min and oliguria developed over one week. Prednisolone 60 mg daily was given for nine days at this stage.

A renal biopsy was performed 20 days after the nephrotic state began, the creatinine clearance then being 15 ml/min and urine protein excretion 8.2 g/day. Examination by light microscopy showed that 10% of the glomeruli were obsolete but the others appeared normal. There was focal tubular damage with regenerating epithelium and mitoses. Immunoperoxidase staining showed that the glomerular capillary walls and mesangium contained tiny amounts of granular IgA and IgM with no IgG, C3, C1q, or C4. Ultrastructurally there were occasional tiny intramembranous and sub-endothelial electron-dense deposits in the glomerular capillary walls and in the mesangium (figure). There was widespread loss of epithelial cell foot processes. Immune complexes were not present in the serum, the complement profile was normal, the DNA binding was in the normal range, and autoantibodies were absent. The patient's lymphocytes did not transform in vitro when cultured with phenylbutazone. Two months later the proteinuria was 4.4 g/day and the creatinine clearance 36 ml/min; by four months the proteinuria had ceased and the clearance risen to 58 ml/min.

Electron micrograph of part of a glomerulus in renal biopsy taken 20 days after onset of nephrotic syndrome. The mesangium is slightly increased in amount and contains small electron-dense deposits (arrows). cap = Capillary lumen (original magnification $\times 11\,400$).

Comment

A similar event was recorded in a 69-year-old Caucasian woman who had taken phenylbutazone 100 mg three times daily for four years because of osteoarthritis. She was taking no other drugs. A nephrotic syndrome with oliguria developed. Phenylbutazone was stopped. A renal biopsy was performed when the blood urea concentration was 17.5 mmol/l (105 mg/100 ml). The glomeruli were normal on light microscopy but electron microscopy showed electron-dense deposits in the glomerular capillary basement membranes. The condition resolved, and 17 months later there was no proteinuria and renal function was normal (Committee on Safety of Medicines, personal communication).

The evidence that phenylbutazone caused the nephrotic state in these two patients is threefold. Firstly, there was a clear relation between drug ingestion and the onset of proteinuria and renal failure. Secondly, the renal condition improved after the drug was stopped. Thirdly, the nephrotic syndrome is uncommon in the elderly: it is seen most frequently in the 3-30 age group.² The severity of the renal failure in both patients may be a feature of the phenylbutazone-related lesion. Glomerular morphology was similar in both patients. The nephrotic syndrome was reported in three patients taking phenylbutazone in 1959,³ but the reported glomerular changes are difficult to evaluate.

Acute interstitial nephritis and papillary necrosis are well-recognised complications of nonsteroidal anti-inflammatory agents. Reversible renal failure and heavy proteinuria may complicate the use of nap-

roxen, fenoprofen, or indomethacin.^{4,5} The two patients cited above, together with the four reported by Brezin *et al*⁴ and Gary *et al*,⁵ had severe renal failure, heavy proteinuria, and glomeruli which were normal on light microscopy. The clinical course of these six patients was sufficiently uniform to produce a characteristic clinicopathological picture.

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Intravenous amiodarone in ventricular fibrillation

Amiodarone is a class III antiarrhythmic agent available in Britain for named patients only. Most clinical experience has been gained on the Continent and in South America. There is little experience in the use of the intravenous formulation.¹ We report its use in two patients with ventricular fibrillation.

Case reports

Case 1—A 45-year-old man sustained an inferior myocardial infarct, complicated in the first six hours by a short episode of complete heart block. Ten days later he had a cardiac arrest and was found to have ventricular fibrillation. He responded to 300 J cardioversion after 100 mg disopyramide had been given. Despite a lignocaine infusion (4 mg/min) and continued disopyramide infusion (0.5 mg/min) he developed ventricular fibrillation eight times, each requiring cardioversion. Bretylium (100 mg) followed by an infusion (3 mg/min) also failed to prevent frequent ventricular fibrillation. After 18 hours and a total of 35 cardioversions a temporary transvenous pacing wire was inserted. Over the next 36 hours he remained stable while paced at 130/min but when the pacing rate was reduced R-on-T ventricular ectopic beats heralded the return of ventricular fibrillation. Procainamide (serum concentration 7.2 mg/l) and then mexiletine (100 mg immediately followed by 0.5 mg/min) failed to control this phenomenon. Ventricular fibrillation occurred twice while the pacing rate was 130/min. Fifty-four hours after the initial cardiac arrest and after 41 cardioversions 200 mg amiodarone was given intravenously over 30 seconds. Systolic blood pressure fell abruptly to 55 mm Hg, the pacemaker was turned off, and sinus rhythm at 80/min returned with no ventricular ectopic beats. Blood pressure rose over the next 10 minutes to 95 mm Hg. A total of 800 mg amiodarone was infused over 24 hours, after which he continued with oral amiodarone 600 mg daily. At follow-up two months later he was well with no cardiac symptoms, taking amiodarone alone.

Case 2—A 65-year-old man underwent aortic valve replacement, repair of an aneurysmal ascending aorta with woven Teflon, and two coronary artery vein grafts. Eight weeks later a leak from the lower end of the Teflon aortic repair was resutured. After the second operation he had various arrhythmias, including multifocal ventricular ectopic beats, which were treated with lignocaine and procainamide durules (500 mg thrice daily). Nine days later he had a cardiac arrest and was found to be in ventricular fibrillation, unresponsive to an initial 400 J cardioversion. Cardiopulmonary resuscitation was started; the lignocaine infusion was increased and supplemented by a 50 mg bolus. The serum potassium concentration was corrected from 3.2 mmol

(mEq)/l to 4.5 mmol/l. The ventricular fibrillation was unresponsive to a further 10 cardioversions. A total of 400 mg disopyramide was given but after 75 minutes of resuscitation and 15 cardioversions he remained in ventricular fibrillation. Amiodarone 200 mg was then given intravenously over 30 seconds. Two to three minutes later a final 400 J cardioversion restored sinus rhythm. A total of 600 mg amiodarone was infused over the next 24 hours and then discontinued. His course continued to be stormy but he remained in sinus rhythm and was discharged home eight weeks after his cardiac arrest.

Comment

Amiodarone has been shown to be effective when given by mouth for a wide variety of arrhythmias. There is a latent period of three to seven days before the effects are noted.²⁻³ Experience with intravenous amiodarone suggests, however, that it is rapidly effective for supraventricular tachycardias with a maximum effect 10 minutes after injection.⁴ In ventricular arrhythmias excellent results have been observed when sufficient time has elapsed for oral amiodarone to take effect. Success was reported in 34 out of 44 cases of recurrent ventricular tachycardia and in six of eight patients with recurrent ventricular fibrillation.²

Amiodarone has a protective effect against ventricular fibrillation induced by coronary artery ligation in dogs² and rats.⁵ Protection in rats was shown when the drug had been administered within two minutes by the intravenous route. Clinical experience suggests that intravenous amiodarone is also rapidly effective against ventricular ectopic beats and ventricular tachycardia success being reported in 19 out of 35 cases.⁴

Our report shows that the use of intravenous amiodarone may extend to the control of highly dangerous arrhythmias in acute cases.

We thank Mr D J Parker and Dr D Bennett for permission to report the case histories of patients under their care.

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Paroxysmal atrial tachycardia provoked by swallowing

Although bradycardia after swallowing is fairly common and is due to exaggerated vagal reflex activity, deglutition tachycardia, which was first reported in 1926,¹ is uncommon and its mechanism remains unclear. Several explanations have been postulated to explain previous examples of deglutition tachycardia.²⁻⁵ We report on a patient with tachycardia induced by swallowing who underwent full evaluation.

Case report

A 52-year-old man presented with a three-month history of palpitations associated with light-headedness, pallor, and discomfort in the lower chest that occurred only on swallowing. The symptoms were worse with solids than liquids, and occurred with most meals but not at other times. He denied any other cardiac symptoms, and the only other relevant symptom was occasional dyspepsia. A barium-meal examination performed three years previously had been normal.

Clinical examination was normal, apart from mild hypertension. All routine haematological and biochemical investigations, chest-x-ray film, resting electrocardiogram, and echocardiogram were normal. Barium swallow

disclosed a small sliding hiatus hernia and absent oesophageal peristalsis. On swallowing, runs of irregular atrial tachycardia at rates of 160-220 beats/min occurred (figure). The QRS complexes of the tachycardia occasionally showed intraventricular aberration and functional atrioventricular block. The tachycardia was consistently produced by inflating a balloon within the oesophagus, using 4-20 ml of air and placing the balloon anywhere between 25-45 cm from the incisors. With large volumes the tachycardia was initiated immediately the balloon was inflated and continued until deflation.

Episode of paroxysmal atrial tachycardia provoked by swallowing (arrow indicates initial act of swallowing).

The effects of various physiological and pharmacological manoeuvres were studied with the balloon placed 30 cm from the incisors. Vertical tilt to 60° reduced the response to balloon inflation but shortened the average duration of the tachycardia cycle from 320 ms to 275 ms. Both quinidine and propranolol appreciably reduced the response to balloon inflation and increased the average duration of the tachycardia cycle to 375 and 400 ms respectively. Temporary right stellate ganglion block, atropine, and carotid sinus massage had no effect. Disopyramide totally abolished the tachycardia response to balloon inflation.

An intracardiac study showed normal conduction intervals, sinus node function, and refractory periods. In response to oesophageal balloon inflation tachycardia arose in the high lateral right atrium but could not be initiated by programmed extrastimulation.

Comment

Physiological and pharmacological evaluation of this uncommon form of tachycardia was facilitated by using a simple and reproducible method of provoking tachycardia. Because the tachycardia could be provoked at will an effective form of antiarrhythmic treatment was easily and rapidly designed and assessed. As in this case, it may be apparent from the clinical history which methods of initiating tachycardia should be evaluated before having recourse to invasive stimulation techniques.

The mechanism of deglutition tachycardia remains in dispute. The repetitive and reproducible nature of the tachycardia and its fixed relation to the act of swallowing suggest either a direct mechanical effect or a neural reflex. In this case a direct mechanical effect was suggested by the abnormal oesophagus and the fact that the tachycardia was initiated immediately by balloon inflation and sustained throughout the inflation but was relatively short lived in response to swallowing. The tachycardia arose in the right atrium and was initiated by stimulation of almost the entire oesophagus, so a direct effect on the left atrium is therefore unlikely. The lack of effect of atropine, right stellate ganglion block, and carotid sinus massage suggests that neural reflex mechanisms are not important. The dramatic effect of tilting and the appreciable effect of beta-blockade, however, favour a neural mechanism affecting the sympathetic limb of the autonomic nervous system.

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