

### SYSTEMIC ARTERIAL VASOSPASTIC SYNDROME: FAMILIAL OCCURRENCE WITH VARIANT ANGINA

The observation that migraine headaches and Raynaud's phenomenon are occasionally associated with variant angina has raised the possibility of a systemic arterial vasospastic (SAV) syndrome [1]. A familial basis for this syndrome, however, remains uncertain. We report a family in which three generations have developed manifestations of a SAV disorder.

**Case Reports. Mother.** An apple orchard owner with a history of classical migraine headaches since childhood developed, at age 48, intermittent substernal chest pain at rest. Coronary angiography revealed only minor luminal irregularities, but diffuse coronary artery spasm and her typical symptoms developed after the intravenous administration of 0.15 mg of ergonovine maleate. Subsequently, with discontinuation of her  $\beta$ -blocker and an increased dose of isosorbide dinitrate, her symptoms abated.

**Daughter.** An animal researcher with a history of Raynaud's disease and classical migraine headaches since her early teen years developed intermittent chest pain and shortness of breath at age 37. During an exercise treadmill test, the patient developed 1- to 2-mm ST elevation and hyperacute T waves in leads V<sub>3</sub>, V<sub>4</sub>, and V<sub>5</sub> (Figure 1), consistent with coronary vasospasm [2]. Coronary angiography revealed normal arteries. Ergonovine was not administered because the patient required continuous intravenous nitroglycerin to control her symptoms. The patient finally achieved relief of her symptoms on a regimen of diltiazem, isosorbide dinitrate, and terazosin. Neither her brother nor sister has a history of chest pain, but her sister has had classical mi-

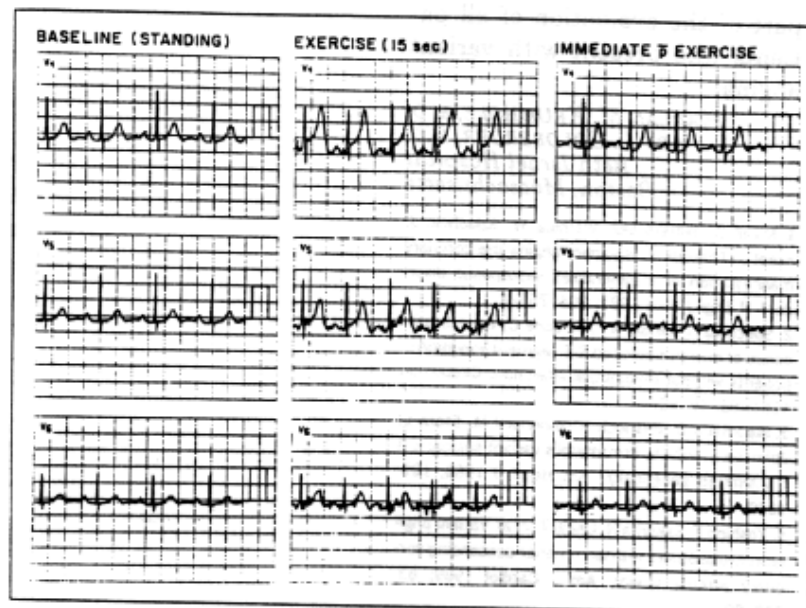


Figure 1. At rest (left panels), the electrocardiogram was normal. Within 15 seconds after beginning treadmill exercise (middle panels), the patient developed substernal chest discomfort with lateral lead ST-segment elevations and increased T-wave positivity. After exercise (right panels), the ST elevations then returned to normal.

graine headaches since childhood.

**Granddaughter.** A 14-year-old high school student has a 6-year history of Raynaud's disease. She currently has no other symptoms. None of her three other siblings have a history of Raynaud's disease, chest pain, or migraine headaches.

**Comments.** There is controversy about whether a hereditary form of variant angina exists [3-6]. Yoshino and colleagues [4] reported two brothers with left anterior descending coronary arterial spasm, demonstrated with the use of ergonovine maleate during cardiac catheterization. Madias and O'Connor [5] also reported two brothers with variant angina, diagnosed by typical chest pain, transient ST elevation, insignificant fixed coronary artery disease, and response to nitroglycerin. The possibility of a genetic susceptibility is further supported by one study demonstrating a low frequency of HLA-DQ $\omega$ 3 in patients with variant

angina as compared with patients with normal and atherosclerotic arteries [7].

In 1981, Miller and colleagues [1] reported the association of migraine headaches and Raynaud's phenomenon in patients with variant angina. The clinical entity of systemic arterial vasospasm has also been previously reported within a family. Fournier and associates [6] reported two siblings with a familial history of migraine and coronary artery spasm.

We extend these previous observations by reporting a family in which a mother, daughter, and granddaughter have manifestations of a SAV syndrome, raising the possibility of a genetic predisposition. The basis of the vasospastic diathesis in these patients remains poorly defined, although a role for altered  $\alpha$ -adrenergic tone is suggested. The familial association of this syndrome, nevertheless, may be more common than previously recognized, and a careful family history should be

part of the evaluation of all patients who present with variant angina.

**HARLAN M. KRUMHOLZ, M.D.**  
**ARY L. GOLDBERGER, M.D.**  
*Beth Israel Hospital  
Boston, Massachusetts*

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**FAMILIAL OCCURRENCE WITH  
VARIANT ANGINA  
AND  
MIGRAINE  
AS  
MANIFESTATIONS OF  
GENERALIZED  
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The occurrence of variant angina in two brothers and Raynaud's phenomenon in a sister are reported. The variant angina was associated with a normal level of coronary artery vasospasm (CAV) on a 24-hour ambulatory electrocardiogram. A family history of a similar disease involving variant angina and Raynaud's phenomenon was also reported. A family history of a similar disease involving variant angina and Raynaud's phenomenon was also reported.

Two brothers with variant angina and a sister with Raynaud's phenomenon are reported. The variant angina was associated with a normal level of coronary artery vasospasm (CAV) on a 24-hour ambulatory electrocardiogram. A family history of a similar disease involving variant angina and Raynaud's phenomenon was also reported.

Raynaud's phenomenon is a common disorder characterized by reversible digital vasospasm. It is often associated with connective tissue diseases, but can also occur in isolation. The pathogenesis is unclear, but it is thought to be related to abnormal vasoconstriction of the digital arteries. Variant angina is a clinical entity characterized by transient ST-segment elevation on the electrocardiogram (ECG) in the absence of obstructive coronary artery disease. It is thought to be caused by transient coronary artery vasospasm. The pathogenesis is unclear, but it is thought to be related to abnormal vasoconstriction of the coronary arteries. In this report, we describe a family with variant angina and Raynaud's phenomenon, suggesting a generalized vasospastic syndrome.