peridol and fluphenazine.\(^1\) Bromocriptine, a selective D2 dopaminergic agonist, also stimulates ADH secretion in normal subjects,\(^2\) and has been reported to cause hyponatraemia, probably by this mechanism.\(^3\)

Hence it is possible that chronic blockade of dopamine receptors on magnocellular neurons by flupenthixol, a combined D1 D2 dopaminergic antagonist, may have rendered them supersensitive to the effects of dopamine formed from the prescribed L-dopa. Recent studies of the reflex control of ADH release from magnocellular neurons suggest that the system is not inflexibly 'hard-wired', but functionally adaptive, reflecting complex and plastic interactions between magnocellular and other dopaminergic agents. Its occurrence following the inadvertent use of L-dopa/carbidopa in a patient with drug-induced parkinsonism suggests that this is an effect of the drug per se and not a reflection of underlying neuropathology.

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**References**


**Cutaneous leukocytoclastic vasculitis preceding renal cancer**

Sir,

Cutaneous leukocytoclastic vasculitis (CLV) has been sporadically reported in association with malignant haematological diseases.\(^1\) Three cases of CLV preceding renal carcinoma have been reported.\(^1,2\) I describe a patient in whom the occurrence of CLV led to the discovery of clear cell renal carcinoma.

A 56 year old man presented with a one week history of palpable purpura of lower limbs evolving into papular, vesicular and pustular lesions with umbilications, and fever and arthritis of the right ankle joint. Skin biopsy revealed small vessel vasculitis with intense intravascular and perivascular neutrophil infiltration, leukocytoclasia, fibrinoid necrosis of the vessel walls, and extravasation of erythrocytes.

Ultrasound of the abdomen showed a right renal tumour. A tumour measuring 4 × 5 cm without capsular, vascular or lymph node involvement was removed at nephrectomy. Histopathology revealed clear cell renal carcinoma and crescentic glomerulonephritis suggestive of microscopic polyarteritis.

One month after nephrectomy, the urine showed proteinuria (1+), and numerous dysmorphic erythrocytes. He was put on oral cyclophosphamide (100 mg/day) and prednisolone (60 mg/day). Over the next 3 months, the urinary abnormalities cleared and renal function returned to normal. Repeat computed tomographic scans showed no tumour relapse or metastases. Twenty months after nephrectomy, purpuric lesions and arthritis similar to those of the initial presentation appeared with active urinary sediment and deranged renal function (BUN 7 mmol/L; creatinine 146 mmol/L). The recurrence as with the original episode was anti-neutrophil cytoplasmic antibody negative. In view of the recurrence of CLV and microscopic polyarteritis of the solitary left kidney, therapy with cyclophosphamide and prednisolone was reinstituted, and one month later neither vasculitis nor tumour metastases was seen. The patient was seen 24 months later without relapse of CLV or neoplasia.

Paraneoplastic manifestations of renal cancer (internist's tumour) are frequent and numerous.\(^4\) Renal tumour antigen may bind up in circulating immune complexes and induce CLV\(^1\) by activating the complement cascade causing lysosomal enzyme release from the accumulated polymorphonuclear cells leading to vessel wall injury, thrombosis, and haemorrhage.\(^5\) CLV has not hitherto been recognized as a cutaneous paraneoplastic syndrome. It should perhaps be included in the long list of paraneoplastic manifestations of renal cancer, although the relapse of CLV without apparent recurrence of tumour suggest coincidence.

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**References**

Subclavian vein thrombosis in a patient with Raynaud's disease

Sir,

Axillary or subclavian vein thrombosis (ASVT) accounts for 1–2% of all deep venous thrombosis. There are three general aetiologies of ASVT: (a) spontaneous; (b) catheter-associated; and (c) miscellaneous causative factors, including trauma, tumours, intravenous drugs abuse, and systemic disease.1 We would like to report a case of subclavian vein thrombosis complicated with pulmonary embolism in a patient with Raynaud's disease. To our knowledge, there has been no previous report of this clinical association.

A 26 year old woman with a 2 year history of Raynaud's phenomenon presented with gradual swelling of the left arm. There was no history of trauma, strenuous exercise, or superficial thrombophlebitis nor previous deep vein thrombosis. She was not taking birth control pills. Examination showed the left arm was swollen and there were prominent, distended superficial veins; all other systems were normal. Laboratory values including white blood cell count, haemoglobin, platelets, ESR, prothrombin time, partial thromboplastin time, fibrinogen level, SMA-12 and urinalysis were all normal, as well as a chest X-ray. A venogram showed thrombosis of the left subclavian vein with collateral flow. Heparin therapy was started. Some hours after admission, the patient reported sudden onset of pleuritic left-sided chest pain without dyspnoea or haemoptysis. A perfusion lung scan showed segmental defects in the right middle and left lower lobes. A radionuclide venography of the legs was normal. Treatment with heparin was continued, symptoms gradually subsided, and the patient was discharged 8 days later with oral warfarin. During the hospital course, tests for rheumatoid factor, anti-nuclear antibodies, VDRL, cryoglobulins, antibodies to extractable nuclear antigen (ENA), serum electrophoresis, and the cervical spine and mains X-ray films were negative or normal. After stopping warfarin 6 months later, a coagulation study including prothrombin time, partial thromboplastin time, thrombin time, Howell time, fibrinogen, anti-thrombin III, protein C, plasminogen, tissue thromboplastin inhibition (TTI) test and platelet neutralization procedure (PNP) test, was normal; serum anti-cardiolipin antibodies were negative and a nailfold capillaroscopy was normal.

Raised blood viscosity, enhanced platelet aggregation and abnormalities in coagulation–fibrinolytic activity, have been reported in patients with Raynaud's phenomenon, especially in the secondary form.2–5 In view of those abnormalities all leading to a hypercoagulable state, it is tempting to speculate that our patient's subclavian vein thrombosis was associated with her underlying disease, although her basic coagulation study was normal. We await further reports of similar cases, which would strengthen this impression.

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References

Acute granulocytopenia in concomitant treatment of clozapine and methimazole

Sir,

The major agents employed in the chemotherapy of thyrotoxicosis are drugs of the thionamide class. Methimazole is one of the most widely used anti-thyroid agents. Adverse reactions occur in a small percentage of patients taking methimazole. The most significant of these are skin rash, drug fever, and agranulocytosis (0.1%). Of these, the last reaction is the most serious and occurs in a fraction of 1% of the patients. Agranulocytosis, like the other adverse reactions, generally occurs within the first few weeks or months of treatment. It is accompanied by fever and sore throat, and hence, when therapy is begun, the patient should be instructed to discontinue the drug and notify the physician immediately should these symptoms develop. This precaution is more important than the frequent measurement of leucocytes counts, since agranulocytosis may develop within a day or two.12 A patient with paranoid schizophrenia and methimazole-control led Graves' disease, with hallucinatory symptomatology unrestrained by typical neuroleptics was switched to clozapine, a neuroleptic that needs weekly blood cell count for its potential to induce agranulocytosis, and suddenly developed granulocytopenia.

A 48 year old woman presented a 23 year history of paranoid schizophrenia with auditory hallucinations, anxiety and systematized delusions. In 1990 Graves' disease was diagnosed and methimazole 150 mg per day was started. She was treated in the last years with haloperidol 15 mg per day, anti-cholinergic compounds and lorazepam 5 mg per day. She also entered trials with...
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