Ablation for Managing Symptomatic Bradycardia. First Experience in Argentina

Cardiac neuroablation (CNA) is a new technique for management of vasovagal syncope and arrhythmias triggered by parasympathetic autonomic hyperactivity.

This procedure, described for the first time in 2005 by Dr. Pachón et al., (1,2) proposes parasympathetic denervation to eliminate post-synaptic neuronal connections of the parasympathetic afferent and thus improve the sinus rate and atrioventricular (AV) node conduction.

Unlike the sympathetic nervous system, which presents its post-ganglionic neurons at the level of the paravertebral ganglia of the sympathetic chain, the parasympathetic post-ganglionic neurons are located in the para-cardiac ganglia of the epicardial fat. For this reason, they can be subjected to radiofrequency ablation from an endocardial approach, without generating long-term effects on the sympathetic afferent.

Four main para-cardiac ganglionated plexi (GP) have been described, and their exact location may slightly vary among individuals. To date, there is no agreement on the number of GP and their exact anatomical location. For this reason, identifying their location in each patient is essential for successful CNA (Figure 1) (3).

Cardiac neuroablation is a therapeutic option in patients without intrinsic damage of the conduction system who remain refractory to hygienic, dietetic, and pharmacological measures, as an alternative to pacemaker implantation.

Although several groups have reported good results with the CNA technique, with adequate success rate and low percentage of complications, there are some controversial issues with the standardization of the procedure and the verification of adequate denervation. These aspects, together with the scarce but growing scientific evidence on the long-term effectiveness and safety of the procedure, are the reasons why CNA is not a globally accepted technique by the electrophysiology community. (4,5)

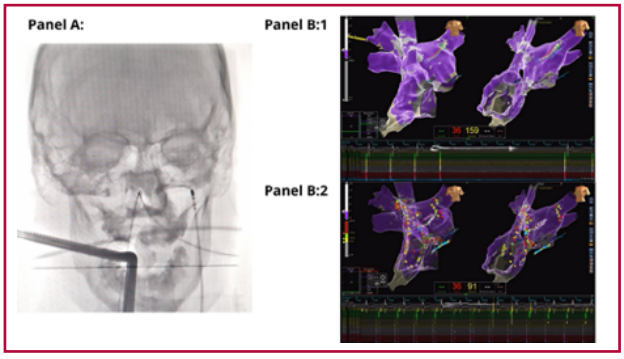

Fig. 1. Panel A- Catheter positioned for vagal stimulation at the level of the left internal jugular vein in antero-posterior view. Panel B- Fractionation mapping of both atria, surface electrogram (white), and intracardiac electrograms: ablation catheter (yellow) and HD grid in left atrium (green, ochre, white and red) and coronary sinus (light blue). Panel 1 shows a sinus pause of 8002 ms after vagal stimulation (the interference of the stimulation waves in the surface electrogram is recorded). Panel 2 shows the radiofrequency lesions performed at the level of the ganglionated plexus 4 and the absence of pauses or changes in AV conduction after vagal stimulation

In this paper we report the first case of CNA in Argentina, with the use of extracardiac vagal stimulation.

A 19-year-old patient was referred to our center to evaluate the implantation of a pacemaker. He had a history of dizziness due to AV block. The 24-h Holter monitoring reported sinus rhythm (average heart rate 49, minimum 19 and maximum 104 beats per minute, SDNN 307.31 ms) with episodes of second-degree AV block Wenckebach type, 2:1 AV block and episodes of high-grade AV block with pauses of up to 5281 ms. On 12-lead exercise stress test, baseline heart rate was 65 bpm, and reached a maximum of 130 bpm with AV block Wenckebach type; AV conduction improved with exercise. Two-dimensional Doppler echocardiography showed normal left ventricular dimensions and function, left ventricular ejection fraction of 72%, mild tricuspid regurgitation and normal atrial volumes.

With these findings, a suspected diagnosis of functional AV block was made, and CNA was decided. Support and assistance were provided by Dr. Miguel Ángel Franco and Dr. Juan Carlos Zerpa of *Hospital del Corazón* in Sao Paulo, Brazil.

An electrophysiological study was scheduled to evaluate AV node function. The right femoral vein was accessed under sedation with propofol, using 2 quadripolar catheters. After baseline intervals, antegrade Wenckebach point and refractory period of the AV node were measured and vagal stimulation was performed (vagal stimulation system by Pachón et al.) from the right and left jugular vein with and without atrial pacing (Figure 1, panel A). Then, the same maneuvers were repeated after intravenous bolus injection of 2 mg of atropine (Table 1).

As these findings confirmed the absence of infra-His block and the exaggerated response to vagal stimulation, parasympathetic ganglia ablation was decided. The intervention was scheduled 48 h after the electrophysiological study to ensure loss of the muscarinic receptor block produced by atropine.

Cardiac neuroablation was performed under general intravenous anesthesia with remifentanil 5 ng/mL and propofol 1.8-3 mcg/mL using continuous infusion (Bran Space infusion pumps). Rocuronium was used for muscle relaxation. The airway was instrumented with an endotracheal tube and ventilation was maintained using a Drager Fabius Plus XL anesthesia machine. Patient monitoring included electrocardiogram (ECG), non-invasive pressure, body temperature and

Table 1.

Parameter	Pre-atropine	Post-atropine
HR (bpm)	70	105
AH interval (ms)	109	79
HV interval (ms)	54	57
AWP (ms)	660	490
RR interval (ms)	857	571
SNRT at cycle length of 600 ms pre-atropine/550 ms post-atropine (ms)	1216	843
SNRT at cycle length of 500 ms pre-atropine/400 ms post-atropine (ms)	1294	798
SNRT at cycle length of 400 ms pre-atropine/300 ms post-atropine (ms)	1152	561
5-second left vagal stimulation	Pause of 10,279 ms	Sinus bradycardia
5-second right vagal stimulation	Pause of 8693 ms	Sinus bradycardia
5-second vagal stimulation with atrial stimulation.	Complete AV block for 9873 ms	

HR: heart rate. AWP: antegrade Wenckebach point. SNRT: sinus node recovery time

end-tidal carbon dioxide (ETCO2).

The moment of vagal stimulation deserves a special mention. Electrical stimulation produces abrupt and sustained contraction of the muscles of the neck. Flexion of these muscles and contraction of the masseter muscles can cause injury to the tongue. Therefore, this structure must be adequately protected. The patient's head is separated from the pillow and bent to one side. This movement should be supported but not restricted, ensuring that there is an adequate distance between the skull and the fluoroscopy tube.

The right femoral approach was performed with three venous punctures and the left femoral approach with one venous puncture. A deflectable quadripolar catheter (Johnson) was advanced through the left femoral vein into the left internal jugular vein for vagal stimulation. The right femoral access was used to insert a Livewire duodecapolar catheter (St Jude Medical) for right atrial and coronary sinus mapping, a FlexAbility irrigated ablation catheter (Abbott Laboratories), and a transseptal kit. The left atrium was accessed under transesophageal echocardiography guidance and anticoagulation was initiated to maintain an activated clotting time (ACT) between 300 and 400 seconds. A HD Grid mapping catheter (Abbott laboratory) and an ablation catheter were advanced to the left atrium.

The EnSite Precision cardiac mapping system (Abbott Laboratories) was used for activation and fractionation mapping of the pulmonary veins, left atrium, right atrium, and superior and inferior venae cavae.

At the beginning of the procedure, the patient presented an atrial rhythm with heart rate of 36 bpm, PR interval of 180 ms, and antegrade Wenckebach point of 1080 ms. Finally, vagal stimulation was performed from the left internal jugular vein with a neurostimulator (Pachón et al.) before ablation, and a sinus pause of 8002 ms was recorded (Figure 1, panel B1).

Fractionation mapping based on spectral analysis of atrial depolarization was used to recognize parasympathetic GP location. The ganglia were approached in an upwards direction from GP 4 located at the level of the left pulmonary veins, followed by GP 3 at the level of the mouth and the roof of the coronary sinus, GP 2 at the level of the postero-septal interatrial region and finally GP 1 located at the level of the superior vena cava. Right phrenic nerve mapping is recommended before radiofrequency delivery in GP 1; in this patient, mapping the trajectory of this nerve prevented a continuous ablation line between both venae cavae.

Ablation lesions were delivered via an Ampere RF generator (Abbott Laboratories) to achieve energy up to 35 watts with a maximum temperature of 43 °C. When energy was delivered to GP 2, the Wenckebach point progressively increased to 510 ms, heart rate increased to 85 bpm and sinus rhythm was observed. Vagal stimulation was repeated for final verification of the effect of denervation, without sinus pause or AV block during atrial pacing. Finally, 2 mg of atropine were administered intravenously, without causing changes in heart rate (Figure 1 panel B2).

The patient was monitored for 24 hours and remained in sinus rhythm at the time of discharge, with a heart rate between 85 and 105 bpm. A 24-h Holter monitoring performed 1 week after CNA reported sinus rhythm (average heart rate 88, minimum 38 and maximum 125 beats per minute, SDNN 90.20 ms) with episodes of second-degree AV block Wenckebach type and 2:1 AV block during sleep and absence of pauses. He remained free of symptoms at the moment this scientific letter was submitted.

This is the first CNA procedure reported in Argentina with the use of vagal neurostimulator. Although we understand that the result was conditioned by the impossibility of performing a continuous ablation line in the right atrium due to the risk of phrenic nerve injury, denervation resulted in an increase in baseline heart rate and AV node conduction, eliminating patient's symptoms. Follow-up at the medium- and long-term is still pending.

The result of this study shows a safe and effective therapeutic option to avoid pacemaker implantation in patients with conduction disorders due to parasympathetic hypersensitivity.

Ethical considerations

Not applicable.

Conflicts of interest

Abbott Laboratories collaborated with the logistics of bringing Dr. Zerpa and Dr. Franco with us..

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Acute Liver Failure due to Intravenous Amiodarone, a Rare but Potentially Fatal Complication

We report the case of a 74-year-old woman, with a history of hypertension and type 2 diabetes, who was under cardiology surveillance due to type 1 bicuspid aortic valve disease with moderate stenosis, and moderate mitral regurgitation. After two months of malaise, chest pain and exercise-induced dyspnea, she visited the emergency department of her referral hospital. On admission, the patient presented hypotension and atrial fibrillation (AF) with rapid ventricular response. The laboratory tests showed data suggestive of infection, with elevated C-reactive protein and procalcitonin, high white cell count with a left shift and a reduced glomerular filtration rate. As the patient had poor hemodynamic tolerance to AF, cardioversion with intravenous amiodarone was decided with a loading dose of 300 mg, followed by continuous infusion, with reversion to sinus rhythm within a few hours.

Based on the history of valvular heart disease and the fact that there were no other infectious foci, empirical antibiotic treatment for infective endocarditis was initiated. The diagnosis was confirmed by transesophageal echocardiography, which revealed a large paravalvular aortic abscess measuring 5 x 2 cm, with a possible vegetation on the aortic side of the valve. Blood cultures were positive for *Abiotrophia defectiva*. A diagnosis of complicated infective endocarditis was made, and the patient was transferred to the coronary care unit of our institution for urgent surgical treatment.

The patient underwent aortic and mitral valve replacement with bioprostheses, and reconstruction of the mitroaortic junction and atrium with pericardial patch. After the intervention she presented favorable clinical and hemodynamic outcome. As the patient remained in sinus rhythm, maintenance treatment with amiodarone was discontinued but had to be resumed with a bolus of 300 mg over 20 minutes, followed by an infusion of 300 mg over 8 hours due to a new episode of AF. On the same day, she developed bradypsychia and flapping. The laboratory tests revealed an increase in markers of hepatic cytolysis (maximum ALT and AST of 3266 U/L and 1416 U/L respectively), coagulopathy (activated partial thromboplastin time 47 seconds, INR of 3), and ammonium level of 30 μg/L. In addition, acute renal failure was detected again with a minimum glomerular filtration rate of 14 ml/min/1.73m^2 and oliguria. As acute liver failure due to amiodarone was suspected, the drug was discontinued and treatment with intravenous thiamine and enemas was initiated. To rule out other etiologies, workup was completed with serologic tests to detect hepatotropic viruses (cytomegalovirus, hepatitis A, B and C viruses), which resulted negative, and a CT scan was performed which ruled out signs of acute brain disease and hepatic hypoperfusion.

The patient experienced progressive recovery, with normalization of liver enzymes, improvement of mental activity and absence of flapping. The glomerular filtration rate increased to 32 ml/min/1.73m^2, with recovery of diuresis.

Amiodarone is a class 3 antiarrhythmic drug widely used, which can be administered orally or intravenously. Chronic oral use commonly causes hepatotoxicity, evidenced by elevated transaminases in 15-50% of cases. (1) Elevation of transaminases is usually chronic, mild and reversible, and < 1% of patients require discontinuation of the drug for evidence of hepatitis. (2)

Amiodarone-induced acute liver failure is rare with an incidence < 3%, (3) and has a different nature than that associated with chronic oral administration.

The underlying mechanism is not well established, but free radicals released due to decreased hepatic perfusion could be involved, causing hypoxic injury to hepatocytes. (3) A retrospective case-control study suggests that hepatotoxicity caused by intravenous amiodarone cannot be differentiated from ischemic hepatitis due to concomitant hypotension. (2) It has been postulated that rather than amiodarone itself, polysorbate 80, a substance used to dissolve the drug,

may be the responsible agent for acute liver damage via a direct toxic effect on hepatocytes. (4)

This acute complication occurs within 24 h after starting intravenous amiodarone, has a predominant increase in transaminases > 10 times the upper reference limit, renal impairment or coagulation disorders are less common, and improves after the drug withdrawal. (4) Centrilobular necrosis is found on histologic examination. (2) It is a potentially fatal condition and encephalopathy is the most common cause of death. (3) Considering that this complication is rare, additional etiologies of acute liver failure should be ruled out, such as viral hepatitis, hypoperfusion, and other hepatotoxic drugs. (5)

Our patient started with manifestations of encephalopathy approximately 10 hours after intravenous administration, in addition to elevated transaminases > 10 times the upper limit of reference and coagulopathy. Viral hepatitis was ruled out, and as she did not present episodes of hypotension or signs of hypoperfusion during or after amiodarone administration, hepatic hypoperfusion was not a possible diagnosis. The patient received other drugs during the episode, as morphine, norepinephrine, furosemide, gentamicin and ceftriaxone. Elevation of liver enzymes has been described with the use of gentamicin and ceftriaxone, but without significant hepatic failure. Once other causes have been ruled out, and considering the temporal relationship with drug administration, the score obtained in the Naranjo Adverse Drug Reaction Probability Scale (7, probable adverse reaction), and the improvement after discontinuing the medication, intravenous administration of amiodarone seems to be the most probable cause.

Although acute liver failure due to intravenous amiodarone is a rare entity, clinicians should be aware of this potentially lethal complication. Early identification through monitoring of mental status, transaminase levels and coagulation status is essential to avoid a possible fatal outcome.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

Ethical considerations

Not applicable.

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Pharmacomechanical Treatment of Deep Venous Thrombosis in an Anatomical Variant of the May-Thurner Syndrome

We report the case of a 49-year-old woman with a history of type 1 diabetes, gravida 3, para 3, and use of contraceptive patches who had been resting for 20 days due to right eye vitreous hemorrhage. She visited the emergency department due to tense edema of the left lower extremity, which was warm and red, and complaint of claudication while walking a few meters since the past 24 hours. The lower extremity venous ultrasound showed dilatation, lack of venous compressibility and flow of the left lower extremity in the external iliac vein, common femoral vein, superficial femoral vein, popliteal vein and saphenous veins; thus, the diagnosis of deep vein thrombosis (DVT) was confirmed. With these findings, the patient underwent thorax and abdomen computed tomography angiography, which revealed right segmental and contralateral subsegmental pulmonary embolism, associated with subsegmental pulmonary infarction and thrombus extension to the inferior vena cava. There was no external compression of the venous system affected (Figure 1 A-C).

As it was necessary to start anticoagulation, a consultation was made with the department of ophthalmology. The fundoscopy revealed reabsorption of the vitreous hemorrhage in the context of diabetic retinopathy as a possible cause of bleeding, so there were no contraindications for anticoagulation and possible use of thrombolytics. The patient was admitted, and anticoagulation was initiated with unfractionated heparin in continuous infusion, adjusted for body weight.

On reevaluation 24 hours later, the edema had reduced moderately, with persistence of heat, numbness and difficulty walking. For this reason, the multidisciplinary team decided to include pharmacomechanical angioplasty into the established therapy.

Under general anesthesia the patient was placed in the prone position. The procedure was performed via the popliteal access under ultrasound guidance, and a

5 French introducer was used. The venography of the left lower extremity confirmed vascular occlusion extending from the proximal segment of the superficial femoral vein to the inferior vena cava, with highly developed collateral circulation and an intraluminal filling defect suggestive of recent thrombus (Figure 1D). A 0.035-inch guide wire Roadrunner® and 4 Fr vertebral catheter were advanced through the occlusion of the iliac axis until reaching the inferior vena cava. The guide wire was removed, leaving the catheter in position, and the contrast agent was injected to confirm adequate positioning in the inferior vena cava. A dedicated Option Elite™ retrievable filter was implanted through the same access and released into the inferior vena cava below the renal vein drainage. Then the catheter was exchanged for an 11 Fr introducer, and a Zelante DVT™ catheter was advanced to infuse the thrombolytic agent (Alteplase 20 mg diluted in 100 cm^3) using Power Pulse™ system. Thrombolytic therapy was completed in 30 minutes. Then angiography was performed, which showed restoration of blood flow in the left venous axis up to the vena cava, with persistence of the intraluminal filling defect (Figure 2A). The procedure continued with active thromboaspiration using the AngioJet™ isovolumetric system for 130 seconds, with evident improvement in vascular flow and significant decrease in the thrombotic burden. There was no evidence of imprinting or filling defect in the ostium of the left iliac vein (Figure 2B), a finding that does not correspond to the usual anatomy of May-Thurner syndrome (MTS), defined as extrinsic compression of the iliocaval veins by the arterial system. The evaluation continued with intravascular ultrasound (IVUS), which demonstrated a reduction in lumen diameter of the proximal primitive iliac vein (in the direction of flow) in the topographic area of the internal iliac artery, and absence of abnormalities in the ostium of the left primitive iliac vein (Figure 2 C-E). Based on these findings, a 15 x 40 mm balloon (Figure 2F) was used for predilation and a 20 × 100 mm Abre™ venous self-expandable stent was implanted (Figure 2G).

The patient presented immediate clinical improvement. Twelve hours later, as the vascular ultrasound confirmed that the stent and iliac axis remained patent, anticoagulation therapy was shifted to low molecular weight heparin, and clopidogrel was started until completing 90 days of therapy.

Deep venous thrombosis is isolated in 2/3 of cases and is proximal in 80%. Long-term complications include post thrombotic syndrome (PTS), defined as chronic venous symptoms or signs secondary to DVT, and is the most common complication at two years in 30-50% of cases with proximal DVT. Risk factors associated with PTS are previous ipsilateral DVT, proximal location (ilio-femoral > popliteal) and significant residual obstruction. (1)

Few publications have compared invasive thrombolytic therapy (ITT) versus anticoagulation and have reported higher risk of intracranial hemorrhage and a greater need for transfusions with ITT, with a modest reduction in PTS. However, a recently published Cochrane Collaboration systematic review (2) that included 19 randomized studies with a total of 1943 patients and compared TTI with standard anticoagulation in acute DVT concluded that TTI effectively produces clot lysis with evidence of moderate certainty. At this point, there is evidence from studies in rodents (3) that early restoration of blood flow may improve experimental resolution of DVT by reducing

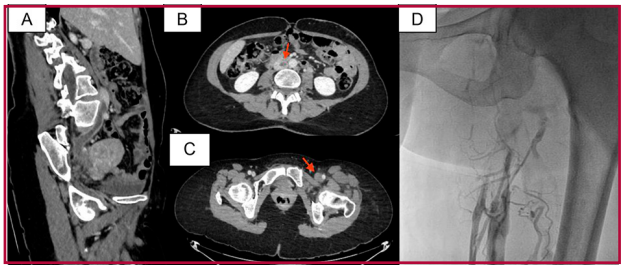

Fig. 1. A: Computed tomography scan of the abdomen, parasagittal section, showing thrombosis of the inferior vena cava extending into the iliac vein. **B-C:** Computed tomography scan of the abdomen, axial sections, showing venous thrombosis in the left venous axis (red arrows indicate the areas of thrombosis). **D:** Venography of the left lower extremity confirming vascular occlusion extending from the proximal segment of the superficial femoral vein to the inferior vena cava, with highly developed collateral circulation and intraluminal filling defect suggestive of recent thrombus

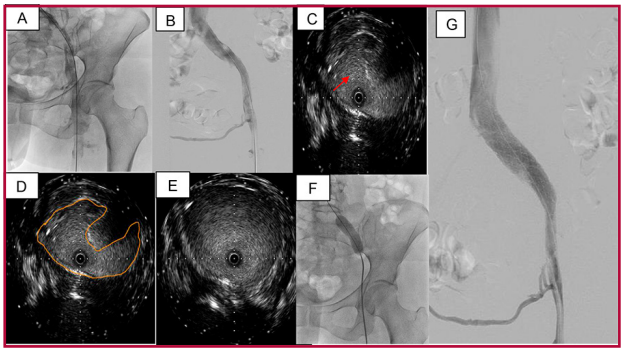

Fig. 2. A: Angiographic image after thrombolytic infusion with a Zelante DVT™ catheter using the Power Pulse system. **B:** Angiographic image after active thromboaspiration using the AngioJet™ isovolumetric system during 130 seconds, with evident improvement in vascular flow and significant decrease in the thrombotic burden, without evidence of imprinting or filling defect in the ostium of the left iliac vein. **C:** intravascular ultrasound which evidences the zone of decrease in the caliber of the light with the Red Arrow **D:** intravascular ultrasound which evidences the zone of decrease in the caliber of the light where is indicated the contour of the vessel.. **E:** Intravascular ultrasound showing the normal diameter of the vein without compression. **F:** Angiographic image showing the15 x 40 mm balloon insufflated in the iliac vein; the red arrow indicates the waist corresponding to the area of compression documented by intravascular ultrasound. **G:** Angiographic image showing the final result after implanting a 20 x 100 mm Abre™ venous self-expandable stent.

the thrombotic burden and vein wall fibrosis. Furthermore, the authors performed a post hoc analysis of the ATTRACT study (4) and showed that those participants who received pharmacomechanical treatment (PMT) within 4-8 days since the onset of symptoms had the greatest benefit in terms of PTS symptoms. Nowadays, treatment of large vein thrombosis should include four main steps: adequate local infusion of low-dose thrombolytic agents, thromboaspiration, angioplasty, and implantation of dedicated stents.

This is a case of venous thrombosis secondary to venous compression within the pelvis at an atypical site, which does not correspond to MTS. Compression of the left iliac vein by the internal iliac artery has been described in other case reports as a variant of MTS. (5,6) The CT scan images did not demonstrate a clear area of compression. The use of IVUS within the procedure allowed identification of the area of stenosis and guided its treatment.

Conflicts of interest

None declared.

(See authors conflicts of interest forms in the website/ Supplementary material).

Ethical considerations

Not applicable.

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Carcinoid Heart Disease

We report the case of a female patient who complains of fatigue, malaise, anorexia, weight loss of 35 kg associated with non-dysenteric diarrhea (5-6 depositions/ day), and face, thorax and lower extremities erythema. These symptoms have been present over the past 8 months. The abdominal circumference is increased due to a mass in the right hypochondrium (the abdominal ultrasound showed a solid nodule in the left upper lobe of the liver). On cardiovascular examination the patient has signs of systemic fluid overload, ascites and lower extremity edema. 5-hydroxyindoleacetic acid is measured in urine to confirm the diagnosis, with a positive result (44.2 mg in 24 hours, with a normal cut-off value of 1-10 mg in 24 hours). The patient undergoes imaging tests.

The abdominal ultrasound shows an enlarged liver due to presence of a 109 x 76 mm heterogeneous lesion. (Figure 1) A contrast-enhanced computed tomography (CT) scan of the chest, abdomen and pelvis reveals heart enlargement, a 125 x 120 x 80 mm nodule in liver segment V with contrast agent uptake, diffuse thickening of the adrenal glands, moderate ascites, and isolated mesenteric lymph nodes. The transthoracic echocardiogram shows normal left ventricle diameters, left ventricular ejection fraction 76%, paradoxical septal motion, intact interatrial septum with normal Qp/ Qs ratio, normal left atrium dimension, dilated right atrium, right atrial pressure of 20 mm Hg, and dilated right ventricle with a diastolic diameter of 44 mm and normal systolic function. There is mild mitral regurgitation; the tricuspid valve apparatus is hyperechoic and the valve leaflets are fixed in a semi-open position throughout the entire cardiac cycle, with severe tricuspid regurgitation, increased antegrade velocity and an estimated systolic pulmonary artery pressure 28 mm Hg. The main pulmonary arteries and branches are preserved, and there is severe pulmonary regurgitation with flow reversal in the pulmonary branches. There are no intracavitary masses (Figure 2).

The patient is evaluated jointly with the oncology service which, given the stage of the disease, proposes palliative treatment. The patient requests voluntary discharge from our hospital to return to her city of origin in the province of Formosa, where she later dies.

Neuroendocrine tumors (NETs) are rare malignant neoplasms, with an incidence ranging from 2.5 to 5 cases per 100,000; 30-40% of the cases develop carcinoid syndrome. Carcinoid heart disease has been reported in 40% to 50% of patients with carcinoid syndrome. (1) The diagnosis of carcinoid syndrome is

based on the detection of urinary 5-hydroxyindoleacetic acid, a metabolite that is a product of serotonin degradation which is also a predictor of the development of carcinoid heart disease. (2)

Most NETs occur in the small bowel, particularly in the ileum, and in the bronchopulmonary system. Less commonly, NETs arise from other sites within the gastrointestinal tract, including the colon, rectum, and stomach. Some of these tumors, particularly small bowel NETs, release vasoactive substances, including serotonin, tachykinins, prostaglandins, histamine, and kallikrein. (3) The liver inactivates these substances when they are released into the portal circulation, but when a serotonin-producing NET metastasizes to the liver, the direct access to the systemic circulation results in carcinoid syndrome and carcinoid heart disease. (3)

Cardiac involvement is caused by the secretory activity of the tumor, and the release of these substances into the systemic circulation, producing fibrous plaques in the endocardium, particularly on the right side of the heart, tricuspid valve and pulmonary valve, causing injury of both valves. (4) In most cases the lesion is limited to the right side because the metabolites are inactivated in the pulmonary circulation, with tricuspid valve involvement in 90% of the cases.

The diagnosis and management of carcinoid heart disease is based on biomarkers and echocardiography. Clinical screening with NT-proBNP measurement should be performed every 6 months. A cut-off value of 260 pg/mL of NT-proBNP has a sensitivity and specificity of 92% and 91%, respectively, for the detection of carcinoid heart disease, (5) with a negative and positive predictive value of 98% and 71%, respectively. A value > 260 pg/mL indicates the need for echocardiographic assessment.

Echocardiography is the gold standard for the detection of carcinoid heart disease, a relatively late manifestation of neuroendocrine tumors, but with important impact on the prognosis of these patients. Thus, early diagnosis and treatment is mandatory in each patient with a carcinoid syndrome. (4)

Once the diagnosis of carcinoid heart disease has been established, it is necessary to distinguish between mild cases, in which clinical and echocardiographic follow-up should be performed every 6 months, and moderate or severe cases, in which clinical and echocardiographic follow-up should be performed every 3 months. In case symptoms of severe cardiac disease develop, surgical management (valve replacement) should be considered. Without operation, only 10% of patients survive 2 years after the onset of NYHA functional class III or IV symptoms. Valve replacement is the only effective treatment option for patients with symptomatic carcinoid heart disease and is associated with improved symptoms and longer survival. (6)

Although somatostatin analogs should be used in all cases, as they inhibit hormone hypersecretion by binding to the receptors present on most neuroendocrine tumor cells, both octreotide and lanreotide have demonstrated to improve symptoms, but not survival. There is evidence that both symptoms and survival improve when the patient is managed by a multidisciplinary team.

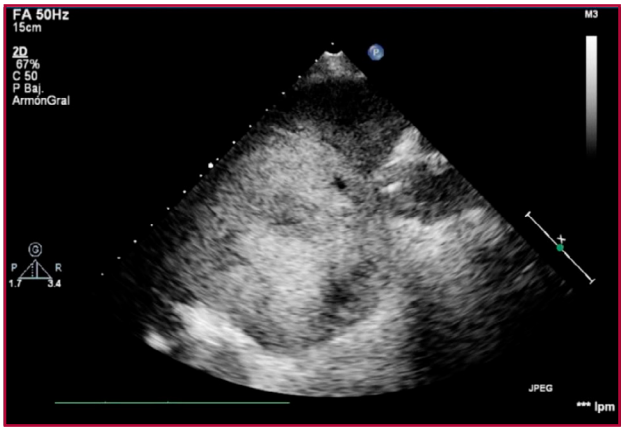

Fig. 1. Image of liver tumor

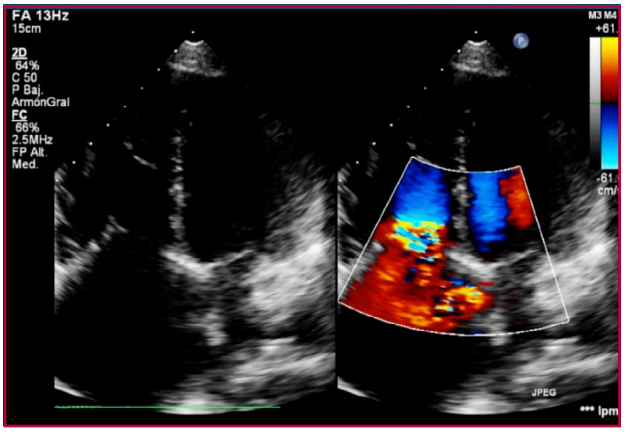

Fig. 2. Severe tricuspid regurgitation with valve leaflets fixed in a semi-open position.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

Ethical considerations

Not applicable

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