likely cause and concomitant lentiginosis prompted evaluation for a unifying diagnosis. Disorders of pigmentation have been reported in association with various cardiac abnormalities, but classification remains controversial. Features of both cardiomypathic lentiginosis and LEOPARD syndrome,\(^2\) a mnemonic code for lentiginosis, ECG changes, ocular hypertelorism, pulmonic stenosis, abnormal genitalia, growth retardation, and deafness, were present. Pectus excavatum, skull defects, and other skeletal abnormalities as well as anomalies of the genitalia, such as undescended testicle, are frequently encountered whereas involvement of the urinary tract is believed to be rare. Somatic retardation is common. The presence of brain atrophy may indicate that mental impairment, one of the syndrome’s key features, might ensue in the future. Finally, additional cases among the kindred of this patient were not detected; this suggests that a novel mutation may have occurred.

Both LEOPARD syndrome and cardiomypathic lentiginosis, originally proposed to be distinct entities, have salient features in common, not the least of which is their mode of inheritance as an autosomal dominant trait and their preponderance to affect tissues of neural crest origin. It, therefore, seems intriguing to assume that both reflect variable penetrance and expression of the same genetic defect.\(^2\) Among other features, atrial myxoma, mitral regurgitation, and, recently, recurrent arterial dissection have been reported in lentiginosis and may be variant forms of the disorder. The genetic basis of lentiginosis syndromes, however, remains entirely unknown, thus preventing proper classification and diagnosis.

**CONCLUSION**

Lentiginosis must prompt thorough evaluation since it may be part of a multifaceted syndrome that cannot only be associated with considerable morbidity but may even place patients at risk for sudden death. Although identification of patients in need of prophylactic treatment will remain difficult, pacer-cardioverter-defibrillator device therapy is believed to be indicated and beneficial in survivors of out-of-hospital ventricular fibrillation.

**REFERENCES**


**Coronary Artery Spasm Complicating Anaphylaxis Secondary To Skin Disinfectant**

Viviane M. A. Conraads, MD; Philippe G. Jorens, MD; Didier G. Ebo, MD; Marc J. Claey, MD; Johan M. Bosmans, MD; and Christiaan J. Vrints, MD

We report a patient in whom presumed vasospasm of an angiographically normal coronary artery led to severe transmural myocardial ischemia. To our knowledge, this is the first case in which an allergic reaction to locally applied chlorhexidine caused such a severe reaction. (CHEST 1998; 113:1417-19)

**Key words:** anaphylaxis; chlorhexidine; coronary; vasospasm

A patient sustained two anaphylactic reactions accompanied by severe myocardial ischemia caused by presumed coronary artery vasospasm. Immunologic testing indicated chlorhexidine as the culprit substance. This case emphasizes the fact that severe anaphylaxis can result in dramatic cardiac changes secondary to the systemic and local release of vasoconstrictive mediators. It should be stressed, however, that subclinical coronary atherosclerosis can be unmasked, merely by the fact of severe vasodilative shock.

**Case Report**

A 53-year-old man with no history of cardiac disease was referred for curative resection of the upper lobe of the left lung because of adenocarcinoma. Ten minutes before anesthetic induction, a test dose of cefazolin was administered. The patient subsequently received propofol, sufentanil, and atracurium. Fifteen minutes later, profound hypotension developed (BP, 45-30 mm Hg; pulse rate, 130/min) and the monitor showed diffuse ST depression. The patient was resuscitated with ephedrine, 40 mg; epinephrine, 0.2 mg; colloid; methylprednisolone, 300 mg; and ranitidine, 50 mg. In the ICU, IV nitroglycerin was administered to prevent recurrent myocardial ischemia. Recovery was uneventful and resection of the left upper lobe was performed 2 days later. Cefazolin was replaced by erythromycin for antibiotic prophylaxis. The peri- and postoperative phases were without problems.

The next day, Hbitane (2% chlorhexidine digluconate, 70% alcohol solution) was applied to the skin and the patient again developed severe hypotension and chest pain. The ECG was compatible with inferoposterior myocardial infarction (Fig 1, A). After IV administration of 1 g of tranexamic acid, infusion of nitroglycerin 2.5 μg/kg/min, and promethazine 50 mg, ST segments normalized rapidly (Fig 1, B). Serially determined cardiac...
enzyme levels excluded myocardial necrosis. Findings from coronary arteriography were completely normal. After two episodes of life-threatening shock and only several days after major surgery, it was considered medically inappropriate to proceed to pharmacologic testing for coronary spasm.

An extensive immunologic investigation was performed; tests included serum-specific IgE measurement and immediate skin testing for various antibiotics, analgesics, muscle relaxants, and disinfectants. Whereas healthy volunteers failed to react to the substance, a prick test with 2% chlorhexidine digluconate in 70% alcohol was strongly positive in the patient, clearly suggesting that Hibitane was the culprit.

**DISCUSSION**

Severe anaphylaxis may induce bronchospasm, profound vasodilation, and angioedema. In such cases, underlying subclinical coronary atherosclerosis can become clinically evident. Anaphylaxis may induce an acute ischemic burden due to the combination of reduced coronary perfusion pressure, tachycardia, and sometimes severe hypoxia. This combination of events may hamper an adequate cardiac response to the extreme vasodilation and even lead to a reduced cardiac output and further deterioration.

The therapeutic administration of α-agonists (eg, ephedrine, epinephrine) will induce an inotropic and chronotropic response that leads to peripheral and possibly coronary vasoconstriction. An acute rise in shear stress can elicit disruption of an unstable coronary plaque, resulting in platelet aggregation and the release of potent vasoconstrictors (thromboxane and serotonin). This creates the ideal environment for coronary occlusion. Moreover, Kovanen et al demonstrated the presence of activated mast cells at the site of ruptured coronary artery plaques, raising the question of whether an allergic reaction, by triggering the release of mast cell contents, could promote plaque disruption.

Since no underlying coronary artery disease was detected in our patient, the theory of a pure coronary spasm is preferred. Coronary vasoconstriction is a well-established feature of anaphylaxis, which is characterized by a massive systemic release of several mediators. These substances include histamine, catecholamines, serotonin, leukotrienes, and prostaglandins, which are all capable of modifying coronary tone and significantly influencing platelet aggregation and thrombosis. Perivascular and cardiac mast cells have been implicated in the pathogenesis of coronary artery spasm. The effects of histamine on cardiac function (chronotropism, dromotropism, inotro-
pism, bathmotropism) are mediated via $H_1$ and $H_2$ receptors. Vigorito et al. showed, in a human model, that the IV administration of histamine could elicit two different reactions. In a subgroup of patients with atypical angina or valvular heart disease and normal coronary arteries, the stimulation of $H_1$ receptors induced vasodilation of small coronary resistance vessels. However, in a substantial proportion of patients with vasospastic angina independent of coronary artery disease, histamine provoked vasoconstriction of large capacitance coronary arteries. This finding supports the role of the systemic and local release of histamine during anaphylaxis complicated by coronary vasospasm. Ginsburg et al., in a model of isolated human epicardial coronary arteries, showed that histamine has a very potent vasoconstrictive effect, probably mediated via $H_1$ receptors, whereas $H_2$ receptor stimulation induces vasodilation. The vasoconstrictive effect of histamine in patients with vasospastic angina and morphologically normal coronary arteries is most probably the result of a defective endothelial nitric oxide-mediated vasodilation due to subclinical early coronary atherosclerosis. Although coronary vasospasm has been reported during allergic reactions against wasp stings, antibiotics, nonsteroidal anti-inflammatory drugs, glafenine, and contrast agents, to our knowledge this is the first reported case initiated by a locally administered substance. In conclusion, anaphylactic reactions can cause such major hemodynamic changes that unmask previously unknown coronary disease. In such situations, fast recovery from the extreme peripheral vasodilation and tachycardia is crucial. On the other hand, the massive release of potent coronary vasoconstrictive mediators may lead to coronary vasospasm, mimicking acute myocardial infarction. Coronary angiography may be needed to define coronary anatomy. Immunologic identification of the causative factor is crucial in order to prevent similar catastrophes in an anaphylactic patient.

REFERENCES


False Elevation of Serum Creatinine Following Skin Absorption of Nitromethane Complicates the Clinical Diagnosis of Rhabdomyolysis*

Andrea Gabrielli, MD; and Catherine Hamnett-Stabler, PhD

A patient had extensive blunt trauma from a high-speed crash in which nitromethane fuel erupted from the fuel tank and soaked into his protective multilayer jumpsuit. The clinical diagnosis was complicated because the absorption of nitromethane fuel through the skin and by inhalation falsely increased the serum creatinine value when a modified Jaffee reaction was used in the laboratory. This spurious value was “unmasked” by the use of an enzymatic method to measure the serum creatinine level. A high serum creatinine value disproportionate to the level of BUN and recent skin exposure to nitromethane were the clinical indications that suggested the differentiation of massive rhabdomyolysis from spurious hypercreatininemia. This spurious value was a confounding factor in the diagnosis of crush syndrome and rhabdomyolysis.

(CHEST 1998; 113:1419-22)

Key words: absorption; nitromethane; rhabdomyolysis; skin

Rhabdomyolysis results when skeletal muscle is injured and toxic intracellular components are released into the systemic circulation. Biochemical hallmarks of this syndrome include increased serum creatine kinase level, ...

*From the Departments of Anesthesiology (Dr. Gabrielli) and Pathology, Immunology, and Laboratory Medicine (Dr. Hamnett-Stabler), University of Florida College of Medicine, Gainesville.

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