Coronary artery spasm as a manifestation of anaphylactoid reaction to iodinated contrast material

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Anaphylactoid reactions following the parenteral use of contrast material during cardiac catheterization are uncommon.[1,2] We report the case of a severe anaphylactoid reaction following selective coronary arteriography in which the electrocardiographic changes and the response to intravenously administered nitroglycerin suggested that coronary artery spasm is one of the cardiac manifestations of anaphylactoid reactions to iodinated contrast material.

Case report

A 33-year-old man was admitted to hospital for coronary arteriography following an anterior myocardial infarction 2 months previously. His risk factors for coronary artery disease included obesity, borderline hypertension, mild hypercholesterolemia and the consumption of 40 cigarettes a day.

His past medical history revealed significant atopy, with eczema, allergic rhinitis and asthma during childhood. There was no history of anaphylaxis, exposure to contrast media or recent asthmatic attacks. The electrocardiogram (ECG) before cardiac catheterization is shown in Fig. 1 (ECG I).

The patient was given Pantopon (total opium alkaloids), 10 mg intramuscularly, and Phenergan (promethazine hydrochloride), 25 mg intramuscularly, half an hour before the procedure. Following retrograde catheterization of the aorta from the right femoral artery, left ventriculography was performed with an injection of 45 ml of Renografin-76 (diatrizoate meglumine and sodium). Selective coronary arteriography was carried out in multiple views by Judkins' technique. An average of 5 ml of contrast medium was used per injection, for a total of 50 ml.

The patient had no angina, arrhythmias or apparent side effects during the study, and the catheter was removed. Ten minutes later he complained of a sudden onset of dyspnea, wheezing, nasal obstruction, rhinorrhea, nausea and epigastric pain.

Examination revealed mild peripheral cyanosis, expiratory rhonchi and a respiratory rate of 35/min. The systolic blood pressure was

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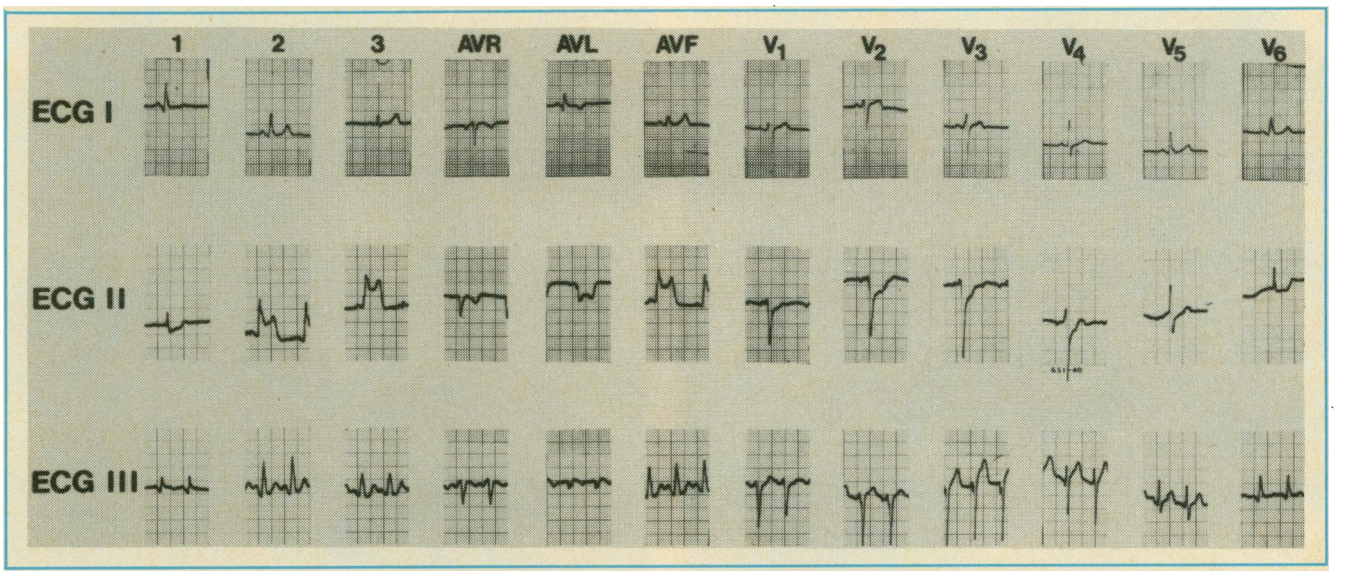

FIG. 1—Electrocardiograms (ECGs) of 33-year-old man. ECG I demonstrates sinus rhythm, with minimal elevation of ST-segments and T-wave inversions in leads V_2 and V_3. Note normal ST-segments in leads 2, 3 and AVF. ECG II demonstrates marked elevation of ST-segments in leads 2, 3 and AVF, with reciprocal changes in anterior leads. ECG III demonstrates return of ST-segments in leads 2, 3 and AVF to normal after intravenous administration of 0.4 mg of nitroglycerin.

found to be 60 mm Hg by palpation, and the heart rate was 85 beats/min. The ECG showed marked elevation of the ST-segments in leads 2, 3 and AVF, with reciprocal changes in the anterior leads (Fig. 1, ECG II). The oxygen tension in the patient's arterial blood was 46 mm Hg.

He was immediately given high-flow oxygen as well as 5 mg of chlorpheniramine maleate and 150 mg of hydrocortisone sodium succinate intravenously. There was no change in the ECG or in his clinical status. Therefore, despite significant hypotension, 0.4 mg of nitroglycerin was given intravenously over a 2-minute period. There was a prompt increase in the heart rate, to 140 beats/min, without a change in the systemic blood pressure. Over the next 4 minutes the ST-segments returned to normal (Fig. 1, ECG III) and the epigastric pain subsided, but there was still severe bronchospasm.

Fifteen minutes after the nitroglycerin infusion the ST-segments became persistently elevated in the inferior leads. There was no response to another infusion of nitroglycerin, but his clinical status gradually improved over the next several hours with intravenous infusions of aminophylline, 500 mg every 8 hours. Rhinorrhea, itchiness of the nasal passages, conjunctivitis and skin irritation persisted for approximately 48 hours. Cardiac enzyme levels determined serially were consistent with a recent infarction, and a myocardial scan with technetium 99m pyrophosphate substantiated this diagnosis.

Review of the coronary arteriograms demonstrated a proximal saccular aneurysm of the right coronary artery but no occlusive lesions (Fig. 2). The left coronary artery showed an occluded first diagonal branch of the left anterior descending artery and a 95% narrowing of the distal circumflex vessel (Fig. 3).

The patient's subsequent hospital course was uneventful.

Discussion

The incidence of severe anaphylactoid reactions following the parenteral use of contrast material is less than 2%.[3,4] Previous reports have dealt primarily with reactions following intravenous pyelography. Although minor reactions have been reported following the use of contrast material in selective coronary arteriography, severe reactions have been rare.[1,2] In 5250 cases reviewed by Bourassa and Noble[1] in 1976 and in over 10 000 cases previously studied at our laboratory there were no serious allergic reactions following coronary arteriography.

The term anaphylactoid reactions refers to any reaction that mimics another type of well defined immediate-type allergic reaction; features include the sudden onset of bronchospasm, cyanosis, severe hypotension and local allergic manifestations (rhinorrhea, conjunctivitis, facial edema and pruritus). From available data we surmise that the chain of events may include the activation of factor XII, clotting, clot lysis, the complement cascade, release of an anaphylatoxin and degranulation of basophils and mast cells, with resultant release of histamine.[5]

In this case continuous electrocardiographic monitoring before and during the anaphylactoid reaction allowed us to observe that marked elevation of ST-segments coincided with the onset of bronchospasm and the other anaphylactoid manifestations. Despite persist-

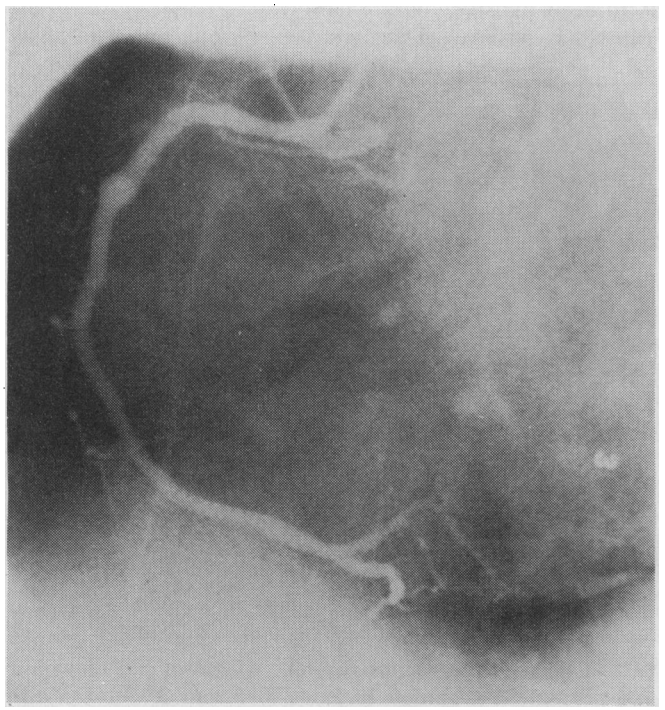

FIG. 2—Right coronary arteriogram, demonstrating proximal saccular aneurysm but no significant occlusive disease.

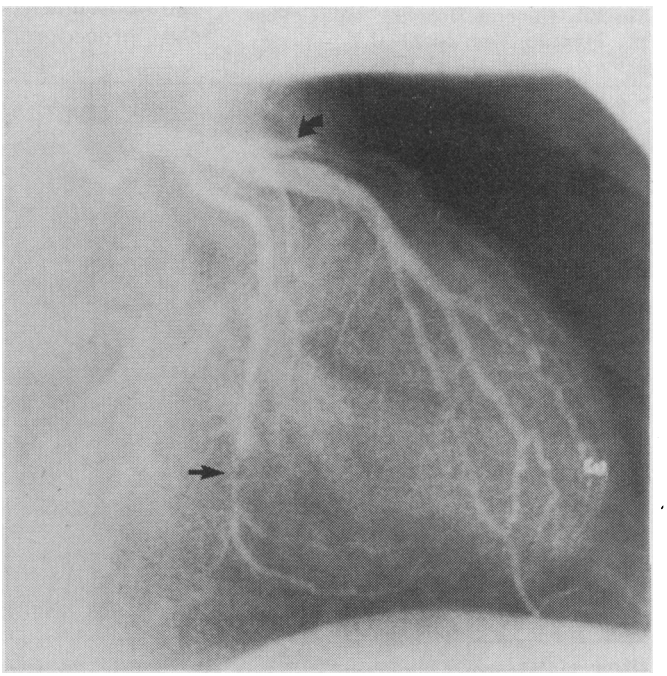

FIG. 3—Left coronary arteriogram, demonstrating occluded first diagonal branch of left anterior descending artery (curved arrow) and subtotal narrowing of distal circumflex coronary artery (straight arrow).

ing severe hypotension nitroglycerin, administered parenterally, effected a prompt return to normal of the ST-segments. It has been shown that nitroglycerin preferentially relaxes large coronary arteries,[6-9] and Fleckenstein and associates[10] and Schnarr and Sparks[7] have demonstrated that nitroglycerin relaxes coronary arteries by inhibiting the influx of calcium ion.

An alternative explanation for the transmural myocardial ischemia evidenced by the ST-segment elevation could be hypoxia, acidosis and hypotension. However, it is unlikely that there was significant early improvement in the acidosis or hypoxia, since the patient remained in severe respiratory distress, with bronchospasm and cyanosis, during the period that the ST-segments returned to normal. Similarly, the blood pressure was unchanged after nitroglycerin administration and the return to normal of the ECG. The response of the ST-segments to intravenously administered nitroglycerin suggests that coronary artery spasm occurred during the anaphylactoid reaction and produced ischemia, which led to infarction.

The previous reports noting ECG changes with anaphylaxis suggested that the ST-segment and T-wave changes were secondary to (a) a direct antigen–antibody reaction in the myocardium, (b) a pharmacologic effect of the mediators released during anaphylaxis, (c) the effects of the agents used for treatment or (d) pre-existing heart disease.[11-13] Studies with animals have demonstrated that the heart is a target organ in anaphylaxis, and histamine release in the myocardium has been documented in guinea pigs during anaphylaxis.[14] Histamine, along with other vasoactive substances either released or used for the treatment of anaphylaxis, could directly affect either normal coronary arteries or those with obstructive lesions. Our case suggests that coronary artery spasm may be an additional factor in the pathogenesis of myocardial injury during anaphylactoid reactions.

Certain recommendations have recently been made concerning studies involving iodinated contrast material in patients at high risk of an anaphylactoid reaction. These include obtaining informed consent and pretreating the patient with prednisone (50 mg orally every 6 hours beginning 18 hours before the proposed study) and Benadryl (diphenhydramine hydrochloride, 50 mg intramuscularly 1 hour before the study). The use of this regimen reduces the incidence and severity of reactions to the contrast material.[5,15]

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References

1. Bourassa MG, Noble J: Complication rate of coronary arteriography. *Circulation* 1976; 53: 106–144
2. Adams DF, Fraser DB, Abrams HL: The complications of coronary arteriography. *Circulation* 1973; 48: 609–618
3. Scott AA, Hobbs BB: *The Management of Reactions to Contrast Media*, Can Assoc Radiol, Montreal, 1976
4. Witten DM, Hirsch FD, Hartman GW: Acute reactions to urographic contrast medium. *Radiology* 1973; 119: 832–840
5. Lieberman P, Siegle PL, Taylor WW Jr: Anaphylactoid reactions to iodinated contrast material. *J Allergy Clin Immunol* 1978; 62: 174–180
6. Winbury MM, Howe BB, Hefner MA: Effect of nitrates and other coronary dilators on large and smali coronary vessels: an hypothesis for the mechanism of action of nitrates. *J Pharmacol Exp Ther* 1969; 168: 70–95
7. Schnaar RL, Sparks HV: Response of large and small coronary arteries to nitroglycerin, $NaNO_2$, and adenosine. *Am J Physiol* 1972; 223: 223–228
8. Cohen MV, Kirk ES: Differential response of large and small coronary arteries to nitroglycerin and angiotensin. Autoregulation and tachyphylaxis. *Circ Res* 1973; 33: 445–453
9. Harder DR, Belardinelli L, Sperelakis N, Rubio R, Berne RM: Differential effects of adenosine and nitroglycerine on the action potentials of large and small coronary arteries. *Circ Res* 1979; 44: 176–182
10. Fleckenstein A, Nakayama K, Fleckenstein-Grun C, Byron Y: Interaction of vasoactive ions and drugs with Ca-dependent excitation-contraction coupling in vascular smooth muscle. In Carafoli E (ed): *Calcium Transport in Contraction and Secretion*, North Holland, Amsterdam, 1975: 555
11. Booth BH, Patterson R: Electrocardiographic changes during human anaphylaxis. *JAMA* 1970; 211: 627–631
12. Delage C, Mullick FG, Ivy NS: Myocardial lesions in anaphylaxis. *Arch Pathol* 1973; 95: 185–189
13. Brasher GW, Sanehe SA: Reversible electrocardiographic changes associated with wasp sting anaphylaxis. *JAMA* 1974; 229: 1210–1211
14. Capurro N, Levi R: The heart as a target organ in systemic allergic reactions. *Circ Res* 1975; 36: 520–528
15. Kelly JF, Patterson R, Lieberman P, Mathieson DA, Stevenson DD: Radiographic contrast media studies in high-risk patients. *J Allergy Clin Immunol* 1978; 62: 181–184