bladder. At rest plasma noradrenaline concentration was increased to 14·0 nmol/l (2369 ng/l; normal (SD) 1·42 (0·61) nmol/l (240 (103) ng/l)) but plasma adrenaline concentration was normal (0·13 nmol/l (24 ng/l); normal 0·17 (0·07) nmol/l (31 (13) ng/l)). Before surgical removal of the tumour seven experiments were performed with informed consent.

On day 1 the effects of micturition on blood pressure and plasma catecholamines were studied without treatment (M1) and after one sublingual dose of 10 mg nifedipine (M2, 3, 4). After one week of treatment with nifedipine 10 mg three times daily, another experiment was performed

response to exogenous noradrenaline has been observed during treatment with nifedipine in normotensive patients.[3] Our patient who had very high plasma noradrenaline concentrations after micturition showed a total abolition of the blood pressure response after experiments M3, M4, and M5. This might be explained by the exhaustion of intracellular calcium stores due to chronic exposure to the high circulating noradrenaline concentrations when the agent to block calcium influx has taken effect.[4]
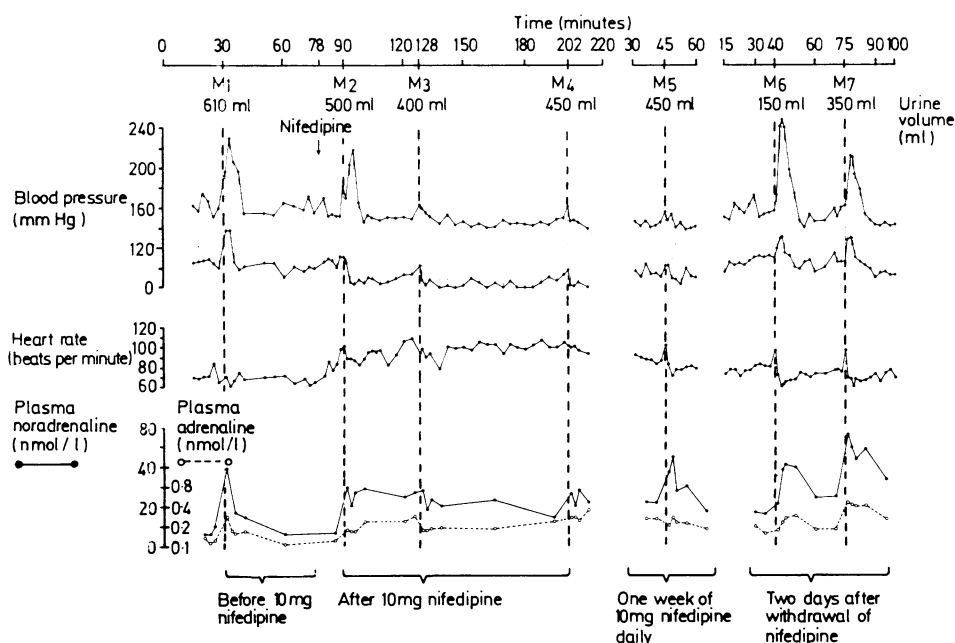
Details of blood pressure, heart rate, and plasma catecholamines (log scale) before and after micturition (M).

(M5). A control experiment was performed two days after stopping nifedipine (M6 and 7). In every experiment the patient voided spontaneously in the supine position. No other medication was used. Before and every two minutes after each micturition blood pressure, heart rate, and plasma catecholamines[2] were measured. Urinary excretion of catecholamines over 24 hours and vanillylmandelic acid content were measured twice both before and during the last two days of treatment with nifedipine.

Without nifedipine, micturition provoked a steep rise in blood pressure (M1, 6, 7), accompanied by a throbbing headache, nausea, and pallor. Acute treatment (M3 and 4) and treatment for one week with nifedipine prevented both the severe rise in blood pressure and all accompanying symptoms, despite similar rises in plasma catecholamines and unchanged urinary excretion of noradrenaline over 24 hours. The noradrenaline concentration was 126 nmol/mmol creatinine and became 131 nmol/mmol creatinine (normal 5-34). Vanillylmandelic acid concentration measured 4·1 nmol/mmol creatinine and afterwards became 4·8 nmol/mmol creatinine (normal 1·2-4·5).

Comment

Our case report shows that an agent which blocks the entry of calcium can prevent severe hypertensive spells which are provoked by the mechanical stimulation of a phaeochromocytoma.

This patient provided an excellent opportunity to study the effect of nifedipine because the rise in blood pressure and plasma catecholamine concentrations could be reproducibly provoked by micturition. Acute and hebdomadal treatment with nifedipine prevented the steep rise in systolic and diastolic blood pressure. The high systolic blood pressure rise after the sublingual dose of 10 mg might be explained by the short interval between the nifedipine dose and M2.

The complete absence of a rise in blood pressure after experiments M3 and M4 might be explained by one of three mechanisms: exhaustion of the release of noradrenaline from the tumour as a consequence of the repeated contractions of the bladder within a short time; inhibition of the release of noradrenaline from the tumour by nifedipine as suggested by Serfas et al[1]; or interference of nifedipine with the action of noradrenaline on the blood vessels and heart. The first possibility is rendered less likely by the persistently strong increments of plasma noradrenaline two days after stopping nifedipine. The increase in plasma noradrenaline after experiment M5 and the unchanged excretion of catecholamines over 24 hours after hebdomadal treatment with nifedipine strongly deny the case for the second possibility.

The third possibility is the most likely. An attenuated pressor

It is most likely that the steep increases in blood pressure in our patient were prevented by the effect of nifedipine on the target organ —that is, vascular smooth muscle.

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Cluster headache and herpes simplex: an association?

A patient presented with cluster headache occurring in association with ipsilateral facial herpes simplex. This suggested that the localised vasodilatation seen during an attack of cluster headache may result from an axonal reflex activated by a latent viral infection in the trigeminal system.

Case report

A 42 year old white man had had bouts of unilateral headache for seven years. These occurred every five or six months, each bout lasting six to eight weeks, during which headaches occurred once or twice each day. A typical attack was strictly confined to the left side, and he would be wakened between 0100 and 0300 by severe boring retro-ocular pain lasting for 30-45 minutes and associated with ipsilateral rhinorrhoea, conjunctival injection, and epiphora. The pain did not spread to the upper teeth or the other divisions of the fifth nerve. Cluster headache was diagnosed, and his symptoms were controlled, initially with ergotamine and methysergide but later with lithium carbonate.

He had had cold sores since the first decade of life, which always occurred on the left upper lip. Initially the blisters developed with symptoms similar to those of flu, but after the onset of cluster headache the blisters developed within four or five weeks after the start of an attack of the headache. The blisters were present with most bouts of cluster headache. There was no history of any other underlying medical condition. He was a chronic smoker (20 cigarettes a day) who used to consume large amounts of alcohol. Examination showed no abnormality apart from a partial left Horner's syndrome during a bout of cluster headache.

Comment

In this patient cluster headache and ipsilateral herpes simplex blisters occurred consistently with a close temporal relation, raising the possibility of an association between the two conditions. Herpes blisters are known to be activated by severe physical or psychological stress. The ipsilateral occurrence of both conditions, however, suggests that herpes simplex may have had a pathogenic role in activating the cluster headache, though this would have been better substantiated had the blisters preceded the cluster headache.

Strict unilaterality of pain in cluster headache suggests that local events may be primarily responsible. Localised vasodilatation of the extracranial vasculature is a feature of cluster headache, but the mechanism for this is not clear.[1] Increased numbers of mast cells have been found on the side of the headache (R Joseph et al, paper presented at fifth international migraine symposium, London, September 1984), mainly in the vicinity of cutaneous nerves.[2] Degranulation of these cells, associated with an axonal reflex, will release vasoactive substances including histamine, substance P, vasoactive intestinal polypeptide,[3] and purine nucleotides,[4] which are mediators of the arteriolar dilatation that produces the flare surrounding cutaneous injury. Such a mechanism has also been thought to be responsible for the localised vasodilatation during attacks of cluster headache.[2] The intermittent recurrence of the axonal reflex may occur from an episodic reactivation of a latent viral infection in the trigeminal system, very much like herpes simplex.[2] The temporal relation between the cluster headache and ipsilateral facial herpes simplex in our patient suggests that such an association may indeed exist.

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Viral infection during chemotherapy for breast cancer

Adjuvant chemotherapy prolongs the disease free interval and increases survival after mastectomy for breast cancer.[1] Cytotoxic treatment may reduce cell mediated and humoral immunity. Viral infection is well recognised in immunosuppressed patients after transplantation, but there have been no studies of viral infection during treatment for breast cancer. This study aimed at investigating the incidence and type of viral infection in patients receiving adjuvant chemotherapy after mastectomy for breast cancer.

Patients, methods, and results

From 1980 to 1982 we studied 124 women who had undergone mastectomy for breast cancer. Sixty four patients were randomised to receive cytotoxic chemotherapy; the remaining 60 patients did not receive any cytotoxic drugs (controls). Chemotherapy consisted of bolus injections of cyclophosphamide (300 mg/m^2), methotrexate (40 mg/m^2), and fluorouracil (600 mg/m^2) given on days one and eight of a 28 day cycle. All patients underwent serological examination every three months to detect viral infection. Samples were tested by standard complement fixation techniques using C3 tagged with fluorescein to detect antibodies to a variety of common viruses. A fourfold increase in antibody titre between sequential samples of serum was considered to be evidence of recent infection. The incidence of viral infection was expressed as the number of infections detected per patient month. The probability of infection in the patients who received cytotoxic chemotherapy was compared with that in the controls using the unpaired Mann-Whitney U test. The types of infections were compared with those reported in Scottish women between 25 and 60 years of age during the same period[2] and the results evaluated by the χ^2 test.

Viral infection was found on 123 occasions during 444 patient months (1:3·6 patient months) in the group treated with cytotoxic chemotherapy compared with only 63 infections during 495 patient months (1:7·8 patient months) in the controls. The probability of infection occurring was much greater in the patients receiving cytotoxic chemotherapy than the controls (p < 0·0001; Mann-Whitney U test).

Twenty four of the patients treated with cytotoxic chemotherapy were also studied after chemotherapy was stopped. In this group 50 infections were detected during 192 patient months while the patients were receiving chemotherapy (1:3·8 patient months) compared with only 25 infections during 249 patient months of follow up after treatment was stopped (1:9·9 patient months). The probability of infection occurring in these patients after cytotoxic chemotherapy was stopped was considerably less than that found during treatment (p < 0·0001; Wilcoxon's signed rank test).

Relative proportions (%) of viral infections in patients given cytotoxic chemotherapy and controls compared with expected proportions in general population of Scottish women during same period

	Cytotoxic chemotherapy	Controls	General population
Herpes simplex	28	26	22
Varicella zoster	3	6	5
Cytomegalovirus	9	6	5
Influenza A	18	17	10
Influenza B	5	5	13
Parainfluenza	18	16	16
Respiratory syncytial virus	12	13	16
Adenovirus	7	11	16

The table shows the relative proportions of the different infections. Herpes simplex was the most common virus in both the treatment and control groups. No significant differences were found in the patterns of infection when each group was compared with the general population ($\chi^2 = 15\cdot51$: p > 0·2). The seasonal variations in herpes simplex and influenza A infections in both groups of patients were also similar to those in the general population (p > 0·1, both cases).

Comment

This preliminary study shows that viral infection is common in patients receiving adjuvant chemotherapy for breast cancer, the incidence being twice that seen in control patients. The type and seasonal variation of infection during chemotherapy are similar to those in the general population, suggesting that the problem is one of decreased resistance to endemic infection rather than of particular susceptibility to unusual organisms.

Recent studies showed that functional variables of the competence of both T and B cells are suppressed during treatment with some cytotoxic agents but recover within three months after treatment is stopped.[3] This study confirms these findings as the incidence of viral infection returned to normal shortly after adjuvant chemotherapy was stopped.

Interestingly, the most common viral infections can produce symptoms of mucositis, conjunctivitis, general malaise, and lethargy and may contribute to the morbidity commonly associated with cytotoxic treatment. Advances in viral prophylaxis[4] would probably improve the quality of life for women receiving adjuvant chemotherapy for breast cancer.

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