and postmortem diagnoses remain woefully high, even when the clinicians are confident about their diagno-

sis. Much might be said for a system where control over the selection of which cases are referred to the coroner, or for hospital necropsy, is removed from those in charge of the subjects before death.

W B BENBOW
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Book reviews

Valproate. Milestones in Drug Therapy.

Valproate has been the subject of over 5000 publications. It was discovered accidentally: it was used as a vehicle for some water insoluble compounds under investigation and found to have an independent anticonvulsant effect. The first clinical reports appeared in 1964. It can justifiably claim its place in the “milestones in drug therapy” series. This book fulfills the main purpose of a monograph. The development, pharmacology, use, and side effects of this drug are all well covered and extensively referenced. Anyone wishing information on valproate would be unlucky indeed not to find it within these covers.

If I have a criticism it would be that the editor has not been strict enough with his contributors. Thus—for example, the chapter on toxicity is almost entirely of clinical interest. The chapter on side effects, and the information on liver damage can be found in several places elsewhere in the book. Some contributions need pruning. The chapter on the use of valproate in children was twice as long as the adult chapter, which was fine except that much of the paediatric chapter was taken up with a description of different paediatric epileptic syndromes; interesting and important information but not directly relevant. The length of the chapter on the use of sodium valproate in headache (20 pages) seems disproportionate in that there are only four double blind, placebo controlled trials in the use of this drug in migraine.

However, these minor criticisms do not detract from the value of this useful book, which should find its place in pharmacy departments and neurology libraries.

R ROBINSON

Chemokines and Cancer. Rollins B, ed. ($125.00.) Humana Press, 1999. ISBN 0 89693 0562 X.

This multiauthor review has 16 chapters, broken down into sections on the physiology of chemokines, tumour infiltration by leuco-
cytes, modulation of host response to cancer, chemokines and tumour growth in carcino-
sis, associations with specific malignancies, and finally effects on stem cell proliferation. Authors are predominantly from US centres, with a scattering of Europeans.

I have to admit to finding this mostly hard going, and, after starting off with good intentions and struggling through half of the book, it was laid aside as more easily digestible and clinically useful things usurped my attention. Half the problem is the multiplicity of chapters. This is a fast moving field, so it is difficult to say what the value of this publication is except as a way mark for the long journey of discovery in cancer research.

There is little here for the working patholo-
gist, but plenty for the chemokine and cancer immunology researcher. I doubt very much whether it will find a general market for interested non-specialists. Mainly one for the library!

G P SPICKEETT
Calendar of events

**Infectious Hazards of Donated Organs**  
28 June 2001, Royal College of Pathologists, London, UK  
*Further details:* Michelle Casey, Academic Activities Coordinator, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel: +44 020 7451 6700; fax: +44 020 7451 6701; www.rcpath.org)

**Recent Advances in Genetics**  
5 July 2001, Royal College of Pathologists, London, UK  
*Further details:* Michelle Casey, Academic Activities Coordinator, 2 Carlton House Terrace, London SW1Y 5AF, UK. (Tel: +44 020 7451 6700; fax: +44 020 7451 6701; www.rcpath.org)

**BSCC Annual Scientific Meeting**  
9–11 September 2001, Majestic Hotel, Harrogate, UK  
*Further details:* BSCC Office, PO Box 352, Uxbridge UB10 9TX, UK. (Tel: +44 01895 274020; fax: +44 01895 274080; email lesley.couch@psilink.co.uk)

**41st St Andrew’s Day Festival Symposium on Therapeutics**  
6–7 December 2001, Royal College of Physicians, Edinburgh, UK  
*Further details:* Eileen Strawn, Symposium Coordinator. (Tel: +44 0131 225 7324; fax: +44 0131 220 4393; email 2.strawn@rcpe.ac.uk; website www.rcpe.ac.uk)

**Current Concepts in Surgical Pathology**  
12–16 November 2001, The Four Seasons Hotel, Boston, Massachusetts, USA  
*Further details:* Department of Continuing Education, Harvard Medical School, PO Box 825, Boston, MA 02117-0825. (Tel: +1 617 432 1525; Fax: +1 617 432 1562; email hms-cme@harvard.edu; web page http://www.med.harvard.edu/conted/)

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