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 hypotensive (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, cyanosis 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 87 g/litre, white blood cell count was 5.5 × 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). Bronchopneumonia was diagnosed; intravenous injections of cefotaxim, clarithromycin, and fluconazole were commenced. After consultation with the virologists the patient also received aciclovir (10 mg/kg) intravenously.

He required intubation, ventilation, and inotropic support within 14 hours of admission. He remained persistently hypoxic despite 100% oxygen, positive end expiratory pressure, inverse ratio ventilation, and nebulised prostacyclin. Oxygenation improved dramatically with prone ventilation. Renal replacement treatment was started on day 3.

On day 4 the rash was noted to be vesicular. 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. Smocking and previous treatment with steroids have been identified as independent risk factors. In the UK, primary 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 large randomised 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 pneumonitis study confirmed, 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. Prophylaxis using 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 licensed 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 we have seen in six years, and the second in an elderly Bangladeshi man taking steroids for lung disease. Although a characteristic chickenpox rash can precede the onset of pneumonitis by three to five days, our group's 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.

D W WAREHAM J BREUER
Department of Medical Microbiology, Barts and The London NHS Trust, London E1 1BB, UK
M T HEALY D R GOLDHILL
Department of Intensive Care, Barts and The London NHS Trust, London E1 1BB, UK


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.1 As the authors state in this editorial, the prognostically and therapeutically important cutaneous 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.2–4 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.5

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 lymphomas 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 ALCL in children. 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.6 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.7 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
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 thereof. The T 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, but where the cause is unknown or when it is well known to the practitioner, but has not consulted in the required preceding 14 days. This is compounded by the variation in attitudes of coroners and their officers to such discussions. It is indeed a "grey area" where needed guidelines are required for doctors and coroners so that it can be determined more precisely when necropsies and inquests are required. To facilitate this process, death certificates and the second part of cremation forms could comprise specific additional questions. These should ascertain the degree to which the certifying practitioner, and the independent practitioner in the case of a cremation form (part 2; form C), are in agreement that the cause of death stated is correct. When such an agreement is not reached, the next of kin clinics, which have been discussed in this journal,1 2 and which target the needs of families attempting to come to terms with the complications 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.

R CHARLTON Centre for Primary Health Care Studies, University of Warwick, Coventry CV4 7AL, UK
roger.charlton@warwick.ac.uk

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 histopathologists 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 refutation of clinical diagnoses. We agree that they might be useful 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 many cases, but discrepancy rates between clinical and postmortem diagnoses remain woefully high, even when the clinicians are confident about their diagnoses. 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.

E W BENBOW Laboratory Medicine Academic Group, University of Manchester, Oxford Road, Manchester M13 9PT, UK
I S D ROBERTS Department of Cellular Pathology, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK


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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