Captopril in the treatment of renovascular hypertension secondary to Takayasu’s arteritis

A case report

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Summary

A case of Takayasu’s arteritis complicated by renovascular hypertension is described. The hypertension was refractory to conventional medical treatment but responsive to captopril therapy. Deterioration in renal function occurred on initiation of captopril therapy; this resolved on reduction of dosage. A captopril-induced disturbance of renal autoregulation was probably responsible for this phenomenon.

Takayasu’s arteritis is an inflammatory disease of the aorta and its branches and occasionally involves the pulmonary arteries. It occurs worldwide, but has a predilection for female orientals. Pathologically, the process is a panarteritis which leads to obliteratoric changes in the aorta and its branches, and to localized aneurysm formation in the aortic and arterial walls. The arteritis is presumed to be of auto-immune origin. More than half of the patients with this disease develop an initial systemic illness characterized by symptoms such as fever, anorexia, malaise, weight loss, night sweats, arthralgia, pleuritic pain and fatigue. This phase subsides and after a variable latent period these patients show symptoms and signs of the obliteratoric and inflammatory changes in the vessels.

The following case report illustrates one of the most common complications of Takayasu’s arteritis, namely hypertension.

Case report

A 22-year-old black man was admitted to Baragwanath Hospital in September 1984, after incidental detection of hypertension while donating blood. He was asymptomatic and regularly played soccer. Examination revealed hypertensive disease: the blood pressure (BP) in the right arm was 220/140 mmHg, and in the left 155/130 mmHg (while on antihypertensive treatment). Diminished left brachial and radial pulses were noted. No bruits were audible. The heart was clinically normal although the ECG showed evidence of left ventricular hypertrophy and strain. Arteriolar narrowing and hard exudates were noted on funduscopy.

Haematological tests were largely unhelpful. The full blood count and prothrombin index were normal, the erythrocyte sedimentation rate was 22 mm/1st h (Westergren), and serological tests for syphilis and antinuclear factor were negative. Albumin constituted 37.8 g/l of a total plasma protein content of 79.6 g/l. The blood urea, creatinine and electrolyte concentrations were normal.

Radiological investigations were more helpful. The intravenous pyelogram showed diminished handling of contrast medium by the left kidney, and a smaller size compared with the right. The disparity in renal cortical size was confirmed by dimercaptosuccinic acid isotope scanning (Fig. 1). The arch aortogram revealed obstruction of the left subclavian artery at its origin with reconstruction of the same artery via collaterals (Fig. 2). The abdominal aortogram demonstrated marked irregularity of the abdominal aorta with partial occlusion of the left renal artery and a well-developed collateral circulation to the left kidney (Fig. 3).

Discussion

The case described is typical of type 3 Takayasu’s arteritis where both the aortic arch and thoraco-abdominal aorta and...
Fig. 2. Arch aortogram showing an absent left subclavian artery (arrow).

Fig. 3. Abdominal aortogram showing irregularity of the aorta and occlusion of the left renal artery (arrow).

branches are involved. This is the commonest type. The obstruction to the left renal artery and the elevated PRA measurements are indicative of the renovascular origin of the hypertension. However, there are other possible mechanisms involved in the production of hypertension in this disease: atypical coarctation of the aorta, reduced elasticity of the aortic wall, aortic regurgitation, and altered baroreceptor activity. Knowing the cardiovascular complications associated with hypertension, it is not surprising that in a Japanese study involving 81 patients with Takayasu’s disease, hypertension (severe) proved a poor prognostic factor. Elevated BP is a particularly common manifestation of this disease and was found in 33 of 48 patients (69%) studied in Singapore; it was severe in 6 (diastolic BP 115 mmHg) and of renovascular origin in 27 patients.

There is no cure for Takayasu’s arteritis because the aetiology is obscure, but corticosteroids are effective in relieving constitutional symptoms in patients with the systemic phase of the disease. These agents may also retard progression of arterial narrowing during the active stage of the disease. Anticoagulants and antiplatelet agents are recommended both for treatment of transient ischaemic symptoms and for prevention of progression of the disease. Their precise efficacy has not been established.

The management of the associated hypertension is complex since it is often unresponsive to standard antihypertensive drugs. An exciting development in this field has been captopril, the first orally active inhibitor of angiotensin-converting enzyme. This drug has been found effective in lowering the BP in renovascular hypertension, and several reports attest to its efficacy in the management of renovascular hypertension associated with Takayasu’s arteritis.

Captopril was used to treat our patient, firstly because the BP proved refractory to a combination of α-methyldopa, hydralazine, atenolol, and a thiazide diuretic; and secondly, because the hypertension appeared to be renin-mediated. A starting dose of captopril 12.5 mg 8-hourly plus hydrochlorothiazide 50 mg and amiloride HCl 5 mg resulted in a prompt reduction in BP. The dose of captopril was gradually increased over a period of several days to a maximum of 75 mg 8-hourly, by which time the BP had dropped to 110/80 mmHg. However, deterioration in renal function was noted at this stage (urea level 11.6 mmol/l and creatinine level 170 µmol/l). The patient had already been discharged from hospital and when he returned for follow-up he had inadvertently been off all treatment for several days. The BP was again elevated, at 165/110 mmHg, but the urea level had dropped to 4.5 mmol/l and the creatinine level to 124 µmol/l. Therapy was recommenced at a reduced dose of captopril — 50 mg 8-hourly. A fortnight later the BP was controlled at 120/90 mmHg but renal function had again deteriorated (urea level 10.9 mmol/l and creatinine level 164 µmol/l). The dosage was further reduced to 25 mg 8-hourly and the diuretic was stopped. Reassessment 1 month later revealed a BP of 120/85 mmHg, and the urea and creatinine levels had returned to normal.

Why the deterioration in renal function in this case? There are several possibilities: firstly, the patient was exposed to a significant amount of potentially nephrotoxic contrast medium over a relatively short period of time during investigation; secondly, a form of membranous glomerulopathy has been associated with captopril therapy; and thirdly, captopril may have inhibited renal autoregulation of blood flow. We favour the latter explanation. The renin-angiotensin system appears to be important in controlling the glomerular filtration rate (GFR) at low renal perfusion pressure; therefore, if captopril is given to patients with various forms of renal artery stenosis, as in this case, this system may be inhibited resulting in an acute deterioration in GFR — which is reversible if captopril therapy is stopped. The facts supporting this contention in our case include the following: (i) deterioration in renal function after initiation of captopril therapy associated with a continuous fall in BP to normotensive levels; (ii) recovery of function after inadvertent cessation of therapy associated with a rise in BP to hypertensive levels; (iii) repeated deterioration of function after reinstitution of therapy; and (iv) a return to
normal renal function when much smaller doses of captopril were used, with control of the BP. The latter suggests that the inhibition of renal autoregulation of blood flow by captopril may in fact be dose-related.

Other techniques used in the management of hypertension in this disorder include complex revascularization and transluminal angioplasty (for atypical coarctation). These procedures require a particular expertise and are not without hazard. The development of captopril has, therefore, given some hope for conservative management of renovascular hypertension secondary to Takayasu’s arteritis.

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REFERENCES


Etomidate infusion for resection of phaeochromocytoma

A report of 2 cases

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Summary

Anaesthesia in patients undergoing resection of phaeochromocytomas is associated with fluctuations in blood pressure and cardiac dysrhythmias. Two patients in whom an etomidate (Hypnomidate; Janssen Pharmaceutica) infusion was used as a supplement to droperidol, fentanyl, pancuronium, air and oxygen anaesthesia are described. Cardiovascular stability was well maintained; the advantages of this technique are discussed.

The anaesthetic management of patients undergoing resection of a phaeochromocytoma has attracted much interest and debate. The potential for serious haemodynamic disturbances has always challenged the anaesthetist, who has consequently assessed the feasibility of different techniques in attempts to minimize these problems.

An intravenous technique for the intra-operative anaesthetic management of phaeochromocytoma is described, but it must also be emphasized that effective pre-operative blood pressure control using adrenergic blocking agents must be instituted according to the criteria of Harrison et al. Efficient pre-operative management with phenoxybenzamine and propranolol has decreased the operative hazards and minimized peri-operative morbidity and mortality. Beta-blockade should never be induced without concomitant a-blockade since this might induce a pressor response resulting in significant increases in arterial pressure.

Anaesthesia has been achieved with varying degrees of success using several anaesthetic techniques, including methoxyflurane, halothane, enfurane, isoflurane and enflurane. None of these techniques is ideal; this prompted a description of total intravenous anaesthesia using droperidol, fentanyl and a continuous infusion of etomidate (Hypnomidate; Janssen Pharmaceutica).

Case reports

Case 1

A 61-year-old woman weighing 60 kg was referred for resection of a phaeochromocytoma. The diagnosis was confirmed by estimation of 24-hour urinary vanillylmandelic acid (VMA) excretion, which was 107 μmol/24 h (normal less than 45 μmol/24 h).