Non-cardiogenic pulmonary oedema after ingestion of chlorothiazide

Dr FRANCIS J BOWDEN (St Vincent's Hospital, Melbourne, Victoria 3065, Australia) writes: A 66 year old woman with longstanding obesity who treated herself with frusemide was admitted to another hospital in July 1986 after suffering the sudden onset of severe breathlessness and wheeze followed by cardiovascular collapse while visiting her sister. On admission she had a blood pressure of 50 mm Hg, and blood gas estimation showed an oxygen pressure of 6 kPa. A chest radiograph showed features of acute pulmonary oedema, electrocardiography showed no ischaemia, and there was no increase in cardiac enzyme activity. She was intubated, resuscitated with intravenous fluids, and transferred to the intensive care unit, where a low wedge pressure was measured. She rapidly improved and was extubated within 48 hours. A gated blood pool scan showed an ejection fraction of 50%. She was discharged well with the diagnosis of non-cardiogenic pulmonary oedema of unknown cause.

In October she returned to her sister's home and within 10 minutes had again developed severe breathlessness and wheeze. The local doctor reported the patient as "wheezy, shutdown, and hypotensive" and treated her with intramuscular frusemide, hydrocortisone, and terbutaline sulphate and then transferred her to the local community hospital. There she required endotrachael intubation and intravenous inotropic support with adrenaline and dopamine. She was noted to be anuric and was transferred to this hospital. On arrival her blood pressure was 70 mm Hg and she was unconscious with no spontaneous movement of the limbs. The pupils were in mid-dilatation and reacted only sluggishly to light. There were fine crackles at both lung bases but there were no abnormal cardiovascular findings on physical examination. A chest radiograph showed bilateral pulmonary opacities consistent with pulmonary oedema but the heart size was normal. An electrocardiogram showed sinus tachycardia only. The pulmonary artery wedge pressure was 7 mm Hg. Echocardiography showed minimal aortic valve thickening, but the left ventricle was of normal size and contraction. Non-cardiogenic pulmonary oedema was again diagnosed. She was treated with intravenous fluid, continued inotropic support, and high dose steroids. She was easily weaned from the inotropes and extubated on day 3. She had a residual quadriparesis (computed tomography showed a right frontoparietal infarct and two left sided peripheral parietal lobe infarcts) and required prolonged rehabilitation.

On the first visit to her sister's house the patient had left her Lasix (frusemide) tablets at home. Her sister suggested that she try one of her Chlotride (chlorothiazide) tablets. About half an hour later she was in the intensive care unit but the Chlotride was not implicated at that stage. On the second visit to her sister she again forgot her Lasix tablets and once again her sister provided her with a Chlotride tablet. This time it was only 10 minutes between ingestion and collapse.

There are at least seven reported cases of non-cardiogenic pulmonary oedema caused by thiazides,[1-7] but this is the first implicating chlorothiazide. The mechanism is not clearly understood but represents a type of anaphylactic reaction with increased permeability of the pulmonary vasculature.[2] Right heart catheterisation typically shows low right atrial and pulmonary artery wedge pressures.[1 3 4] Cardiorespiratory collapse may occur rapidly and the patient requires endotracheal intubation, intravenous fluid replacement, and inotropic support. The use of steroids is widespread but unproved. The association between thiazides and life threatening reactions is not widely known. Our patient had been in the intensive care unit of another hospital with a life threatening illness after ingesting a commonly prescribed drug and the connection was not made until she was again admitted and had suffered a severe degree of global cerebral hypoxia. Non-cardiogenic pulmonary oedema is a rare complication of treatment with thiazide diuretics but should be considered in patients presenting with bilateral pulmonary infiltrates, cardiorespiratory collapse, and evidence of low cardiac filling pressures.

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Pancreatitis associated with pentamidine by aerosol

Drs B HERER, T CHINET, S LABRUNE, M A COLLIGNON, J CHRETIEN, and G HUCHON (Université René Descartes, Hôpital Laënnec, 75340 Paris, France) write: Pancreatitis has been reported during parenteral pentamidine treatment in patients with AIDS with *Pneumocystis carinii* pneumonia.[1] We describe two patients with AIDS who developed pancreatitis after receiving pentamidine by aerosol.[2 3]

Case 1—An HIV positive 51 year old white man was treated for *P carinii* pneumonia with pentamidine mesylate (Lomidine, Specia Laboratories, France) by aerosol 4 mg/kg every 24 hours. Creatinine and glucose concentrations stayed normal, but amylase and lipase activities increased after four days of pentamidine treatment without clinical symptoms. Eight days after the onset of treatment the dose of pentamidine was reduced in frequency to once every 48 hours and serum amylase and lipase values fell. Clinical cure of *P carinii* pneumonia was obtained after 21 days. Tuberculosis was diagnosed and antituberculosis treatment was started and pentamidine stopped; amylase and lipase values remained normal.

Case 2—A 34 year old HIV positive white woman was treated for *P carinii* pneumonia with pentamidine mesylate by aerosol 4 mg/kg every 24 hours. Creatinine and glucose values stayed normal throughout, as did the serum amylase value. On day 18 failure to respond was documented and treatment was changed to co-trimoxazole; 17 days later the patient developed abdominal pain. Serum amylase and lipase values had increased, and a computed tomographic scan of the abdomen showed enlargement of the pancreas. Serum pentamidine concentration (35 days after discontinuation of aerosol treatment) was 15 µg/l. Amylase and lipase values did not return to baseline until 6 weeks after withdrawal of co-trimoxazole, at the same time that the computed tomogram became normal and the serum pentamidine concentration fell below 5 µg/l. Co-trimoxazole was later reintroduced for prophylaxis without relapse of pancreatitis.

Pancreatic lesions in AIDS may be due to opportunistic infections, tumour infiltration, and adverse effects of therapy.[4] In our patients opportunistic infections or tumours were not documented. An iatrogenic pancreatitis seems likely in view of the temporal relation between the biological and morphological changes. The second patient received co-trimoxazole, which has been associated with pancreatitis,[5] but there was no relapse on rechallenge with co-trimoxazole.

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Fatal anaphylaxis associated with ciprofloxacin in a patient with AIDS related complex

Drs B PETERS and A J PINCHING (Department of Immunology, St Mary's Hospital Medical School, London W2 1PG) write: A 32 year old patient was diagnosed as having the AIDS related complex in December 1987 and was prescribed zidovudine 200 mg every four hours. He developed left otitis media with a purulent discharge yielding *Pseudomonas* sp. He initially received a combination of amoxycillin and gentamicin, but after a limited clinical response he was treated with oral ciprofloxacin 500 mg twice daily for 10 days. He made a clinical recovery following the ciprofloxacin and had no adverse effects, specifically no rash. However, the otitis media recurred four weeks later, although, apart from local symptoms, he was well.

He was prescribed a second course of oral ciprofloxacin. Ten minutes after the first dose he developed vomiting, dizziness, dyspnoea, and epigastric pain. On admission a few hours later he was profoundly hypotensive (systolic blood pressure 55 mm Hg), with pulse 110 beats/min, and anuric. Immediate resuscitation included several doses of intramuscular adrenaline 1 ml 1/1000, which initially restored his blood pressure. Blood cultures taken during this period were negative. About six hours after admission he had an asystolic cardiac arrest. Resuscitation restored a normal cardiac rhythm, but he remained unconscious with extensive bilateral brain stem signs and died the next day.

The close temporal relation between drug administration and symptoms make anaphylaxis secondary to ciprofloxacin the likely event, despite the lack of allergic features during the first treatment course.

There have been 22 cases of severe anaphylactic reactions possibly due to ciprofloxacin reported world wide, among which severe hypotension was noted in 14 (unpublished reports submitted to Bayer, October 1988). Two patients died and one of these was a patient with AIDS who developed anaphylaxis with severe hypotension and additionally had Stevens-Johnson syndrome following oral ciprofloxacin. An increased frequency of allergic reactions in patients with AIDS and AIDS related complex has been reported,[1 2] though anaphylaxis has been rare. This case emphasises the need for continued vigilance for adverse drug reactions in such patients, especially with relatively new compounds. Whether or not ciprofloxacin is especially likely to cause anaphylaxis in this group remains to be determined.

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