hormone this may help to explain the association of cigarette smoking with various menstrual disorders, including an early menopause.[2] Thus smoking may have hormonal effects due, at least partly, to an increased release of dopamine.

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Department of Medicine, Dartmouth Medical School, Hanover, New Hampshire 03756, United States of America
JOHN A BARON, MD, MS, associate professor of medicine

Department of Clinical Endocrinology, Imperial Cancer Research Fund, London
R D BULBROOK, PHD, head of clinical endocrinology
D Y WANG, PHD, staff scientist

Netherlands Cancer Institute, Amsterdam
H G KWA, PHD, staff scientist

Correspondence to: Dr Baron.

Leucocytoclastic vasculitis and pneumonitis induced by metformin

We present what is to the best of our knowledge the first reported case of vasculitis and pneumonitis induced by metformin.

Case report

A 59 year old woman was admitted to the department of dermatology because of a purpuric eruption on her legs, thighs, buttocks, forearms, and lower abdomen that had started two weeks previously. During this period the patient had also experienced arthralgia of the ankles without fever. For the past five years she had been treated for non-insulin-dependent diabetes mellitus with glibenclamide, 10 mg/day. Four months before admission she had also been given metformin, 2·55 g/day.

On admission the patient was in good general condition; her blood pressure was 130/80 mm Hg, she had a pulse rate of 82 beats/min, and a temperature of 36·5°C. Slightly indurated purpuric papules were seen on the lower abdomen, thighs, forearms, buttocks, and legs. Some of those on the legs had delicate haemorrhagic vesicles in the centre. Other findings included an apical systolic murmur with normal pulses and a mild, painful swelling of the ankles. Chest radiography showed bilateral basilar pulmonary infiltrates. Specimens taken by punch biopsy of a purpuric papule from the thigh showed an intense perivascular polymorphonuclear infiltrate, fibrinoid deposits in the small dermal vessels, and fragmented neutrophils (nuclear "dust") consistent with leucocytoclastic vasculitis.[1] Direct immunofluorescence did not show evidence of immune deposits of IgM, IgG, or C3. Glibenclamide and metformin were discontinued and replaced with injections of insulin. Prednisone 0·5 mg/kg/day was given orally and rapidly tapered according to her clinical condition. Repeated chest radiography 10 days after beginning treatment showed a clear diminution in the size of the lung infiltrates. The patient was discharged after four weeks and prescribed 20 mg/day of prednisone and daily injections of insulin.

The rapid improvement of the eruption after discontinuing metformin and glibenclamide suggested the possibility of the patient's hypersensitivity to these drugs. Other causes for leucocytoclastic vasculitis were ruled out as the laboratory results—antinuclear factor, latex, Rose-Waaler, C3, hepatitis B surface antigen, protein electrophoresis, and cryoglobulin—were negative or within normal limits.

The patient was admitted to the department of medicine two weeks after discontinuing prednisone. Metformin was reintroduced, and two days later an identical eruption was observed. This eruption disappeared progressively after metformin was stopped.

Comment

Vasculitis is one of the most common and severe forms of drug eruption.[2] The similarity between the experimental Arthus phenomenon and the histological findings, in which fibrinoid and polymorphonuclear infiltrates are predominant features, suggests that immune complexes play a part in the pathogenesis of leucocytoclastic vasculitis.[2] The failure to find immunoglobulin in the lesion may have been due to its rapid clearance—that is, within eight to 18 hours—as in the Arthus phenomenon.

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Departments of Dermatology and Medicine, Hadassah University Hospital, IL-91120 Jerusalem, Israel
L KLAPHOLZ, MD, registrar in dermatology
E LEITERSDORF, MD, lecturer in medicine
L WEINRAUCH, MD, acting head, department of dermatology

Correspondence to: Dr Weinrauch.

Chylopericardium, chylothorax, and hypobetalipoproteinaemia

We describe a patient with chylous effusions in the pericardial and pleural spaces who also had familial hypobetalipoproteinaemia. A family study was performed.

Case report

A 21 year old woman had developed a symptomatic left chylothorax at the age of 9 (1973). A chest *x* ray film after aspiration showed that the heart was enlarged and pear shaped and an electrocardiogram showed low voltage complexes. Further cardiac investigations were recommended but not performed. After reaccumulation of the pleural effusion decortication of the left lung was performed. Preoperative lymphangiography and operative blue dye injections failed to disclose the site of leakage. There were no comments about the heart.

Over the next four years the patient was asymptomatic but chest radiographs showed further, progressive cardiac enlargement. She was admitted for investigation. Pericardial aspiration produced 270 ml chyle. After aspiration the heart size was normal. Serum lipid analysis was not performed.

Over the next three years the pericardial effusion reaccumulated. During three weeks in 1980 she developed anorexia, weight loss, lethargy, dyspnoea, and ankle swelling. On admission she was thin and pale and had the physical signs of a pericardial effusion. This was confirmed by echocardiography. Examination showed nothing else of note. Her haemoglobin concentration was 107 g/l with iron deficient indices and frequent acanthocytes in the blood film. Serum lipoprotein analysis (see table) showed hypobetalipoproteinaemia. Results of the chromium chloride test for protein losing enteropathy, faecal fat estimation, and findings on bipedal lymphangiography were normal.

Plasma low density lipoprotein cholesterol concentrations of members of reported family

Relationship to propositus	Low density lipoprotein cholesterol concentration (mmol/l)	Comment
Propositus:		
Preoperative	1·38	Hypobetalipoproteinaemia
Postoperative	2·00	Hypobetalipoproteinaemia
Sister 1	1·49	Hypobetalipoproteinaemia
Sister 2	0·96	Hypobetalipoproteinaemia
Mother	1·62	Hypobetalipoproteinaemia
Father	1·48	Hypobetalipoproteinaemia
Paternal aunt	2·06	Hypobetalipoproteinaemia
Paternal grandmother	2·78	Normal
Paternal grandfather	—	Dead
Maternal uncle	3·65	Normal
Maternal aunt	2·14	Borderline
Maternal grandmother	3·87	Normal
Maternal grandfather	3·11	Normal

Conversion: SI to traditional units—Cholesterol: 1 mmol/l≈38·6 mg/100 ml.

Laparotomy and exploration of the pericardium through an abdominal approach disclosed an area of lymphangiectasia 1·5 cm diameter in the small bowel mesentery. The pericardium was opened atraumatically and found to contain 1 litre of heavily bloodstained chyle (haemoglobin concentration 47 g/l). The pericardium was only slightly thickened and the heart normal. A pericardial window was formed.

Recovery was uneventful and during the subsequent five years the pericardial effusion did not reaccumulate. Blood films showed scanty if any acanthocytes but lipoprotein values remained consistent with hypobetalipoproteinaemia.

Family study—The table gives the results of lipoprotein analysis in family members. Hypobetalipoproteinaemia is recorded when the low density lipoprotein cholesterol concentration is below the age and sex related fifth percentile in our laboratory. The patient had acanthocytes in her preoperative blood films. Other family members did not. Each family member was found to be asymptomatic and normal on physical examination. Each had a normal chest x ray picture and echocardiogram.

Comment

This patient had familial hypobetalipoproteinaemia. The precise incidence of the condition is uncertain. Only the patient had chylous effusions. Chylothorax presented at the age of 9. We think that she had a pericardial effusion at that time, though chylopericardium was not confirmed until four years later and may have resulted from surgical treatment of the chylothorax.

There have been only three reported instances of idiopathic chylothorax and chylopericardium occurring in the same patient.[1-3] Such idiopathic chylous effusions are probably the result of occult lymphatic abnormalities. Our patient had mesenteric lymphangiectasia. Intestinal lymphangiectasia is well known to be associated with chylous effusions[4] and has been described in hypobetalipoproteinaemia.[5] Chylous effusions and hypobetalipoproteinaemia, however, are not a recognised association. In our patient the coincidence of two rare lipid transport abnormalities may not have been a chance association.

The chylopericardium was cured by formation of a pericardial window without ligation of the thoracic duct.

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St Thomas's Hospital, London SE1 7EH
P T WILMSHURST, MRCP, senior registrar in cardiology
J P BURNIE, MB, house physician, department of medicine
P R TURNER, PHD, research fellow in chemical pathology
A KUBIE, MB, senior registrar in haematology

Correspondence to: Dr Wilmshurst.

Epidemics of fractures during periods of snow and ice

There is an obvious increase in accidents and casualties during periods of snow and ice each winter, but until recently reliable figures indicating the extent of this increase were not available. Winter epidemics of fractures have been monitored in the accident and emergency department at this hospital since 1978. Here we compare the results for the winter 1978-9 with those recorded in the winters of 1981-2 and 1984-5.

Patients, methods, and results

Fractures sustained by pedestrians during periods of snow and ice were monitored in the accident and emergency department at this hospital from 1978 onwards, and the first report recording the casualties in the winters 1978-9 and 1979-80 was published five years ago.[1] To confirm the alarming results fractures sustained during periods of snow were monitored in the winter of 1981-2, and recently a third survey conducted in December 1984 and January to February 1985 was completed. Results of all three surveys were studied.

Snow and ice fractures were those sustained on days when over 70% of walking surfaces were covered with snow or ice, or both, and control fractures were those sustained on dry days with comparable hours of daylight and date. Only patients with fractured limb bones were monitored.

The table shows the results. Of the 824 fractures recorded, 656 occurred during periods of snow and ice—almost two and a half times more frequently than control fractures. Most fractures were caused by pedestrians falling on uncleared pavements, which resulted in a persistent, sharp increase in fractures commonly linked with slipping and landing on an outstretched arm, such as fractures of the arm, lower forearm, and wrist (on certain days fractures of the wrist reached a 15-fold increase). Adults (aged 31-60), and in particular old people (aged 61 and over), were the most common victims of fractures.

The most disturbing and challenging fact to emerge from the study was the undiminished size of these epidemics of fractures during the three surveys.

Comment

The frequency with which injuries occurred during periods of snow and ice in this study was such that in a population of one million there would be 60 new casualties with fractures attending every day, the equivalent of a "major accident" or "moderate disaster."[2-4] Because of the proved reappearance of such fractures with every spell of snow and ice, however, we should now coin a new term, such as "periodical major accident," for this environmental health hazard. The scale of the snow and ice injuries recorded in Cardiff has recently been confirmed by similar results in a multicentre study conducted in a similar way in six other large accident and emergency departments in south Wales, Avon, and the Thames Valley (unpublished observations). Because most of the fractures were sustained by unprotected pedestrians slipping on untreated snow or icy pavements, the cleaning of pavements is even more important for the prevention of fractures than the cleaning of roads, where the number of people injured in vehicles is very small by comparison.

After the first report[1] the size of this problem gained some publicity in the national and local press; there was also a parliamentary inquiry in the House of Commons and talks between the health and local authorities. Although in some areas improved gritting and salting of roads has given the impression that something has been done (it is now common to see pedestrians walking on the cleaned roads in snowy periods as they are safer than the pavements), the real cause, the slippery pavements, remains unattended. Renewed efforts are needed to prompt administrative and legal changes regarding the clearing of pavements if such epidemics of fractures are to be prevented in future.

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Cardiff Royal Infirmary, Cardiff CF2 1SZ
Z A RALIS, MD, FCCS, senior lecturer in orthopaedics and honorary consultant in accident and emergency medicine

Fractures monitored during three surveys 1978-85

	1st Survey (1978-9)	2nd Survey (1981-2)	3rd Survey (1984-5)	All surveys (1978-85)
No of fractures	278	299	247	824
No of snow and ice days	4	12	5	21
No of control days	8	2	3	13
Mean No of fractures per snow and ice day	42·75	23·33	41	31·24
Mean No of fractures per control day	13·38	9·5	14	12·92
% (SE) of fractures occurring on snow and ice days	76·16 (2·55)	71·06 (2·62)	74·55 (2·77)	70·7 (1·59)
Increase in fractures on snow and ice days	×3·2	×2·46	×2·93	×2·4