

Treatment of Penetrating Aortic Ulcer Involving the Aortic Arch Associated with Lesion of the Left Main Coronary Artery

To the Editor

Penetrating aortic ulcer (PAU), described by Shennan in 1934, (1) is still one of the major challenges of cardiovascular surgery. It stands for 5% of acute aortic syndromes, (2) after aortic dissection and hematoma. Histopathologically, it is described as an atherosclerotic lesion with ulceration that penetrates into the internal lamina and allows intramural hematoma formation in the aortic media. (1) Its therapy is less divergent when it is located in the ascending and descending aorta and there are different surgical options when it is located in the aortic arch, which is rare, representing 7% of the total PAUs referred to in the review carried out by Cho et al from the Mayo Clinic. (3)

The association of PAU located in the aortic arch with severe stenosis of the left main coronary artery (LMCA) is an extremely rare and as yet not described entity that entails a significant morbimortality rate.

Clinical report

We present the case of a 69-year-old patient with a history of hypertension, overweight, and physical inactivity who was admitted to the hospital with acute aortic syndrome of 5 days evolution. He referred diagnosis of aneurismal dilatation involving the ascending aorta and aortic arch, followed-up for the last three years. A transesophageal echocardiography showed mild tricuspid valve regurgitation and aneurysm of the ascending aorta with a diameter of 50-52 mm in its tubular portion. Wall thickening suggestive of intramural hematoma was observed at 25 cm of the dental arch.

A helical CT angiography of the thoracic and abdominal aorta showed a 3.1 × 1 cm penetrating aortic ulcer at the level of the aortic arch with adjacent parietal hematoma involving the aortic root, the ascending aorta and the aortic arch. A surgical procedure was decided (Figure 1).

As part of the pre-surgical exam, a coronary angiography was performed showing 50% LMCA stenosis, severe stenosis in the middle third of the left anterior descending artery (LDA), and severe stenosis of the circumflex artery.

Myocardial revascularization surgery was performed without extracorporeal circulation (ECC), with the left internal mammary artery to the LDA, and then in "Y" from that bridge with the right internal mammary artery to the obtuse marginal artery. Then the patient was placed on ECC (total time of 144 min). Aortic clamping (104 min) and circulatory arrest (37 min) were performed, and the ascending aorta and inferior aortic arch were replaced.

After surgery, the patient was under motor, respiratory, and speech and hearing rehabilitation for 19 days, until he was discharged walking on his own.

A follow-up outpatient CT scan was performed (Figure 2).

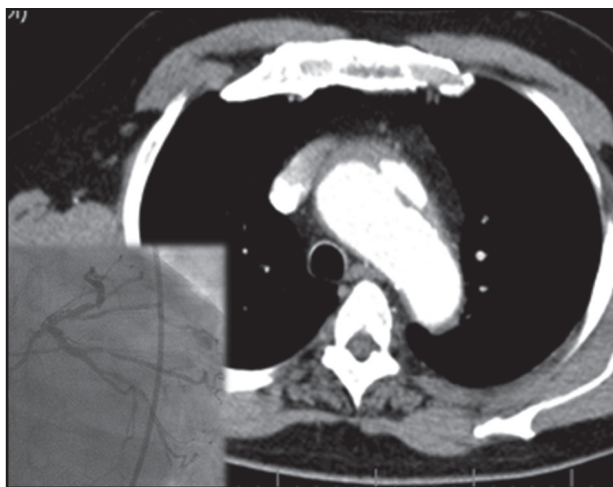


Fig. 1



Fig. 2

Discussion

Penetrating ulcer of the aortic arch stands for less than 0.1% of total acute aortic syndromes. The association of this condition with severe LMCA is an entity that has never been described in the medical literature.

We decided to perform coronary bypass surgery without ECC to reduce pump time. The use of a bilateral internal mammary artery graft avoided proximal anastomosis in aortic prosthesis, in addition to gaining short- and long-term benefits of coronary artery bypass. (5) Ascending aortic replacement was extended up to the PAU, located in the anterior wall of the aortic arch; thus, the hybrid technique of bypass to the supra-aortic trunks followed by aortic arch stenting proposed before as an alternative therapy was prevented. This technique would have put at risk the circulation in the mammary artery bypasses, both of them supplied by the left subclavian artery. (6)

PAUs located in the aortic arch are a challenge for the attending physician, who can now decide among different therapies to minimize the morbimortality associated with this entity.

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Glibenclamide in the prevention of Sudden Cardiac Death

To the Editor

There is a clear association between diabetes mellitus (DM) and cardiovascular diseases; thus, diabetes is considered a definite risk factor for heart disorders. It has been suggested that diabetic patients have a specific electrical vulnerability. (1) Morahem and Mazem, in a multivariate analysis, found that DM was associated with higher risk of ventricular fibrillation (VF), regardless of the presence of heart failure

or coronary artery disease. (2) It has already been observed that glibenclamide (a second-generation sulfonylurea), used in the treatment of type II DM, has antiarrhythmic effects determined by blocking ATP-dependent potassium channels (K⁺-ATP) in the cardiomyocytes.

Under physiological conditions, these channels are closed and do not contribute to repolarization of the cardiac action potential. However, during ischemia, when ATP levels fall, channels open, allowing K⁺ outflow from the cells. This shortens action potential duration and elicits the subsequent partial depolarization due to increased extracellular K⁺ concentration. These elements and the fact that ischemia is confined to an area of the heart tissue cause increased spatial heterogeneity in cardiac fibers and shortening of the refractory period, favoring the development of reentrant arrhythmias, including VF.

Understanding these elements and the ability of glibenclamide to block K⁺-ATP channels in the heart have prompted several research studies about the possible antiarrhythmic effects of this drug. In a study by Lomuscio et al, treatment with glibenclamide resulted in a significant reduction of the incidence of VF in non-insulin-dependent diabetic patients with acute myocardial infarction. (3) In diabetic patients with heart failure assessed by Holter monitoring, Aronson et al observed that those treated with glibenclamide had lower incidence of ventricular arrhythmias compared with patients who received other hypoglycemic agents. (4) In 15 Langendorff perfused hearts explanted from patients with dilated cardiomyopathy, Farid et al, found that blockade of K⁺-ATP channels with glibenclamide promoted spontaneous ventricular defibrillation by attenuating the ischemia-dependent spatial heterogeneity of refractoriness. Such VF self-limitation occurred prematurely. (5)

These research studies show that the usefulness of glibenclamide in DM complicated with coronary artery disease goes beyond the benefits derived from endocrine control. Through this letter, we wish to call the attention on the performance of large sample studies to conclusively demonstrate the advantages of these findings.

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Ectopic Position of Pacemaker Catheter for 22 Years

To the Editor

Malpositioning of a pacemaker catheter –outside the right ventricle– is a rare complication, and its actual incidence is unknown. (1) The catheter may enter the left ventricle through the ventricular septum, an atrial septal defect, (2) or a sinus venous defect, (3) or perforating the right ventricle (4) or atrioventricular septum, (5) or through a patent foramen ovale. (6) Herein, we report the clinical case of a 68-year-old male patient referred to the echocardiography lab for a routine check-up, who had a history of chagasic dilated cardiomyopathy and, due to complete AV block, had a VVI permanent pacemaker implanted in 1989, with a generator change in 2003. Transthoracic echo-Doppler showed dilatation of all four chambers with 28% ejection fraction and moderate mitral valve regurgitation. The right atrial pacing lead passed through the patent foramen ovale into the left atrium, and from there into the left ventricle, affixing to the middle third of the lateral wall (Figure 1). The ECG confirmed pacemaker rhythm with complete right bundle branch block image (Figure 2). While a front view chest x-ray could not determine the precise location of the catheter, the lateral x-ray revealed a posterior location (Figure 3). Given the time elapsed of catheter placement and the patient's stability, conservative treatment and oral anticoagulation were chosen.

Malpositioning of a pacemaker catheter may be potentially harmful due to risk of cardioembolism and perforation of the left ventricle. Oral anticoagulation therapy is recommended for asymptomatic patients, but in the presence of these complications, percutaneous or surgical catheter removal and repositioning are suggested.

Obviously, for early diagnosis of a malpositioned catheter it is always recommended to perform a 12-lead ECG after pacemaker implantation, and if paced beats show an image of complete bundle branch block, an echocardiography should be performed to confirm the position of the catheter.

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Fig. 1

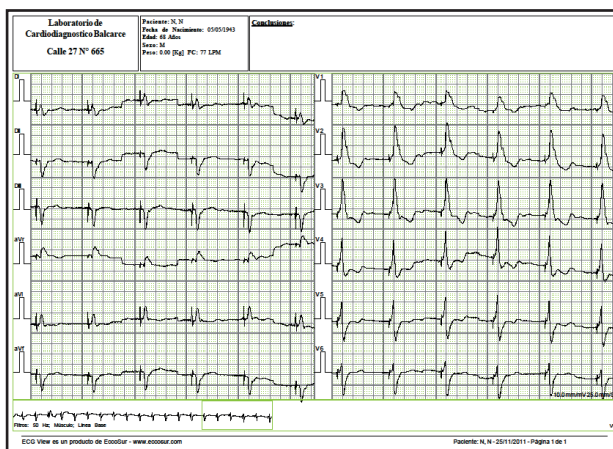


Fig. 2.

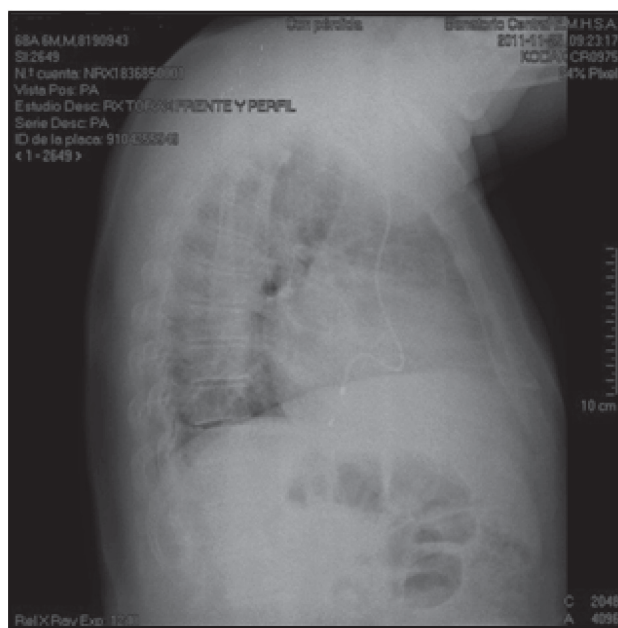


Fig. 1

April 18, 1955: Albert Einstein Died from a Complex Aortic Abdominal Aneurysm

To the Editor

This year, we are organizing our fourth campaign for the early detection of aortic aneurysm, called “ANEURYSM 0”, at the Hospital de Clínicas. But such an ambitious effort, which implies both the commitment of volunteers from the Damas de Rosa (Ladies in pink) organization, nurses, secretaries, resident and staff physicians, and the different contributions of the industry, will not have a satisfactory result if medical societies related to the disease do not analyze the possible benefits of a check-up campaign on a selected part of our community. It is just going to be a small great effort.

The four trials on screening published in the medical literature are Chichester (1) in the United Kingdom, Viborg (2) in Denmark, the screening trial in Western Australia (3), and the MASS trial (4) in the United Kingdom. As a conclusion, the screening for aortic artery aneurysm (AAA) in the male population > 60 years of age, in regions where the prevalence is $\geq 4\%$, reduces aneurysm-related mortality by almost half within 4 years, mainly through reduction of ruptured aneurysm incidence (Class Ia, Level of Evidence A). (5) There is a great similarity among the trials, particularly regarding the studied population, in relatively high socioeconomic areas mostly inhabited by people of Caucasian origin.

However, there are four potential consequences produced by this campaign: In the first place, there is the anxiety and subsequent effects on the quality of life derived from informing a patient that he/she

suffers from a life-threatening disease. Specifically, the Viborg (2) trial found that the changes experienced by patients were more pronounced in those with bad quality of life at the study baseline, but still, these effects resolved within the first months of screening.

In the second place –perhaps the most important one–, there is the risk of mortality associated with the intervention. If the screening exam is performed safely, and patients are referred to centers specialized in endovascular surgery with a low mortality rate audited for either open or endovascular aneurysm repair, the equation favors check-up. Both approaches (conventional and endovascular) are placed in the same category in recent recommendations published by the AHA, which also point out that choosing one of them depends on the arterial anatomy and the preference of the physician and the patient. (6) However, some patients do not have a suitable anatomy for endovascular treatment with standard stenting. Therefore, there still remains the need for centers to provide elective and open surgery repair at low mortality rate.

In the third place, screening programs may cause a significant increase of surgeries at endovascular surgery units. MASS and other trials demonstrated that the rate for elective repairs doubled after the screening campaigns. For that reason, England, for instance, has articulated the campaign by small territories.

In the fourth place, the campaign focuses on men aged > 60 years, smokers or ex-smokers, or on patients with a family history of aortic aneurysm. However, there is an important group that will not be studied but can potentially develop AAA. At the three recent campaigns carried out at the Hospital de Clínicas in Buenos Aires, nearly 25% of the population who was diagnosed with aortic aneurysm did not meet that condition. Women, non-smokers, or men aged < 65 years are aneurysm carriers and are not considered by the campaign. Hence is the point of broadcasting and informing the population. To disclose the information about this condition through academic and non-academic means is paramount. Making it clear that the selected population is the most prevailing but not the only one is the key.

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Learning Curve in Percutaneous Treatment of Carotid Lesions

To the Editor

Based on their leading expertise on percutaneous transluminal angioplasty (PTA) for carotid artery stenosis (CAS), (1) Bettinotti et al report 72% procedures for symptomatic CAS (SCAS) from 1998 to 2003, and 17.5% (thus, 82.5% were asymptomatic CAS [ACAS]) from 2004 to 2010. In his editorial comment, Pocovi concludes that PTA "...is reserved to patients with severe SCAS and high surgical risk", and that "...we should reconsider indications for revascularization in patients with ACAS, given the low rate of events (...) with current medical treatment". (2)

Firstly, some inconsistencies about the outcomes should be pointed out. Firstly, a total of 69 SCAS (39/54 from 1998 to 2003, and 30/171 from 2004 to 2010) are mentioned. Then, the death/stroke cases reported in SCAS were 3/70 (1 more SCAS). With 2/171 death/stroke cases in the 2004-2010 period, the rate is 1.2%, and not 1.7%. The table of neurological complications shows 7 TIA, 3.1%, but it also shows 7 ischemic strokes (1.8%), whereas this percentage should also be 3.1%; and then 1 hemorrhagic stroke and 1 death, 0.04% each (in fact, 0.4%).

It would have been interesting that the authors explained why PTA was performed three times more in ACAS during the 2004-2010 period than in the 1998-2003 period (and almost five times more ACAS than SCAS). They included patients with ACAS > 80%, with "...high-risk variables", and carotid echo-Doppler "previous to each procedure". If they used the recommended NASCET/ACAS angiographic methods, (3) they must have excluded patients, because with angiography, there is up to 28% discordant measurements compared to Doppler. (4) They considered age > 75 years, "bilateral carotid disease", and contralateral occlusion (CLO) as "high risk" variables, among others. The high-risk limiting age is 80 years. (3, 5) Generically, bilateral disease, which almost all patients have, does not imply high risk. CLO was certainly a high-risk variable in the

SAPPHIRE study of PTA/endarterectomy (CEA), (5) but it was not excluded from the ACAS of CEA/medical treatment (MT). (3) Precisely, in a secondary analysis, patients with CLO and MT had better event-free survival rate than those with CLO and CEA. (6) So far, no study has compared PTA with MT in CLO.

The natural risk for stroke in ACAS > 75% is extremely low -2 -3% annually-, just like the risk for an endarterectomized CAS. (3) For that reason, morbimortality in carotid surgeries for ACAS should not be > 3%. (7) In this series, total morbimortality for ACAS is 3.2%. Although the rate for the 2004-2010 period is promising (1.2%), data suggest that some patients with ACAS submitted to PTA would have also been candidates for CEA, and above all, that many of them could have remained under MT with antiplatelet, lipid-lowering and/or antihypertensive agents, and free from carotid events. We agree with the editorial: indications for revascularization in ACAS should be reconsidered, and in fact, they should be accomplished within the frame of new recommendations. (7) It is possible that more revascularizations in ACAS than those strictly indicated are being performed in our setting despite the presence of stenosis > 80%, which unnecessarily increases the risk for stroke.

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of Neurological Surgeons; Society of Atherosclerosis Imaging and Prevention; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society of NeuroInterventional Surgery; Society for Vascular Medicine; Society for Vascular Surgery; American Academy of Neurology and Society of Cardiovascular Computed Tomography. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. *Stroke* 2011;42:e420-63.

Authors' response

We were pleased to read the letter sent by Dr. Fustini and Dr. Gadda, in which they comment on the impact of baseline neurological symptoms on our outcomes, (1) emphasizing the importance of an appropriate risk stratification. The authors of the letter wonder why indications in asymptomatic patients increased during the second period of our study (2004-2010), and argue that surgical risk was probably tolerable enough for patients to undergo revascularization surgery. Undoubtedly, the high proportion of symptomatic patients undergoing carotid angioplasty in our first period (1998-2003) increased the risk of the procedure. As part of our learning curve, we believe that the improvement in patient selection resulted in a reduced number of symptomatic patients undergoing angioplasty during the second period, and decreased the rate of events. Similarly, the number of asymptomatic patients in our study was comparable to that observed in several international multicenter registries (CAPTURE 86%, REACH 70%, SAPHIRE Worldwide 72.3%, and ARCHER 76%). (2-5) Regarding the risk for our population, 27% had a history of contralateral neurological symptoms, 14% had undergone previous carotid revascularization and almost one third previous coronary artery bypass surgery (27%). (1) In addition, the presence of contralateral occlusion (10%), accessory nerve palsy following carotid endarterectomy (3%), radiation therapy (1.4%), and 15% octogenarian patients might explain certain preference for a percutaneous alternative in our asymptomatic population.

The proper way to assess carotid stenosis is also discussed in the letter. In our practice, we perform digital carotid and cerebral angiography in all cases. The information provided by the angiography allowed us to determine the anatomic risk and the feasibility of the procedure (complex aortic arch, excessive carotid tortuosity, intracranial and extracranial lesions, thrombus, or ulcerated plaques). The degree of carotid stenosis was assessed with the NASCET method, (6) by comparing the diameter of the stenosis with that of the internal carotid artery distal to the lesion. Following the guidelines of the American (7) and European (8) societies, we used a carotid stenosis cut-off point 80% to treat asymptomatic patients.

Certainly, our system was different than the one implemented in the SAPHIRE (9) (carotid Doppler was used to determine the degree of obstruction) and CREST (10) (a lower angiographic cut-off point: >

60% was used in asymptomatic patients) trials.

Our study is not intended to redefine therapeutic concepts but just to reflect an experience of the real world in our setting, taking into account the evolutionary changes derived from experience, along with the technological advances for this procedure, as has been the use of brain protection and new designs for implantable devices.

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Relationship between Neck Circumference and Hypertension in the National Hypertension Registry (the RENATA Study)

To the Director

As mentioned on other occasions, data provided by the RENATA study are valuable for the epidemiological study of hypertension (HT) in our country, Argentina. Its methodological design and the use of techniques to measure its variables with very good reproducibility stand out as two of its strengths.

In the current data analysis (1), neck circumference measurement is a variable that –in its highest values– is associated with greater prevalence of HT both in men and women. This semiological tool provides an indicator of increased fat deposits in the upper half of the body, probably in the same way as the waist circumference represents the lower half of the body, and mainly the visceral fat deposits. Furthermore, the waist keeps a very good correlation with the prevalence of overall and specific cardiovascular risk factors, even adjusting by the body mass index (BMI). These data would be enriched with an analysis that adjusted the neck circumference measurement to BMI. The authors point out that it was not possible due to design and operational issues, although in some previous publications, similar assessments have provided results reproducible with the present ones, even adjusting the regression models by BMI, with lower correlation coefficients and borderline statistical significance for their relationship with increased blood pressure. Variations in the results of the different series may correspond to ethnicity –as has been evident for waist circumference in publications of the last 10 years – and probably to the use of cut-off points and analysis groups that have not been homogeneous among themselves, like the use of population tertiles in most publications as well as in the current one, or quintiles in others, with less sensitivity but greater specificity.

Certain characteristics of the population encourage the analysis of their representativeness and, in any case, their evaluation in a future study: age and gender distribution among groups, determining factors in the incidence and prevalence of HT in the population. The age of the groups, very different among themselves and with a variation that could rule out

the population group with no signs of increased body fat deposit or obesity (without increased neck or waist circumference) as control group, 15 years younger than the clearly obese group with the highest average of both systolic and diastolic blood pressure. Distribution by gender among groups is also different, and the inclusion of premenopausal women in this population entails a bias in HT prevalence. Also, it is interesting to point out that there was a similar average heart rate in the different subpopulations –even despite age, distribution by gender, and increased blood pressure–, taking into account that sympathetic activation is one of the main pathophysiological mediators of HT in these age groups, especially when associated with obesity.

Finally, it is very interesting to observe the similarity among intermediate groups with the presence of only one of the two obesity variables, one with neck obesity and the other with abdominal obesity, in all their determinations. This seems to be one of the major strengths of the current series, and places measurement of neck circumference as an alternative variable to others for overweight and obesity, more comfortable for both patient and doctor.

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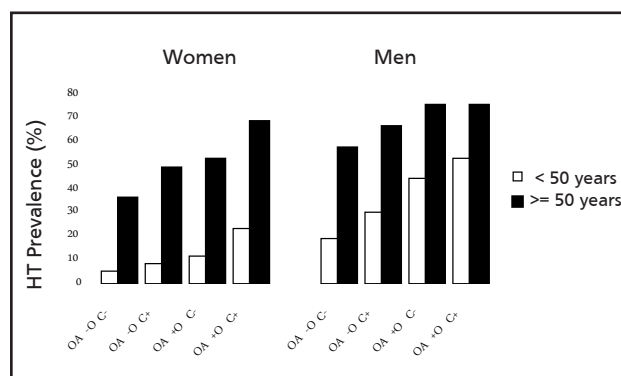
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Authors' response

Dr. Obregón's comment gives us the opportunity to enhance the wealth of information presented in our article. Both hypertension and obesity are related with each other and at the same time, both are strongly associated to age and gender. This is reflected in Table 2 of the article. Prevalence of hypertension according to the absence or presence of abdominal (AO) and/or neck obesity (NO) is compared in that Table. On average, the group of individuals without AO or NO is younger, with a predominance of females. However, logistic regression analysis allowed us to prove that the effect of AO and NO on the prevalence of hypertension was independent of age and gender.

To clarify Dr. Obregón's concern, we have included a chart illustrating the effect of AO and NO on the prevalence of hypertension, stratifying respondents by gender and age. The chart shows that AO and NO are associated with an additive increase of hypertension prevalence, which occurs in young and elderly men and women ($p < 0.001$, chi square test in each of the four subgroups, respectively).



This chart shows the effect of AO and NO on the prevalence of hypertension, stratifying respondents by gender and age (< and $\geq$ 50 years). The chi-square test showed $p < 0.001$ for increased prevalence of hypertension both for men and women in each age group.

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Cardiovascular Complications Associated with Type 1 Neurofibromatosis

To the Editor

Type 1 neurofibromatosis is a relatively common genetic disorder, characterized by skin and neurological manifestations, as well as at other levels. Cardiovascular complications associated with this disorder include aortic valve involvement, aortic aneurysm, ischemia, and HT. We present the case of a patient affected by this disorder, together with a review of his cardiovascular complications management.

Clinical report

This is the case of a 49-year-old male patient diagnosed with type 1 neurofibromatosis, who led a normal active life. A month before the current episode, the patient began with progressive dyspnea, and was transferred to our center due to acute pulmonary edema requiring orotracheal intubation, diuretics, and intravenous vasodilators.

On admittance, physical examination showed a neurofibroma in the neck and café-au-lait spots, with no signs of heart failure. Cardiopulmonary auscultation revealed II/VI holosystolic murmur in the mesocardium radiating to the apex, and crackles at the lung bases. No abdominal mass, murmur or other findings were identified.

While in the Coronary Care Unit, the patient presented several episodes of difficult-to-control atrial fibrillation with rapid ventricular response, and blood pressure of up to 190/80 mm Hg, requiring intravenous drugs. Increased myocardial damage or ECG changes were not observed, and vascular disease and pheochromocytoma were ruled out with a thoraco-

abdominal CT scan.

A transesophageal echocardiography was performed, revealing severe aortic regurgitation (Figure 1), a dilated LV with mild systolic dysfunction and mitral valve prolapse with severe impairment secondary to chordae tendineae rupture (Figure 2), with no other findings. An additional coronary angiography ruled out ischemic chordae tendineae rupture.

The case was presented in a clinical session, surgical repair of the valvulopathies was decided, and uneventful double valve replacement with mechanical prostheses was performed. After surgery, the patient showed progressive improvement and was discharged in good condition.

Type 1 neurofibromatosis is an autosomal dominant genetic disorder, characterized by the presence of neurofibromas, café-au-lait spots, pigmented iris hamartomas, and learning disabilities. (1) The association of this disorder with cardiovascular complications is well established. (2)

Valve involvement has been previously described, and cases of severe aortic regurgitation with LV dysfunction similar to that in our patient have been published. (3, 4) The explanation for this involvement can be the endothelial dysfunction secondary to impaired neurofibromin, typical of this disorder. (3) Cases of mitral valve prolapse with severe impairment have also been described. (4, 5) In some cases, this involvement has been associated with difficult-to-control supraventricular arrhythmias, as was the AF in our patient. (6)

Other cardiovascular complications, such as aneurysms or coarctation of the aorta, are also common. (2) HT secondary to pheochromocytoma occurs in 1% of the cases; (7) this complication was suspected in our patient due to his high blood pressure, but then it was ruled out.

Finally, we had to exclude ischemia as the cause of chordae tendineae rupture given the higher incidence of AMI in these patients. (1) Rupture might be explained by the presence of vasospasm secondary to increased catecholamines caused by a pheochromocytoma (8) or by cardiac compression due to pericardial neurofibromas. (1) Both suppositions were ruled out in our patient.

Therefore, cardiovascular complications associated with type 1 neurofibromatosis, particularly valve diseases, are a documented fact, explainable by the disease, which must be studied in these patients. Management of complications is similar to that in any other patient, with a favorable prognosis.

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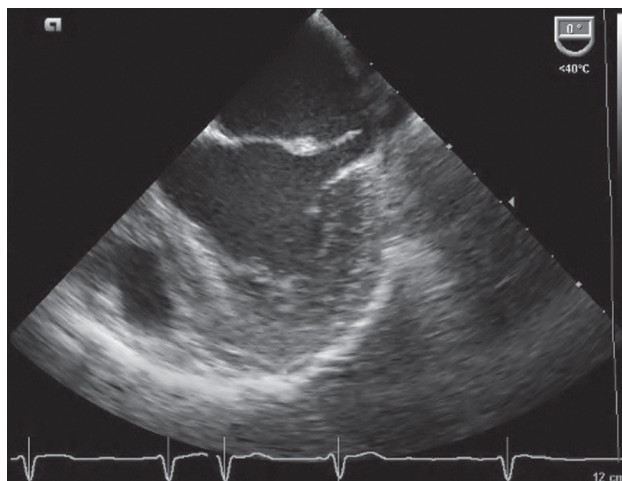


Fig. 1

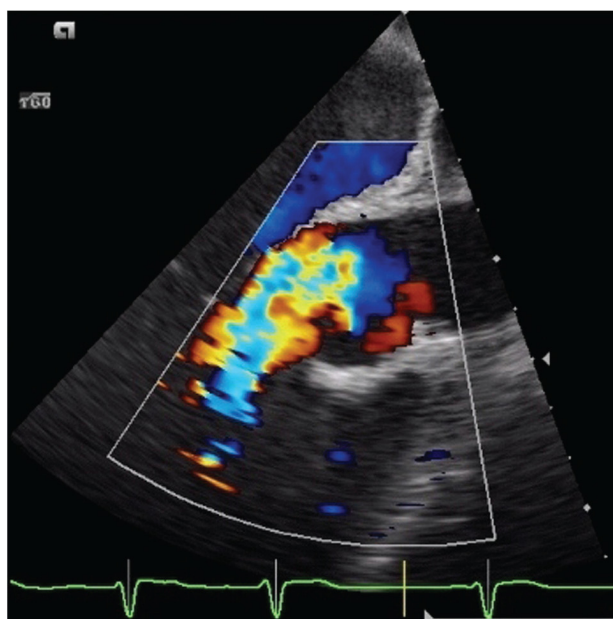


Fig. 2