Exacerbation of Goodpasture’s syndrome after inadvertent exposure to hydrocarbon fumes

Circumstantial evidence suggests that an association exists between Goodpasture’s syndrome and exposure to hydrocarbon fumes, but there are no studies that either quantify industrial exposure or document abuse of hydrocarbon products. We report a case indicating that Goodpasture’s syndrome may occur in seemingly benign environments and may be reactivated by further exposure to hydrocarbons.

Case report

A 16 year old girl presented with a cough of six weeks’ duration and haemoptysis and dyspnoea of nine days’ duration. For 10 months she had worked as a student typist in a bank, where she was exposed to methylene chloride and 1,1,1-trichloroethane when the printing machine was cleaned. There had been no exhaust ventilation. On admission she was pale and scattered expiratory crepitations were noted. She was anaemic (haemoglobin 8.5 g/dl, normocytic, normochromic) with lymphocytopenia (731 with white cell count 4.3 x 10^9/l) and renal impairment (creatinine concentration 0.11 mmol/l (1.24 mg/100 ml), urea 6.0 mmol/l (359 mg/100 ml) and creatinine clearance 53 ml/min/1.73 m^2). Microscopy of centrifuged urine showed 25,000 red cells/ml (normal <500), 105 red cell casts/ml, and 45 granular casts/ml. Urinary protein excretion was 1.03 g/24 h. Results of intravenous pyelography were normal. Chest x ray examination showed a diffuse pulmonary infiltrate. Arterial blood gas tensions (room air) were pH 7.45, arterial oxygen pressure 11.9 kPa (89 mm Hg), and arterial carbon dioxide pressure 5.1 kPa (38 mm Hg). Forced expiratory volume in one second was 2.31 (92% of predicted value) and vital capacity 2.41 (78% of predicted). Single breath carbon monoxide pulmonary diffusion capacity was 73.6%, and alveolar-arterial oxygen tension difference was 5.9 kPa (44 mm Hg) (normal 1.6 kPa (12 mm Hg)). Antiglomerular basement membrane antibody was present in serum; results of blood immunology tests were otherwise normal, and infection titres were insignificant. HLA typing yielded A1, A11, Bw39, B7, and DR4.

Renal biopsy findings included focal fibrinoid necrosis, one capsular adhesion, and one focal crescent out of 40 glomeruli, with bright linear IgG and moderate linear complement on immunofluorescence. By day six, after treatment with methylprednisolone 1 g/day for three days followed by prednisolone 100 mg/day, cyclophosphamide 2 mg/kg/day, and blood transfusion, chest x ray appearances had returned to normal. Creatinine clearance improved to 103 ml/min/1.73 m^2 by day 14, but 24 hour urinary protein loss was 1.5 g and carbon monoxide diffusing capacity was 58%; and alveolar-arterial oxygen tension difference was 4.4 kPa (33 mm Hg) on day 14, when she was discharged.

Ten days after discharge and two days after inhaling an insect spray she presented again with bilateral loin pain and macroscopic haematuria. Haemoglobin concentration was 10.3 g/dl, creatinine concentration 0.15 mmol/l (1.69 mg/100 ml) mmol, creatinine clearance 55 ml/min/1.73 m^2, urinary protein 3.9-5.4 g/24 h, and carbon monoxide pulmonary diffusing capacity 50%; arterial blood gas tensions, chest x ray appearances, and results of spirometry remained normal. Renal biopsy showed more extensive and prevalent focal necrotising glomerulonephritis with crescents. Immunofluorescence findings were unchanged.

Methylprednisolone 1 g was administered, prednisone 120 mg/day and cyclophosphamide were continued, and 12 plasma exchanges of two litres each were performed over three weeks. Symptoms subsided within three weeks. Antinuclear and basement membrane antibody was persistently absent after the eleventh plasma exchange. Eight weeks after the start of plasma exchange the creatinine clearance was 114 ml/min/1.73 m^2, urinary protein 2-3 g/24 h, and creatinine 0.09 mmol/l (1.02 mg/100 ml) and urine microscopy showed 24,000 red cells and 15 hyaline casts/ml.

Comment

This report shows the association between exposure to hydrocarbon fumes and Goodpasture’s syndrome. This association is further suggested by exacerbation of disease activity in this patient after inadvertent rechallenge with inhaled hydrocarbons. The initial hydrocarbon exposure was seemingly inconsequential and shows that a causal relationship with the work environment is necessary in all patients with Goodpasture’s syndrome.

Exacerbation of symptoms in this girl occurred after inhalation at home of an insect killer that contained trichloroethane, and, although this does not prove cause and effect, there was no other apparent cause for this exacerbation. A subsequent investigation of non-listed components of many domestic products showed that almost all aerosols contain trichloroethane and, moreover, that methylene chloride is used to decaffeinate coffee in Australia. Hydrocarbons are thus readily available, and as they may exacerbate Goodpasture’s syndrome inhalation of all products containing hydrocarbons, particularly aerosols, should be avoided by patients with the disease, particularly in its early phase.

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Potentiation of oral anticoagulants by ketoconazole

The oral antifungal agent ketoconazole (Nizoral) has been available for the past two to three years. Currently the manufacturer’s data sheet gives no reference to potential interaction of this drug with oral anticoagulants. I report a case in which treatment with ketoconazole potentiated the anticoagulant effect of warfarin.

Case report

A 75 year old woman had been treated with warfarin for three years. In 1976 she had suffered a myocardial infarction complicated by a pulmonary embolism, after which she received three months’ treatment with warfarin. In 1980, after an episode of chest pain and dyspnoea, recurrent pulmonary embolus were diagnosed and confirmed by ventilation and perfusion scanning. She was given anticoagulant drugs and it was decided to continue these indefinitely. Anticoagulant control presented no major problem, with her British comparative ratio staying in the range 1.6-3.5. Minor adjustments were made to the dosage of warfarin, and the average weekly dosage ranged from 17 to 24 mg.

In March 1983 her general practitioner prescribed ketoconazole 200 mg twice daily for a chronic vaginal thrush infection. The blood clotting ratio two days after ketoconazole was started was 1.9; her average weekly dosage of warfarin was 19 mg and had been unchanged for the previous 13 months. After three weeks’ treatment with ketoconazole she complained of spontaneous bruising and reported to the clinic, where her British comparative ratio was found to be 5.4. Full blood count, platelet count, and liver function tests gave normal results. Treatment with ketoconazole was stopped and warfarin dosage reduced. She was not receiving any other drugs. Over the next three weeks her warfarin control was reestablished at previous levels.

Comment

In this case no other drug was taken and ketoconazole is therefore clearly implicated in potentiating the effect of warfarin. An extensive list of drugs capable of interacting with warfarin was recently re-
Acute brain stem stroke during neck manipulation

Manipulation of the neck as a cause of infarction of the brain or spinal cord is thought to be rare, but this may not be so. We report the occurrence of brain stem stroke during neck manipulation.

Case report

A 31 year old man in good health consulted an osteopath for relief of neck pain. Neck manipulation by the osteopath proceeded no further than rotation of the head to the right. Immediately the patient complained of tingling of the right side of the face, right arm, and right leg followed by slurred speech, double vision, and difficulty in closing the left eye. He was examined at this hospital one hour after the onset of his stroke. There was an incomplete left facial palsy of the lower motor neurone type, diplopia, and coarse nystagmus on looking to the right, depression of sensation to pinprick and light touch on the right side of the face, dysarthria, and ataxia of the right arm and leg. The tendon reflexes were not exaggerated, and both plantar responses were downgoing. There was no limb weakness but he was unable to stand because of unsteadiness. A bruit was heard over the left carotid artery. Other examination findings were normal.

Full blood count, urea and electrolyte concentrations, liver function values, blood sugar and lipid concentrations, electrocardiogram, results of cardiac ultrasound, and radiographs of skull, chest, and cervical spine were normal. A CT brain scan showed a poorly defined area of low attenuation near the fourth ventricle in the cerebellum but was otherwise normal. An arch aortogram one week after the stroke showed an irregular and narrowed left vertebral artery, with occlusion at the site of its passage between the first and second cervical vertebrae. Some collateral circulation was established (figure). These changes were consistent with a traumatic thrombosis of this vessel. Angiographic appearances of the other cranial vessels were normal.

The patient improved without treatment. Ten days after the stroke he had slight nystagmus to the right, slight ataxia of the right arm and leg, but a pronounced left facial palsy. Six months after the stroke the facial palsy was barely noticeable and he had returned to his job as a fork lift driver.

Comment

This patient apparently had a traumatic occlusion of his left vertebral artery during rotation of the neck, resulting in acute brain stem and cerebellar ischaemia and probable infarction. Careful review of his previous health, family history, and other possible trauma to the neck was unrewarding.

Thrombosis of this vessel during neck manipulation has been recognised as a cause of brain stem, cerebellar, or spinal cord infarction since 1947, but by 1981 only 52 patients had been reported. A recent American survey, however, yielded 360 additional cases. In Germany the Society of Manipulative Medicine has kept a registry of such cases. This injury tends to occur in the relatively young (mean aged 37 years), the mortality tends to be high, and anticoagulants in the period immediately after the stroke have therefore been recommended.

This injury usually occurs at the atlantoaxial level and is determined by the anatomical relations of the vertebral arteries. These vessels are relatively fixed in the transverse foramina between the first and second cervical vertebrae. The atlantoaxial joint is the site of rotation and of some tilting of the head and neck. These factors favour the stretching, temporary occlusion, or thrombosis of the vertebral arteries during manipulation of the neck. Other manoeuvres associated with head turning have also caused strokes—for example, falls, painting the ceiling, yoga, gymnastics, archery, and head turning while driving a car. To our knowledge there have been no other reports from Britain of stroke during neck manipulation. In view of the American and German experience we suspect that such injury may have gone unnoticed or unreported.