Hypersensitivity to dexamethasone

Drs A T C CHAN and M E R O'BRIEN (Department of Medicine, Royal Marsden Hospital, London SW3 6JJ) write: A 39 year old woman presented in March 1989 with inflammatory breast cancer, which was treated with combination chemotherapy followed by surgery and radiotherapy. Local recurrence and bone metastases in February 1990 were treated with tamoxifen 20 mg daily. Further local recurrence in October 1990 was treated with aminoglutethimide 250 mg twice daily with replacement hydrocortisone 20 mg twice daily.

In May 1991 the patient developed pleural and liver metastases. Ibuprofen 400 mg four times a day failed to control pain, and on 4 June 1991 dexamethasone 2 mg three times a day and cimetidine 800 mg once daily were started for symptom control. On 8 June 1991 the patient developed a generalised urticarial rash with bronchospasm, which was treated with intravenous hydrocortisone and chlorpheniramine. Ibuprofen and cimetidine were stopped and dexamethasone continued. She had two further attacks in the next two days. On 11 June 1991 she received chemotherapy with antiemetic cover of intravenous dexamethasone 8 mg and metoclopramide 10 mg followed by dexamethasone 4 mg four times a day orally and had a further urticarial attack associated with bronchospasm. At this point we suspected that she was hypersensitive to dexamethasone and therefore withdrew the drug. There were no further attacks.

This case shows hypersensitivity to dexamethasone in a patient previously taking hydrocortisone for five months with no evidence of hypersensitivity. Hypersensitivity to hydrocortisone has been well documented,^{1,2} and intradermal testing was thought to have a role in predicting safe administration of an alternative steroid. In this case, however, pinprick testing followed by intradermal injections of hydrocortisone sodium succinate 100 g/l and dexamethasone sodium phosphate 4 g/l gave negative results and the patient declined further challenges. Awareness of this hypersensitivity phenomenon is important as dexamethasone is increasingly used as antiemetic therapy and for raised intracranial pressure, acute cord compression, and other common clinical conditions.

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Acute eosinophilic pneumonia induced by inhaled pentamidine isethionate

Drs M DUPON, M MALOU, A M ROGUES, and J Y LACUT (Hôpital Pellegrin, Tripode, 33076 Bordeaux Cedex, France) write: On 9 January 1991 a 25 year old woman with asymptomatic human immunodeficiency virus infection received a first aerosol of pentamidine isethionate for primary prevention of *Pneumocystis carinii* pneumonia: 300 mg of pentamidine isethionate was dissolved in 10 ml sterile water and inhaled in sitting position, over 15-25 minutes, via an ultrasonic nebuliser. She was admitted to hospital on 21 January because of a productive cough and mild dyspnoea which had appeared four days earlier. She had a history of recurrent eczema but no exposure to toxic products. She had smoked one pack of cigarettes daily for six years and was taking no medication. Her temperature was 38.2°C, and chest examination disclosed wheezing and ronchi. The white cell count was $10.22 \times 10^9/l$ with $2.09 \times 10^9/l$ eosinophils. Arterial partial pressure of oxygen was 10.8 kPa. A chest radiograph showed non-systematic disseminated infiltrates, chiefly in the two lower lobes. Bronchoalveolar lavage excluded *P. carinii* pneumonia. Screening for infection gave negative results, but total serum immunoglobulin IgE was high: 7370 IU (normal < 150 IU/l). An oral macrolide antibiotic was administered because we suspected an atypical pneumonia. One week later the symptoms disappeared. Two weeks later the chest radiograph was normal and eosinophils were only $0.58 \times 10^9/l$. On 11 February she received a second pentamidine isethionate aerosol; cough and dyspnoea reappeared two days later and eosinophils rose to $0.95 \times 10^9/l$. A chest radiograph showed recurrence of the pulmonary lesions. She recovered with no treatment, and *P. carinii* pneumonia prophylaxis was stopped. She had no relapse during 18 months' follow up, and results of lung function tests were normal.

Local side effects, including cough and wheezing, during inhalation of pentamidine isethionate occur in 33% of patients.¹ Other adverse reactions due to systemic absorption,

such as hypoglycaemia, rash, and acute renal failure, are rare.² This is the first report of acute eosinophilic pneumonia associated with nebulised pentamidine, whose half life in bronchoalveolar lavage fluid is at least 10-14 days.³ The aerosol device is unlikely to have been the cause.⁴ This adverse reaction is similar to that described for nitrofurantoin, sulphonamides, and penicillins and the mechanism is probably immuno-allergic.⁵

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Visual failure and optic atrophy associated with chlorambucil therapy

Drs P HJI YIANNAKIS and ANDREW J LARNER (Midland Centre for Neurosurgery and Neurology, Smethwick B67 7JX) write: We report a patient with visual failure and optic atrophy who was receiving long term chlorambucil for a low grade non-Hodgkin's lymphoma.

A 65 year old man noticed painless swellings in his neck and was found to have cervical, axillary, and inguinal lymphadenopathy without hepatosplenomegaly or systemic symptoms. Cervical lymph node biopsy showed a non-Hodgkin's lymphoma of follicular type. The patient received local cobalt beam radiotherapy (9 Gy) which produced regression of all lymph nodes, followed by maintenance therapy with chlorambucil 2 mg twice daily. Cessation of chlorambucil after two symptom free years was followed by prompt recrudescence of inguinal lymphadenopathy necessitating further local radiotherapy (18 Gy) and maintenance chlorambucil (2 mg twice daily).

Five years after his illness began the patient complained of progressive visual impairment. In April 1991 his visual acuities were 6/12 right and 6/24 left and the discs were noted to be pale. Goldmann fields showed a marked constriction on the right and obliteration of the central 20° on the left. Slightly raised intraocular

pressures were controlled with timolol 0.25% twice daily but with no improvement in acuity, which by March 1992 had deteriorated to 6/36 right and 6/60 left. Reduction in chlorambucil dose to 2 mg daily had no effect on visual symptoms.

The following investigations were normal or negative: full blood count; biochemical profile; thyroid function tests; serum vitamin B-12 and folate; syphilis serology; chest x ray examination; autoantibody screen; and cerebrospinal fluid pressure, cell count, cytology, and protein. Computed tomography of the brain showed moderate cerebral atrophy. Magnetic resonance imaging of the brain (before and after gadolinium) showed no evidence of intracranial lymphoma. Flash and pattern reversal stimulation failed to evoke clear cortical potentials, and electroretinograms were unrecordable.

By exclusion chlorambucil was the most likely cause of this patient's visual failure and optic atrophy. A direct effect of lymphoma on the optic nerves or chiasm was excluded by the normal magnetic resonance scan, and a non-metastatic complication was unlikely in the absence of lymphadenopathy or systemic symptoms. Failure to record an electroretinogram suggests a global insult to the retina, compatible with drug toxicity.

Chlorambucil has rarely been reported to produce ocular side effects, although these are common with many cancer chemotherapeutic agents.¹ Keratitis, oculomotor disturbances, haemorrhagic retinopathy, and disc oedema have been reported, generally as isolated cases after many years of chlorambucil use.² Textbooks also mention lid oedema, hyperpigmentation and oedema of the conjunctiva, and dry eyes in association with chlorambucil use.³ The Committee on Safety of Medicines (personal communication) has received only a single report of visual disorder associated with chlorambucil—namely, corneal opacity—and the manufacturers (Wellcome) have only a single report of optic neuritis, occurring on day 1 of chlorambucil treatment and not resolving on withdrawal. The mechanism for these various reactions, including the current case, is unknown.

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