Laboratory studies included measures of creatinine (0.84 mg/dL), urea (37 mg/dL), glucose (95 mg/dL), Na (132 mEq/L), K (4.1 mEq/L), and therapeutic lithium (2.32 mEq/L; normal range 0.6–1.2 mEq/L), which confirmed the diagnosis of lithium intoxication. During hospitalization, the lithium regimen was suspended but venlafaxine and lamotrigine were continued on the recommendation of the psychiatry department.

Although the sodium channel blocker lamotrigine is known to be associated with arrhythmogenesis and a relationship has been reported between venlafaxine and a long PR interval and bundle branch block, the disappearance of neurological symptoms and the recovery of sinus rhythm at 60 beats/min on normalization of the lithium level led us to attribute the bradyarrhythmia to lithium intoxication.

Chronic lithium intoxication generally presents with nonspecific symptoms and its diagnosis requires a high degree of diagnostic suspicion. In 2001, a review of the literature[2] found that the most important predictors of lithium intoxication were: (a) diabetes insipidus (nephrogenic secondary to chronic lithium treatment); (b) age >50 years; (c) hypothyroidism, and (d) deterioration in renal function.

The symptoms most frequently associated with lithium intoxication are gastrointestinal (i.e. nausea, vomiting and diarrhea) and neurologic (i.e. neuromuscular excitability, trembling, muscle weakness, ataxia, and confusion or delirium). Cardiologic signs and symptoms appear in only 20%–30% of patients.[3] The most frequent ECG findings are T wave changes (i.e. flattening). Bradyarrhythmias have also been described: namely, sinus node dysfunction and varying degrees of atrial block, which occasionally require temporary pacemaker implantation. In a series of 19 patients, Talati et al.[4] reported a variety of symptoms associated with overdoses: syncope (7), dyspnea (2), central nervous system toxicity (4), atypical chest pain, and weakness or lethargy. Eight patients presented with a lithium concentration <1.5 mEq/L. Sinoatrial block was the most frequent cardiac repercussion, followed by sinus bradycardia. In most patients, these changes were corrected by lithium withdrawal. The cardiovascular signs and symptoms of lithium toxicity typically appear after the neurologic symptoms. Although infrequent, arrhythmias, which are potentially fatal with lithium overdoses, have been reported.[5]

In conclusion, given that the cardiotoxicity induced by lithium is reversible once the concentration returns to normal, it is important to bear in mind that ECG changes observed in patients being treated with lithium may be linked to the plasma concentration, even in the absence of an overdose.

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REFERENCES

1. Hansen HE, Admisen A. Lithium intoxication (Report of 23 cases and review of 100 cases from the literature). Q J Med. 1978;47:123–44.
2. Oakley PW, White IM, Carter GL. Lithium toxicity: an iatrogenic problem in susceptible individuals. Aust N Z J Psychiatry. 2001;35:833–40.
3. Serinken M, Karcioglu O, Korkmaz A. Rarely seen cardiotoxicity of lithium overdose: complete heart block. Int J Cardiol. 2009;132:276–8.
4. Talati SN, Aslam AF, Vasavada B. Sinus node dysfunction in association with chronic lithium therapy: a case report and review of literature. Am J Ther. 2009;16:274–8.
5. Mitchell JE, Mackenzie TB. Cardiac effects of lithium therapy in man: a review. J Clin Psychiatry. 1982;43:47–51.

Acute Myocardial Infarction Probably Related to Severe Coronary Vasospasm During Pheochromocytoma Crisis

Infarto agudo de miocardio probablemente secundario a severo vasospasmo coronario durante crisis de feocromocitoma

To the Editor,

Pheochromocytomas are neuroendocrine tumors that are often present in one of the adrenal glands. Among the systemic abnormalities associated with release of catecholamines, cardiac involvement is among the most frequent,[1] with reported conditions including transient myocardial dysfunction, acute coronary syndrome (ACS), and ventricular arrhythmias.[2–4]

We present the case of a 39-year-old woman with no pertinent history, who was referred to us for primary angioplasty due to inferior ST-elevation ACS (STEACS), defined as angina of 6 h duration associated with 2.5 mm ST-segment elevation (Fig. 1A). Of note in the examination were sinus tachycardia (145 beats/min) and arterial hypertension (180/110 mmHg). She was treated initially with aspirin and a loading dose of clopidogrel (600 mg). During transfer to our hospital, she experienced psychomotor agitation and required sedation. On admission, she was in a stupefied state, with persistent sinus tachycardia, arterial hypertension (systolic blood pressure, 60 mmHg) and a lower ST-segment elevation. An emergency coronary angiogram was performed (2000 IU of unfractionated heparin with coadjuvant treatment). This revealed normal coronary arteries (Fig. 1B); ventriculography revealed inferior hypokinesis-akinesis with an ejection fraction of 55% (Fig. 1C). After the procedure, the patient experienced a deterioration in her state of consciousness and hypoxemia requiring infusion of vasoactive drugs and orotracheal intubation. A computed tomography scan of the brain did not show any intraparenchymal bleeding, although subarachnoid hemorrhage could not be ruled out due to the presence of perimesencephalic contrast. The laboratory tests performed on admission revealed a creatinase level of 1026 IU/L (normal range, 25–140 IU/L), MB creatinase isoform of 304 IU/L (normal range, 0–24 IU/L), and troponin T of 8.9 ng/mL (normal range, 0–0.1 ng/mL). The patient was admitted to the intensive care unit with marked hemodynamic instability and suffered a cardiorespiratory arrest that did not respond to cardiopulmonary resuscitation maneuvers. She died 2 h after admission.

In the autopsy, a pheochromocytoma measuring 3.5 cm in diameter was found in the right adrenal gland (Fig. 2A). In addition, a massive bilateral pulmonary hemorrhage was observed (Fig. 2B) and subarachnoid hemorrhage (Fig. 2C). These were identified as the most probable causes of death. The coronary arteries had mild intimal hyperplasia with no luminal occlusion (Fig. 2D). Nevertheless, an established acute myocardial infarction (AMI) of between 2 and 12 h duration was observed, with involvement of the inferior and posterior walls of the left ventricle (Fig. 2E).
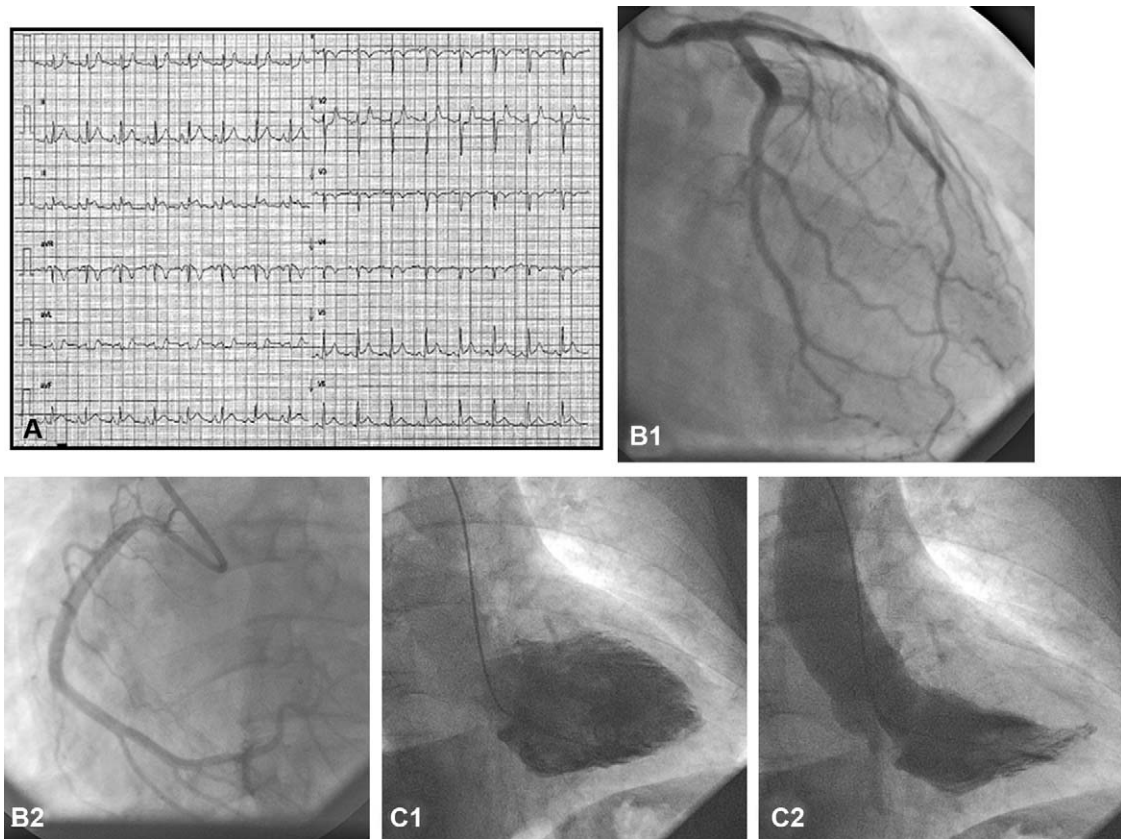
Figure 1. A: ST-segment elevation. B: Normal coronary arteries. C: Inferior hypokinesis-akinesis with ejection fraction of 55%.
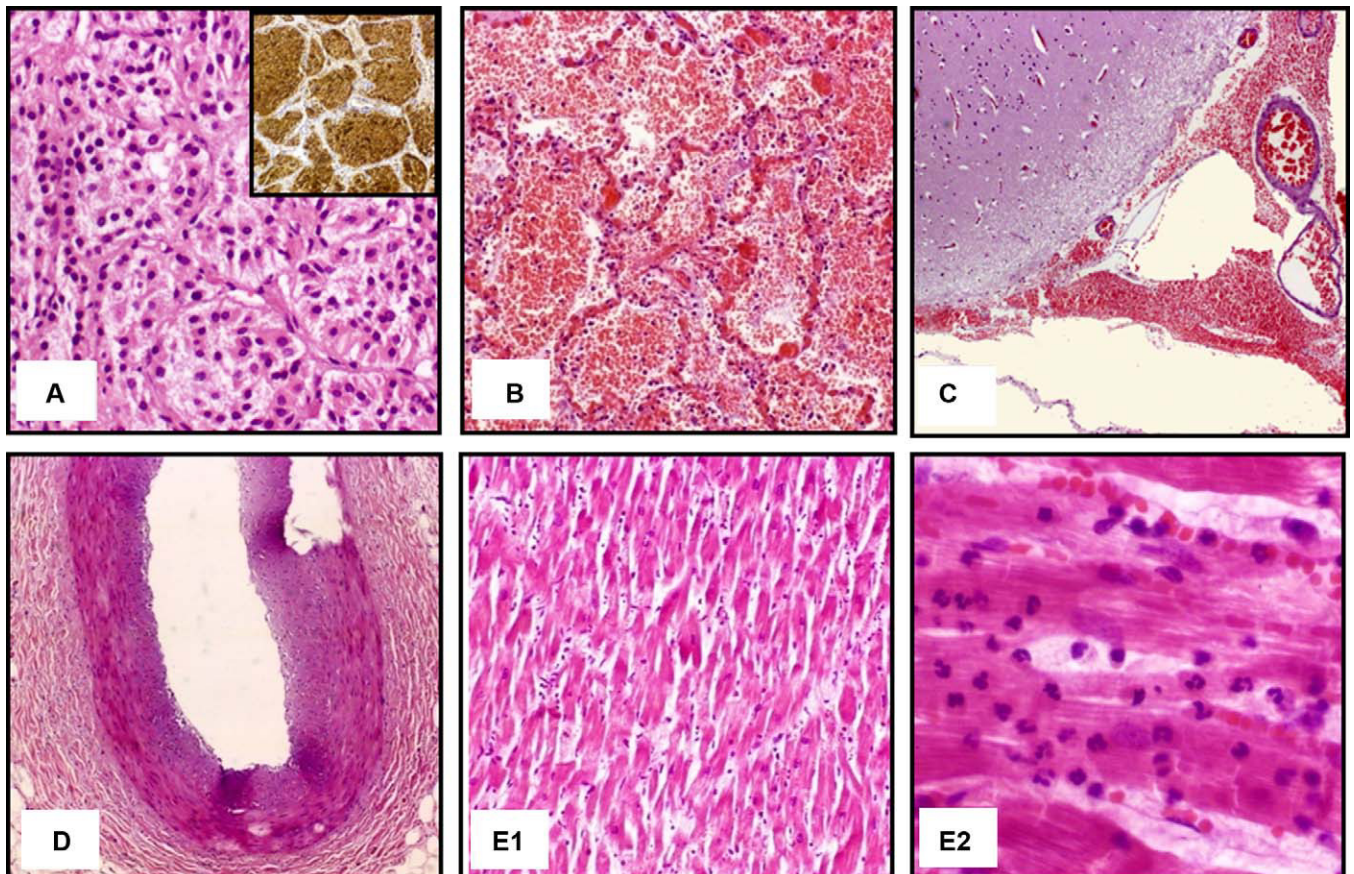
Figure 2. A: Hematoxylin-eosin and immunohistochemical staining that confirm diagnosis of pheochromocytoma. B: Pulmonary vascular congestion and intra-alveolar hemorrhage. C: Hemorrhage in subarachnoid space. D: Mild intimal coronary hyperplasia. E: Degenerative myocardial changes characteristic of acute myocardial infarction.

In this atypical case resulting in death, the first sign of the hyperadrenergic state was STEACS. Pheochromocytoma crises resembling AMI have been reported.[5,6] The abnormalities were explained in terms of severe coronary vasospasm, direct myocardial damage by catecholamines, and increased oxygen uptake as a result of tachycardia and increased afterload. Characteristically, the abnormalities were transient, with normalization after treatment of the tumor. Darzé et al[5] reported a similar case, but with no abnormal cardiospecific markers and with total recovery after treatment with α-blockers. Our case had the particular feature of clinical, laboratory, and pathological confirmation of established AMI in a patient with no obstructive lesions in her coronary arteries. The involvement of the inferior and posterior walls in the electrocardiogram, ventriculography findings, and the autopsy point to an unusually prolonged coronary vasospasm in the right coronary artery as the most probable trigger of the events experienced by the patient.

Although the patient was transferred for treatment of ACS, the fatal outcome was related to massive brain and pulmonary hemorrhage, probably as a result of hypertensive crises or direct vascular damage caused by the hyperadrenergic state. In any case, administration of antiplatelet agents and anticoagulants as treatment for STEACS may have exacerbated the patient's condition.

In conclusion, the present case highlights one of the characteristics of adrenergic crises. It also points to the wide range of possible presentations that can make an accurate diagnosis so complicated in emergency situations.

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REFERENCES

1. Liao WB, Liu CF, Chiang CW, Kung CT, Lee CW. Cardiovascular manifestations of pheochromocytoma. Am J Emerg Med. 2000;18:622–5.
2. Barriales-Villa R, Hevia S, Santamarta-Liébana E, Morís C. Miocardiopatía producida por feocromocitoma o miocardiopatía por estrés secundaria a feocromocitoma: ¿necesidad de una nueva denominación? Rev Esp Cardiol. 2008; 61:432–3.
3. Magalhaes AP, Pastor A, Núñez A, Cosío FG. Taquicardia ventricular como manifestación clínica inicial de feocromocitoma. Rev Esp Cardiol. 2007;60:450–1.
4. Suárez-Peñaranda JM, Gómez-Otero I, Muñoz JI, Pedreira-Pérez M. Muerte cardiaca asociada a ganglioneuroma suprarrenal. Rev Esp Cardiol. 2008;61:551–2.
5. Darzé ES, Von Sohsten RL. Pheochromocytoma-induced segmental myocardial dysfunction mimicking an acute myocardial infarction in a patient with normal coronary arteries. Arq Bras Cardiol. 2004;82:178–80.
6. Yebra Yebra M, Martín Asenjo R, Arrue I, Paz Yepes M, Bastante Valiente MT, Prieto S. Isquemia miocárdica aguda y trombosis ventricular asociadas a feocromocitoma. Rev Esp Cardiol. 2005;58:598–600.

Acute Aortic Syndrome and Rheumatoid Arthritis

Síndrome aórtico agudo y artritis reumatoide

To the Editor,

Rheumatoid arthritis (RA) is an inflammatory immune system disorder that is associated with a higher level of morbidity and mortality than found in the general population, mainly because of cardiovascular disease. In Switzerland, mortality due to RA increased by >50% and, in England, it was 1.5–1.6 times higher, principally due to myocardial infarction but also to valvular dysfunction.[1,2] We report the case of a patient with RA who was admitted for acute aortic syndrome (i.e. an aortic intramural hematoma developing into a dissection). A literature search carried out using PubMed and the keywords "rheumatoid arthritis" AND "aortic dissection" revealed no evidence of an association between the two, which we believe is a possibility.

The patient was a 47-year-old man who smoked 70 cigarettes/day and had high blood pressure of recent onset, which was being treated with enalapril. He had been diagnosed with RA 7 years earlier and was currently receiving methotrexate, leflunomide, indometacin, folic acid, and deflazacort. He presented with severe retrosternal pain that radiated to the neck and back and which was associated with autonomic symptoms. On admission, his blood pressure was 110/60 mmHg and his heart rate was 80 beats/min. A hemogram and biochemical study gave normal results: the erythrocyte sedimentation rate was 79 mm/h. Thoracic multidetector computed tomography CT (Fig. 1) showed an aortic hematoma associated with a Stanford type-B dissection (i.e. distal to the left subclavian artery). The patient was admitted to intensive care unit where his blood pressure was maintained at <120/80 mmHg. The chest pain disappeared and subsequent examinations revealed partial resolution of the aortic hematoma. An aortic endoprosthesis was used to stabilize the patient's condition.

The association between RA and loss of elasticity in the aorta is principally due to inflammatory changes and structural alterations, such as smooth muscle hypertrophy and changes in the extracellular matrix characterized by an increase in collagen and a reduction in elastin, all of which predispose to increased rigidity of the arterial wall. Moreover, smooth muscle cells can produce bioapatite (they express osteoblastic markers under inflammatory conditions) which causes calcification of the aortic tunica media. Perivascular inflammation and cellular infiltration around the vasa vasorum have been observed to result in ischemia.[3] It is widely recognized that aortic intramural hematoma is caused by rupture and bleeding from the vasa vasorum. We believe that these mechanisms (principally ischemic phenomena in the vasa vasorum themselves) may have triggered the condition in our patient. Moreover, in RA, a type of peripheral neuropathy caused by necrotizing vasculitis of the vasa vasorum has been reported.[4]

Hollan et al.[5] studied changes in the aortic wall (i.e. inflammatory changes) in specimens obtained following coronary artery revascularization surgery, and compared findings in patients with and without RA. They excluded patients with infiltration close to the intima, which can occur in normal individuals, and focused on observations in the tunica media and tunica adventitia. They concluded that the observed changes were greater in patients with RA and that they could represent an