Native Mitro-Aortic Infective Endocarditis Secondary to Brucellosis

Brucellosis is a zoonosis with worldwide distribution, but it rarely causes endocarditis. Brucella infective endocarditis (BE) is an entity with subacute presentation, characterized by extensive valve destruction and myocardial abscess formation, usually requiring combined medical and surgical therapy. Without prompt treatment, it progresses to heart failure and death. (1) The following is a case of infective endocarditis secondary to Brucella.

We describe the case of a 40 year-old male patient, farmer, smoker, who was admitted to the department of cardiology due to 1-week history of progressive dyspnea and persistent fever. On admission, he was febrile (38,5 °C), with blood pressure of 110/70 mm Hg, good peripheral perfusion, tachypnea (35 per minute), and heart rate of 95 bpm. Auscultation revealed a grade 4/6 diastolic murmur in the aortic area and grade 3/6 systolic murmur in the mitral valve area, and crepitant rales at both lung bases. Palpation revealed hepatomegaly, and ankle edema was observed in both legs. The electrocardiogram showed sinus rhythm with left ventricular overload, and the chest x-ray revealed enlarged heart and signs of flow redistribution in both lungs. Lab tests detected high erythrocyte sedimentation rate (55 mm) and 12,100/mm3 white blood cell count with initially negative blood cultures. The transthoracic echocardiography showed increased left ventricular (LV) diameters (diastolic diameter, 61 mm, systolic diameter, 33 mm) and increased tricuspid aortic valve diameter. A highly mobile vegetation of 25 x 11 mm attached to the left coronary leaflet was found at the level of the ventricular outflow tract, with extensive prolapse in the LV outflow tract. Severe aortic regurgitation without stenosis was observed. The mitral valve presented a severe regurgitant jet originated in the mid portion of the anterior mitral leaflet, at the level of the mitral-aortic intervalvular fibrosa, and image consistent with sessile vegetation of 10 x 9 mm in the atrial aspect of the anterior mitral leaflet (Figures 1 & 2). Positive serologic test for Brucella abortus was obtained during follow-up, together with a positive Rose-Bengal test, positive agglutinations to Brucella at 1/640, and a titer of 1:1024 determined by the indirect immunofluorescence test. Treatment was started with doxycycline, streptomycin, and rifampicin.

Due to persistent heart failure, aortic valve replacement with mechanical prosthesis (size 21), and mitral valve repair was performed.

Culture of material excised at the operation was positive for Brucella abortus. Postoperative course was uneventful, with clinical improvement and absence of fever, and reduction of Brucella antibody titers. A 6-week course of antibiotics was indicated by the Department of Infectious Diseases due to the patient's good progress, who is currently on follow-up.

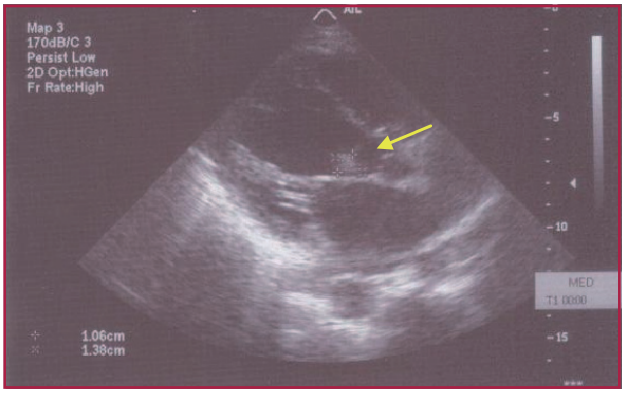

Fig. 1. Transthoracic echocardiography. Parasternal long axis view showing vegetation of 1.0 x 1.3 cm diameter attached to the ventricular wall is observed, close to the left ventricular outflow tract.

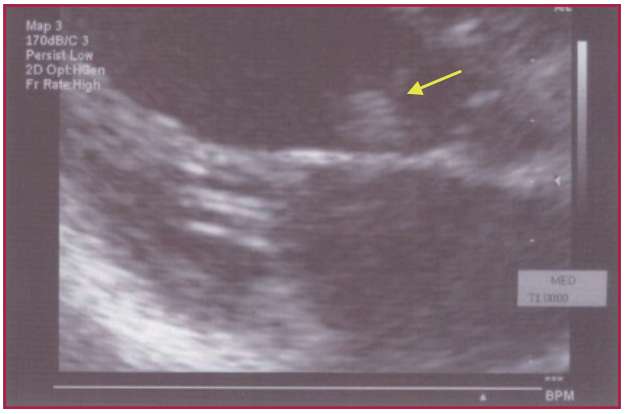

Fig. 2. Transthoracic echocardiography. Parasternal long axis view with zoom on the formation described above, showing lower echo-refraction with respect to the valve structure, and the vegetation occupying almost 50% of the of the left ventricular outflow tract diameter

While brucellosis is a rare disease, it occurs in Asia, Middle East, and South America. It is a systemic infectious disease caused by gram-negative bacilli of the genus Brucella, which in the case of humans, generally corresponds to the Brucella melitensis strain. Typically, it is a mild, asymptomatic disease that can affect multiple organs as it progresses, with an incubation period of 2-6 weeks though it may occasionally be much longer. (2)

Endocarditis is a rare but severe complication of brucellosis, affecting 2% of the cases and is the main cause of mortality (80%) in these patients. It mostly affects the left coronary valves, predominantly the aortic valve (29%), also causing abscesses in the ascending aorta. Morbidity rate is high, with focal complications in 30-40% of cases. As in the case of our patient, a history of work in rural areas in contact with unpasteurized food (particularly milk) or infected animals are common risk factors. (3)

Even with a high level of suspicion, diagnosis may be difficult to confirm. Serologic tests are more sensitive than blood cultures, but they are not specific and are difficult to interpret in endemic areas. They may also be negative in early stages of the disease. The most common tests are Huddleston, Rose-Bengal, Wright, 2-mercaptoethanol, and complement fixation. As a result of the slow growth of the bacteria and the need for specific culture media, the negative blood culture rate is higher than for other types of bacterial endocarditis. (4) Due to the high valvular endocardial damage, treatment is rarely limited to the use of antibiotics alone and surgical procedures are also necessary. (5)

Indications for surgical intervention include refractory heart failure, sepsis resulting from a myocardial abscess, severe valvular dysfunction, and embolism. Valve replacement with aggressive debridement of infected tissue is the most important part of the treatment, and should be complemented with a course of antibiotics before and after surgery. (6)

Brucella infective endocarditis is a rare entity with a high morbidity rate, and also represents the most common cause of death in patients with brucellosis. A high index of suspicion for this disease is necessary to diagnose it in potentially exposed patients in endemic areas. In Argentina, it is a mandatory reportable disease.

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Epicardial Cryoablation of Ventricular Tachycardia in Chagas Disease: Emergency Hybrid Treatment

Ventricular tachycardias (VT) associated to nonischemic structural heart disease present larger scars in the epicardial area than in the endocardial area. At the same time, the density of slow conduction channels within the epicardial scar is higher than in the endocardium. (1) The combined (epicardial and endocardial) ablation of VT achieves high success rate and low recurrence; (2) however, it is a major challenge to avoid lesions in the coronary arteries during the procedure.

We describe the case of a patient with Chagas disease and electrical storm, where the left ventricular epicardial and endocardial voltage mapping was fused with a multidetector computed tomography angiography (MDCTA) to directly visualize the relationship between the myocardial scar and the coronary arteries. A hybrid treatment with radiofrequency and cryoenergy was used in order to minimize risks.

A 69-year-old male patient with dilated Chagas cardiomyopathy (ejection fraction 28%) was referred to our center due to electrical storm. He had been treated with implantable cardioverter defibrillator (ICD) 12 months before as primary prevention of sudden cardiac death.

He had incessant sustained monomorphic ventricular tachycardia (SMVT) without hemodynamic decompensation, with multiple ICD shocks, refractory to amiodarone treatment. Surface electrocardiogram (ECG) met epicardial VT criteria (3) (Figure 1).

The patient underwent an emergency catheter ablation procedure. The pericardial cavity was reached using Sosa's technique. (4) Voltage mapping determined a large anterolateral epicardial scar region in basal and medial segments. The VT breakout site was obtained with activation mapping in the basal anterolateral region. At this level, ventricular fractionated and mid-diastolic potentials were observed, and the slow conducting zone of the tachycardia circuit (isthmus) was localized with entrainment maneuvers. Previously, a MDCTA was performed and merged with the epicardial voltage mapping. As a result, it was possible to determine the exact relationship between the scar and the coronary arteries. The use of radiofrequency on that site interrupted the arrhythmia in a few seconds (3.4 sec.), as shown in Figure 2, top.

Then, the VT substrate was treated using the dechanneling technique with an 8 mm tip focal cryoablation catheter, to reduce the risk of coronary artery lesion (Figure 2, bottom) until the abnormal electrograms, described by Haissaguerre (5) (LAVAs), were eliminated.

A different VT morphology was induced, which did not present electrocardiographic criteria for epicardial VT. A transseptal puncture was performed to access the left ventricle and voltage mapping was created. A slow conduction zone (isthmus) was localized at the endocardial level, on a voltage channel that divided the scar into two. The use of radiofrequency interrupted the VT in 3.9 sec. (Figure 3).

Several consolidation lesions were targeted on this point to close the voltage channel. (5) No VT was induced by any protocol of programmed ventricular

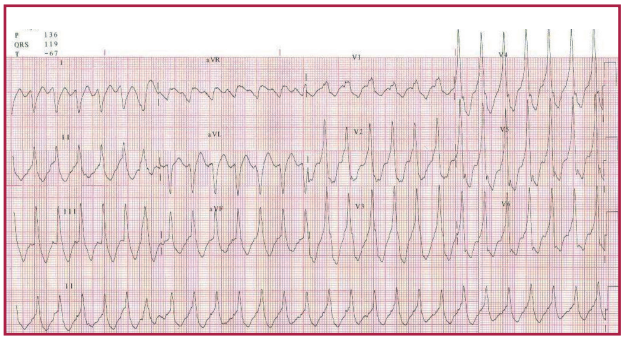

Fig. 1. Monomorphic ventricular tachycardia with epicardial origin: absence of Q-waves in inferior leads; pseudo-delta wave > 75 ms; MDI > 0.59.

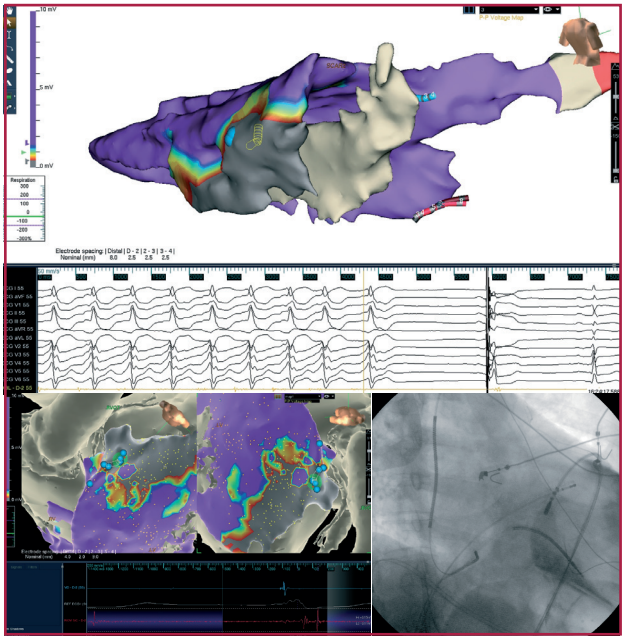

Fig. 2. *Top*: Epicardial voltage mapping delimiting the anterolateral region of the scar. The blue dots correspond to the effective ablation site (circuit isthmus). *Bottom*: Mid-diastolic potentials recorded by the ablation catheter placed in the circuit isthmus during sustained monomorphic ventricular tachycardia (yellow). Notice the prolongation of the ventricular tachycardia cycle before its interruption. *Bottom, left*: Fusion of multidetector computed tomography angiography and epicardial voltage mapping. The blue dots correspond to a slow conduction channel from the edge to the inside of the scar (double ventricular electrogram in red: ROV SC D2). Targeted focal cryoablation was performed to eliminate the conduction within the scar. *Bottom, right*: Right anterior oblique projection. Subxiphoid approach and fluoroscopic catheter position at the epicardial level, on the effective ablation site in the lateral left ventricular wall.

stimulation. The ICD was rescheduled, and the patient was discharged after 72 hours, without complications. During the 3-month follow-up, the patient did not present VT episodes or defibrillator discharges.

About 25% of the patients with ICD develop electrical storm during the course of 4-5 years, increasing mortality rate despite the ICD. Catheter ablation of VT should be performed as emergency procedure in patients with electrical storm, both with ischemic or non-ischemic cardiomyopathy. It can be performed electively in cases of SMVT even in episodes stored in the ICD. VT ablation is complementary to ICD implantation, and should be performed early to reduce the number of ventricular arrhythmia episodes and shocks.

There are different signs suggestive of epicardial VT. In our case, we used the criteria proposed by the Marchlinsky group: absence of Q-waves in inferior leads; pseudo-delta wave >75 ms; MDI > 0.59 (interval between the onset of QRS to its maximum amplitude/duration); Q wave in L1. Those criteria have 96% sensitivity and 93% specificity.

Coronary angiography is used to correlate the position of the ablation catheter and the coronary vessels; however, this method only provides two-dimensional information, which can lead to errors. We chose to perform a MDCTA and merge it with the pericardial voltage mapping, thus allowing three-dimensional visualization of the relationship between the scar, the coronary arteries and the position of the ablation catheter. (6)

In critical areas of the epicardial circuit (isthmus), radiofrequency was used as ablation procedure. To treat the substrate (epicardial scar) with the dechanneling technique, we used a focal cryoablation catheter, given its improved biophysical profile. Cryoenergy preserves endothelial indemnity, reduces the formation of superficial thrombus, generates homogeneous lesions without extending beyond the surface of the ablation electrode, and reduces the incidence of lesions to vascular structures due to the convection or "ther-

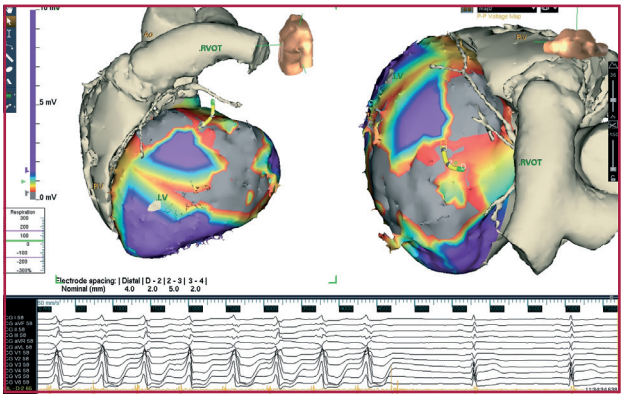

Fig. 3. *Top*: Endocardial voltage mapping. A large anterolateral region of the scar is delimited (gray) separated by an intermediar voltage channel (red), where the ablation catheter is placed. *Bottom*: Radiofrequency application in the voltage channel, and interruption of ventricular tachycardia. At this level, *entrainment* maneuvers were consistent with the circuit isthmus location. Notice the electrogram recorded by the ablation catheter, without conduction to the ventricular myocardium at the moment of interruption.

mal washing" effect produced by coronary blood flow. These characteristics turn it into an attractive technique for catheter ablation of epicardial arrhythmias with risk of coronary artery injury. While there are no prospective clinical trials to validate these results, the biophysical profile of cryoablation offers clear advantages on epicardial arrhythmogenic substrates. This is because the formation of lesions is limited by the convection warming effect produced by coronary blood flow. This method could also be applied to other techniques of substrate treatment, such as ablation of scar edges, scar transection, and scar homogenization.

Catheter ablation should always be considered as an emergency therapeutic method in case of electrical storm. The use of imaging methods, such as multidetector computed tomography angiography and cryoenergy, to complement conventional ablation techniques in complex arrhythmogenic substrates could reduce intraoperative risks. The effectiveness of these methods should be evaluated with prospective protocols.

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Aortic Hypoplasia, an Extremely Rare Cause of Hypertension

In the study of refractory hypertension (HT), the importance of imaging tests to identify its etiology is well established. We describe the case of a male patient who underwent a transthoracic echocardiography and a chest CT angiography, resulting in the definitive diagnosis of the extremely rare cause of his HT.

We describe the case of a 49-year-old male patient with a history of amaurosis fugax (normal brain CT scan). During the study of refractory HT, a transthoracic echocardiography was performed, showing the bicuspid aortic valve with raphe between the right and left coronary cusps. No significant transvalvular aortic gradient was detected, with mild eccentric aortic regurgitation. Valve annulus was 25 mm and the ascending aorta was dilated (44 mm).The aortic arch was 32.6 mm, narrowing just before the beginning of the descending thoracic aorta at the level of the supra-aortic trunks (diameter 15.6 mm), with end-systolic acceleration of flow at that level but no significant gradient (Figures 1A & B). There was evidence of normal left ventricular size and thickness, with preserved systolic function.

In view of these findings, a chest CT angiography was performed, showing aneurysmal dilation of the ascending thoracic aorta (anteroposterior diameter, 44 mm), and a caliber change in the region of the aortic arch with diameter of 18 mm, and descending aorta of 22 mm (Figure 2).

All the findings were consistent with hypoplasia of the thoracic aorta, causing the patient's refractory HT.

Coarctation of the aorta is defined as a significant narrowing of the aortic lumen that causes severe obstruction of blood flow. This process affects an isolated short segment of the aorta.

Coarctation is most often found at the junction of the ductus arteriosus and the thoracic aorta, representing a 98% of all aortic coarctations.

When the narrowing affects longer portions of the aorta, it is known as tubular hypoplasia of the aorta, an exceedingly rare anomaly (1) on which there are very few reports in the literature associating it with secondary HT. (2)

First described by Quain, (3), the etiology of this condition is not well known and congenital and acquired causes have been proposed, (4, 5) although most of the authors turn to a congenital origin.

In the case of our patient, the diagnosis of hypoplasia of the thoracic aorta was associated with the presence of bicuspid aortic valve.

Symptoms typically occur within the first three decades of life and include HT, lower extremity claudication, and mesenteric ischemia.

One of the most severe complications is the HT resulting from this condition. Hypertension is often severe and, if untreated, can lead to potentially life-threatening complications, such as stroke, heart failure or kidney failure. In our case, the patient had a history of amaurosis fugax, with no evidence of changes in the brain CT scan.

Diagnosis is made using imaging techniques, such as echocardiography or CT angiography.

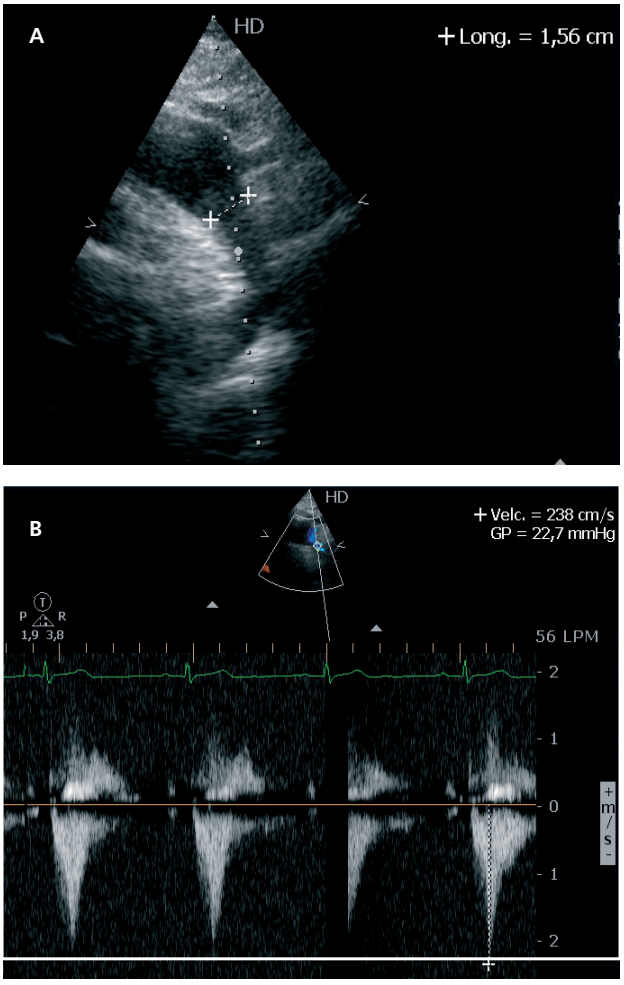

Fig. 1. Transthoracic echocardiography. **A.** Suprasternal view showing the aortic arch and the descending thoracic aorta; an evident change in diameter and narrowing just before the beginning of the descending thoracic aorta (diameter, 15.6 mm) at the level of the supra-aortic trunks are also seen. **B.** Suprasternal view with continuous Doppler at the beginning of the descending thoracic aorta, showing end-systolic acceleration of flow at that level but with no significant gradient.

Reconstructive surgery is the optimal treatment option and must be tailored depending on the characteristics of the disease. Balloon dilation has been used in the treatment of coarctation of the aorta. However, this method has not proved to be effective in patients with aortic hypoplasia affecting long segments. (6)

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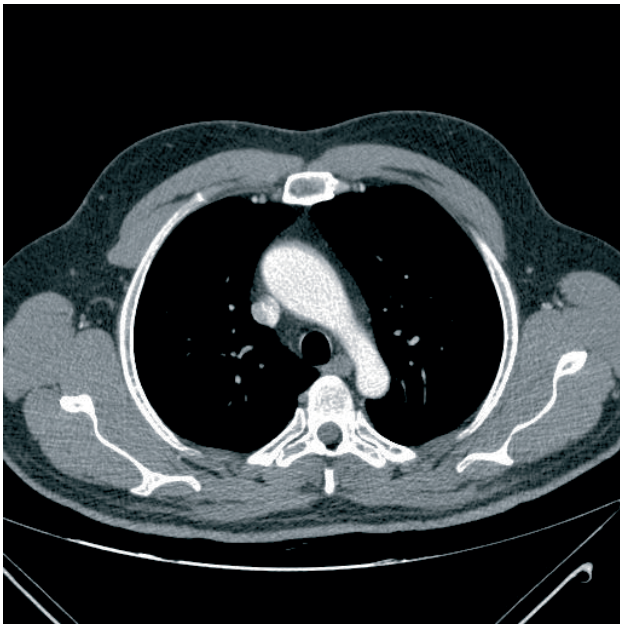

Fig. 1. Contrast-enhanced chest CT scan, showing aneurysmal dilation of the ascending thoracic aorta (anteroposterior diameter, 44 mm), and a caliber change in the region of the aortic arch with diameter of 18 mm, and descending aorta of 22 mm.

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Carcinoid Syndrome

We present the case of carcinoid syndrome with cardiac involvement in a 53 year-old female patient with a history of (poorly controlled) hypertension, eclampsia, and chronic renal failure (CRF). She consults a cardiologist for palpitations and dyspnea in variable functional class. During the guided interrogation the patient referred a long-term history of flushing and a two-year history of diarrhea.

Physical examination showed grade 2/6 systolic murmur in the mesocardium, jugular ingurgitation of 4 cm, painful hepatomegaly 4 cm below the costal margin, hard, mobile, painless inguinal adenopathies, facial, chest and lower limb telangiectasias, and mild infrapatellar edema.

Doppler echocardiography revealed mild right and left atrial enlargement, mildly increased right ventricular diameter with preserved systolic function, mild posterior pericardial effusion, tricuspid valve with sclerosis, thickening and hypomobile leaflets with severe regurgitation (Figure 1), and pulmonary valve with sclerosis, high transvalvular velocity, and mild regurgitation (Figure 2).

In view of the characteristics of the heart condition, the presumptive diagnosis was carcinoid syndrome and several complementary tests were performed to identify the carcinoid tumor. The chest, abdomen and pelvis CT scan revealed round hypodense images on the right liver lobe, small amount of perihepatic fluid, isolated enlarged lymph nodes in the retroperitoneal prevertebral space, and internal iliac lymph node chains. An abdominal ultrasound and a cardiac MRI with gandolinum were performed, which were consistent with the CT scan and the echocardiography.

The patient was hospitalized due to impregnation syndrome two months after the first consultation, presenting anemia, pain in the right hypochondrium, and CRF of prerenal origin, exacerbated by diarrhea and use of diuretics. A retroperitoneal lymph node biopsy revealed sarcoid granulomas, and a wedge biopsy of the liver parenchyma marked with CK7, enolase, chromogranin, synaptophysin, and Ki67 showed total parenchyma replacement by atypical cell proliferation defining nests, cords and trabeculae of small, polygonal-shaped cells with clumped chromatin and fibroconnective and vascular pattern with ecstatic vessels without necrosis, a morphology consistent with well-differentiated neuroendocrine carcinoma.

Plasma serotonin and chromogranin and urinary 5-hydroxyindoleacetic acid were measured with positive results, confirming the diagnosis of carcinoid syndrome with unknown primary tumor.

A total-body positron emission tomography (PET) was performed to locate the primary tumor, showing mediastinal enlarged lymph nodes and heterogeneous hepatomegaly with hypodense areas. Since the patient refused to undergo upper digestive tract videoendoscopy and videocolonoscopy (VCC), a capsule endoscopy was performed, showing signs of non-erosive gastropathy without clinical relevance.

The case was presented at a multidisciplinary meeting, in which, given the absence of known primary tumor, the presence of multiple unresectable liver metastases, comorbidities and patient's poor adherence, the decision was taken to apply symptomatic therapy with octreotide. During the course of the disease, the patient had short periods of symptomatic improvement, but the progressive worsening of her

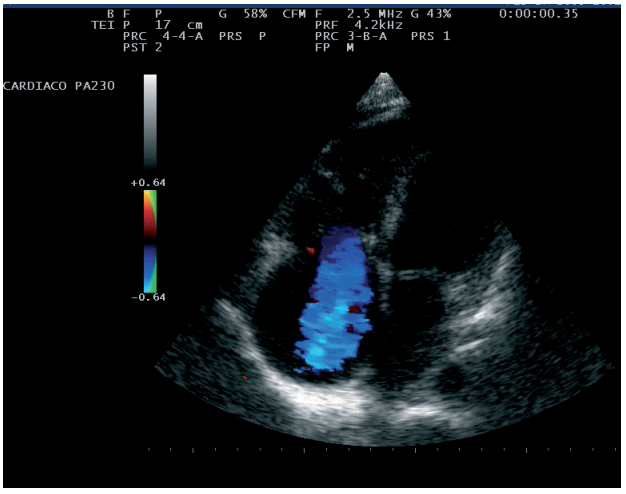

Fig. 1. Transthoracic Doppler echocardiography. Apical four chamber view of mild atrial dilation, mild right ventricular enlargement, mild posterior pericardial effusion, and tricuspid valve with sclerosis, thickening and hypomobile leaflets with severe regurgitation.

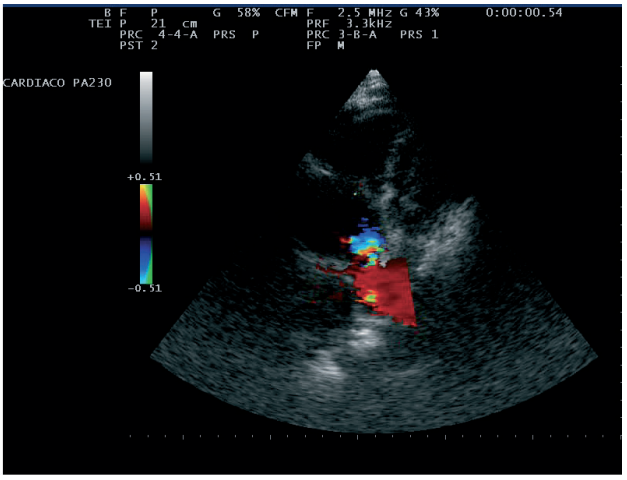

Fig. 2. Transthoracic Doppler echocardiography. Parasternal view of pulmonary artery with sclerosis, high transvalvular velocity, and mild regurgitation.

anemia, CRF, heart failure, and general condition was inevitable, as well as her recurrent hospitalizations. A VCC was performed during one of these hospitalizations, showing a low-grade tubulovillous adenoma in the ascending colon, a finding unrelated to the carcinoid syndrome.

The patient died 30 months after diagnostic confirmation of carcinoid syndrome, in anasarca and with exacerbated CRF.

Carcinoid syndrome is a group of signs and symptoms caused by the metastasis of the carcinoid tumor (rare neuroendocrine malignancy) and by the circulation of the humoral substances it secretes. Tumors of the cecal appendix and the terminal ileum account for 60-90% of the cases; the rest is due to other tumors in

the gastrointestinal system and the bronchi.

The incidence of carcinoid tumors is estimated in 1:75,000 inhabitants, 50% of whom develop carcinoid syndrome, and in turn, 50% of these develop carcinoid heart disease which typically causes abnormalities in the right heart chambers.

Cardiac manifestations are caused by the paraneoplastic effects of humoral substances released by the carcinoid tumor, such as serotonin, histamine, bradykinin, and prostaglandins. These are usually inactivated by the liver, lungs, and brain, but the presence of liver metastases may allow large quantities of these substances to reach the right heart chambers.

Vasoactive substances extend to the left heart chambers only in 5-10% of the patients with multiple liver metastases, bronchial carcinoid, or a patent foramen ovale.

Typically, symptoms are characterized by facial flushing, diarrhea, bronchospasm, and right heart failure.

Many carcinoid tumors follow a prolonged course of up to 20 years from the onset of carcinoid symptoms. However, the development of heart disease in the carcinoid patient heralds a rapid decline in the clinical condition and survival rate is much lower.

Valve regurgitation is the most common complication; about 95% of the patients display moderate to severe tricuspid regurgitation. Pulmonary regurgitation is less common. Both are responsible for right heart failure.

Diagnosis is made with Doppler echocardiography, and is confirmed with serotonin and urinary 5-hydroxyindoleacetic acid assays. Additional complementary tests are only indicative.

In the early phase of the disease, surgical resection of the carcinoid tumor tends to be curative. In some cases, resection or embolization of hepatic metastases can be an option. In patients with the carcinoid syndrome, treatment tends to be palliative; octreotide, analogous of somatostatin, is used for reduction of vasoactive substances and relief of symptoms. Once heart disease has developed, treatment is focused on heart failure.

In selected cases of tricuspid or pulmonary valve stenosis, balloon valvuloplasty produces symptomatic improvement, although recurrent symptoms have been observed after some time. Early valve surgery is the only definitive treatment for severe heart failure. Bioprosthetic valves are preferable, as anticoagulation, which would increase the risk of bleeding secondary to metastasis, can be avoided, and the life expectancy of the patient is likely to be shorter than that of the valve. Patients usually die of severe tricuspid regurgitation rather than of carcinomatosis.

Finally, our diagnostic triad for this disease consists of anamnesis, physical examination and Doppler echocardiography. However, it is even more important for cardiologists to consider carcinoid syndrome as a possible differential diagnosis in tricuspid and pulmonary valve diseases, because it is the only way to provide a better prognosis to our patients.

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Cardioembolic Ischemic Stroke Associated with Mitral Annular Calcification

Mitral annular calcification (MAC) is a chronic degenerative process of the valve fibrous skeleton. MAC has been associated with high risk of systemic embolism, among which cerebral embolism leads to ischemic stroke. We describe a case of stroke secondary to calcific embolization, possibly originated in MAC.

A 78-year-old female patient, receiving eplerenone 25 mg, atorvastatin 10 mg, losartan 50 mg and inhaled bronchodilators on a daily basis, presented with recurrent episodes of expressive aphasia lasting approximately 1 minute. She had several comorbidities, including hypertension (HT), dyslipidemia (DLP), and chronic obstructive pulmonary disease. Twenty days before hospitalization, the patient had been admitted for multiple injuries due to a car accident whereupon a computed tomography (CT) scan of the brain showed no abnormalities (Figure 1). On admission, the neurological examination and lab tests were normal. The ECG showed sinus rhythm, without significant changes. CT scan on admission (Figure 2) revealed bihemispheric subcortical microangiopathic sequelae, mild involutional changes, and punctate calcifications in the cerebellar tentorium and in the M1 segment of the left middle cerebral artery (MCA). During hospitalization, the patient repeated four similar episodes of aphasia with recovery ad integrum. The electroencephalogram revealed left temporal

intermittent slowing, and lamotrigine was prescribed. Magnetic resonance imaging (MRI) of the brain with diffusion sequences showed several acute ischemic lesions at the temporal, lenticular and in the left convexity level, and the magnetic resonance angiography (MRA) of intracranial vessels showed no signal in the left MCA. The magnetic resonance angiography of neck vessels was normal. Total cholesterol was 212 mg/dL, HDL 56 mg/dL, LDL 141mg/dL and triglycerides 77 mg/dL. Echo-Doppler of the lower limbs and iliac veins was normal. The transesophageal echocardiography showed MAC, severe mitral regurgitation, left atrial enlargement, diffuse aortic atheroma, and a 7 × 5 mm mobile calcification associated with the atrial side of the mitral annulus; the interatrial and interventricular septa were complete. A CT angiography of the intracranial vessels revealed partial obstruction in the M1 segment of the left MCA due to calcified embolism. The patient was diagnosed cardioembolic ischemic stroke due to possible calcified embolism. The case was reviewed by the Department of Cardiovascular Surgery, which discarded surgery. The patient was discharged, adding aspirin, atorvastatin, and lamotrigine to her usual therapeutic regimen.

Mitral annular calcification (MAC), described in 1908, is a degenerative fibrocalcification of the mitral valve. Presumably, it is originated as a result of mechanical endothelial disruption followed by migration of macrophages and T-lymphocytes, generating a localized chronic inflammatory response that causes remodeling of the extracellular matrix with reactive fibrosis and calcification. Risk factors (RF) for MAC development are the same as those for cardiovascular disease: HT, diabetes (DM), DLP, smoking, physical inactivity, and age. The main non-modifiable RF is age (which proportionally increases incidence), and the main modifiable RF is HT (some studies consider it an independent RF). (1) Higher prevalence of MAC has been described in chronic inflammatory diseases (such as collagen diseases) and in those altering the phospho-calcium metabolism (such as chronic kidney failure). It was in 1946 that Rytand and Lipsitch described an ischemic stroke in a patient presenting MAC. In 1984, Furlan poses two conclusions about the association between MAC and ischemic stroke: 1) it may be difficult to prove the association between them, and 2) MAC may be better viewed as a marker of atherosclerosis rather than an embolic mechanism. (2) The SSS-TOAST classification system for ischemic stroke (3) assigned MAC a low or undetermined risk for stroke, based on a study from 1992, (4) in which MAC was associated with a 2.2 relative risk of ischemic stroke. In that study, Benjamin et al. analyzed the Framingham cohort population and determined that MAC is an independent cause of ischemic stroke after adjusting for age, sex, systolic blood pressure, DM, smoking, atrial fibrillation, coronary artery disease, and congestive heart failure (RR 2.10, 95% CI 1.24-3.57; p = 0.006). However, MAC is a marker of systemic vascular disease as an association was found between the presence of MAC and carotid stenosis greater than 160%, (5) a variable for which no adjustments were made in the study of Benjamin et al. Kizer et al (6) retrospectively analyzed 2,723 patients from the Strong Heart Study cohort, who were free of prevalent cardiovascular disease. They concluded that MAC provided high risk of ischemic stroke (incidence rate ratio, 3.12, 95% CI 1.77-5.25) after risk adjustment for age, sex, obesity, DLP, serum creatinine, HT, DM, and smoking. MAC was also associated with reduced time to the first ischemic stroke after adjustment for the variables described above and C-reactive protein, fibrinogen (HR 2.42; 95% CI, 1.39-4.21) and echocardiographic markers (left ventricular hypertrophy and left atrial enlargement; HR 1.89; 95% CI, 1.04-3.41). In other studies, when MAC is adjusted with other known RF for stroke, the risk is not increased. MAC was not significantly associated with ischemic stroke (HR 0.76%, 95% CI 0.42-1.36; p = 0.3) in the study by Boon et al, (7) after adjustment of RF for systemic vascular disease, with and without adjustments for RF as carotid artery stenosis, cardioembolic source and atrial fibrillation. In this work, carotid artery stenosis was identified as a potential confounder that explained previous reports of associations between MAC and ischemic stroke. A study published in 2003 demonstrated that the presence of MAC predicts cardiovascular events and death due to cardiovascular disease, and claims that MAC is a marker of subclinical cardiovascular disease. (8) While it is controversial whether MAC is associated with independent increased risk for stroke, there are plenty of studies on ischemic stroke in which a causal association with MAC is postulated. (9, 10) In our case, the absence of calcified lesions in the M1 segment of the left MCA in the CT scan performed 20 days before

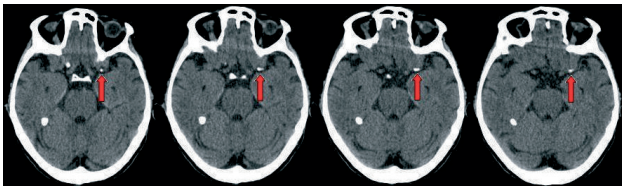

Fig. 1. CT scan on admission. The arrows show endoluminal hyperdense calcification in the M1 segment of the left middle cerebral artery.

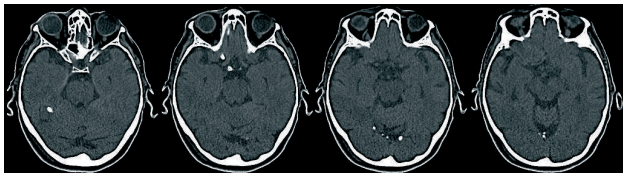

Fig. 2. CT scan prior to admission: hyperdense images consistent with dystrophic calcification in the free edge of the cerebellar tentorium.

hospitalization due to ischemic stroke, suggests an association with MAC. We therefore postulate that the presence of a mobile mass of MAC would increase the risk of detachment and possible embolization. MAC could be not only a marker of vascular disease but also a cause of medium to low risk of cardioembolism in patients with extensive, mobile calcifications.

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