Agenesis of the Internal Carotid Artery and Left Kidney

The absence of the internal carotid artery is a rare anomaly, with a prevalence < 0.01 %, and is usually found incidentally. (1)

This case here reported highlights the relevance of knowing its existence in order to rule out associated conditions and have a pathophysiological interpretation in case a patient suffering from this condition has a stroke, or when there is need of interventional or surgical transsphenoidal hypophyseal procedures or carotid endarterectomy.

We report the case of a 49-year-old male patient with left renal agenesis, followed up due to hypertension and hypertriglyceridemia, with adequate monitoring of his risk factors except for weight (obesity grade I, BMI 32). Despite his aforementioned condition, the patient started to present increased creatinine (1.87 mg/dL, with Cockcroft-Gault glomerular filtration of 64 ml/min and 41.3 ml/min/1.73 m² by CKD-EPI) and microalbuminuria (68 mg/24 hours). In this context, a Doppler ultrasound of the neck vessels was performed to analyze a possible associated vascular disease, with the following findings (see Figure 1):

1. Hypoplasia of the left common carotid artery, with anterior-posterior (AP) short axis of 4.7 mm, and cross sectional (T) axis of 4.6 mm, while the right common carotid artery measured 8.2 mm and 8.1 mm, respectively.
2. Absence (agenesis) of the left internal carotid artery.
3. Vertebral arteries with normal antegrade flow and velocity.
4. Antegrade flow in both ophthalmic arteries.

A magnetic resonance angiography with gadolinium of the ascending aorta, aortic arch, and supra-aortic and intracranial vessels was performed to confirm the diagnosis and rule out associated conditions (Figure 2). The study ratified the ultrasonography findings and ruled out the presence of aneurysms in intracranial vessels, which are described with a prevalence of 25-35%, much higher than the 2-4% reported for the general population. (2) The study revealed ***fetal type*** collateral circulation in which the anterior cerebral artery from the affected side receives compensatory perfusion from the contralateral internal carotid artery through the anterior communicating artery, whereas the mid cerebral artery is perfused from the homolateral basilar artery through a well-developed posterior communicating artery. This is the most frequent type of collateral circulation (around 70% of cases) in the absence of internal carotid artery. (3) The other two types are the ***adult type***, in which the contralateral internal carotid artery supplies, by means of the anterior communicating artery, both the anterior cerebral artery and the mid cerebral artery on the affected side. Finally, there is a third pattern in which the side affected by internal carotid agenesis receives abnormal anastomotic flow: a) from the external carotid artery via the maxillary, ophthalmic, pterygoid canal or accessory meningeal arteries, b) from the cavernous portion of the contralateral internal carotid artery via transsellar intracavernous intercarotid connection, or c) via persistent embryonic vessels.

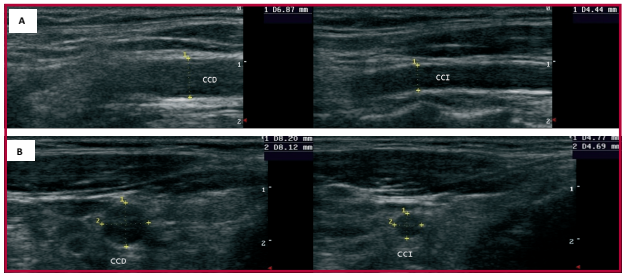

Fig. 1. Doppler ultrasound of the neck vessels. Panel A. Long axis image of the common carotid artery. **Panel B.** Short axis image of the common carotid artery. On the right of the image, notice that the left common carotid artery (LCCA) is hypoplastic, with anterior-posterior (AP) short axis of 4.7 mm and 4.6 mm in its cross-sectional (T) axis, while the contralateral common carotid artery (RCCA) measures 8.2 mm and 8.1 mm, respectively.

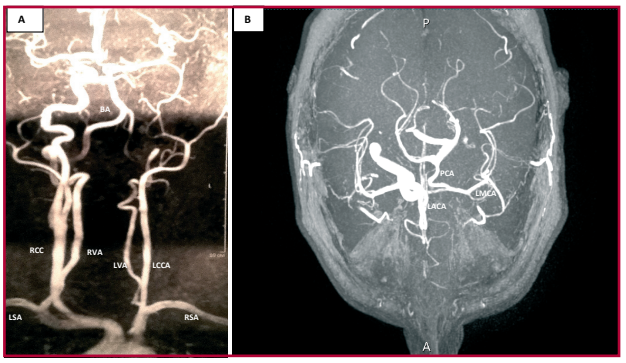

Fig. 2. Magnetic resonance angiography imaging. Panel A. Aortic arch. The first branch emerging from the aortic arch is the right brachiocephalic trunk (RBT), from which the right common carotid artery (RCCA) and the right subclavian artery (RSA) originate; the right vertebral artery (RVA) emerges from the RSA, and together with the less developed left vertebral artery (LVA) form the basilar artery (BA). The origin of the hypoplastic left common carotid artery (LCCA) is seen next. The left vertebral artery originates in the left subclavian artery (LSA). **Panel B.** Intracranial vessels. In the left hemisphere, in the absence of internal carotid artery, the left anterior cerebral artery (LACA) is supplied by the contralateral carotid system, and the left mid cerebral artery (LMCA) of the homolateral basilar system is supplied by a hypertrophic posterior communicating artery (PCA). "Fetal type" collateral circulation.

Differential diagnosis presented in the Doppler study is with internal carotid artery occlusion. The diagnostic suspicion, as pointed out in the literature (4), was to find a clearly hypoplastic homolateral common carotid artery. The primitive carotid artery and the first portion of the internal carotid artery originate from the third aortic arch, while the rest of the internal carotid artery is derived from the cranial portion of the dorsal aorta, and its development is completed in the 6th week of gestation. The origin of the external carotid artery is controversial. Some authors argue that it has a common origin with the internal carotid artery in the third aortic arch, but others claim that it originates independently in the aortic sac because it usually develops normally in the absence of the internal carotid artery.

There may be total absence (agenesis), complete absence with existence of its embryonic precursor (aplasia), or a small caliber internal carotid artery (hypoplasia).

The left unilateral anomaly is more common. (3:1).

A relevant fact is the presence of carotid channel at the base of the skull by means of computed tomography scan; its absence means internal carotid agenesis.

In our case we did not use this method, and after the Doppler results we resorted to magnetic resonance angiography to confirm the diagnosis. Although this condition is often associated with other cardiovascular and central nervous system abnormalities, fortunately that was not the case in our patient. Another finding was a small left facial angioma, and the description of the left renal agenesis he had in association with carotid agenesis was not found in the literature. Renal agenesis is also a rare entity (1: 1000 births), (5) left agenesis and in male subjects being more prevalent. Ovali G Y et al (6) reported a case of right carotid agenesis associated to right multicystic dysplastic kidney. As in our case, an unknown noxa, acting between the 3rd and 5th week during the embryonic origin of both organs, determined its co-occurrence.

Intracranial aneurysms have been ruled out in our patient; the approach will be the strict management of vascular risk factors, taking into account the existing abnormal renal function and his greater dependence on the right carotid axis for vascular supply of both hemispheres.

Conflicts of interest

None declared.

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Cerebral Metastases in Patients with Left Atrial Myxoma

Primary tumors of the heart are extremely rare, with an estimated incidence ranging from 0.0017% to 0.33%. Cardiac myxoma (CM) represents the most frequent benign cardiac tumor. The cells giving rise to the tumor are considered to be pluripotent mesenchymal cells that persist as embryonal residues during cardiac septation, although their origin is controversial. (1)

Complete surgical excision is often curative. Recurrence has been associated with incomplete excision, multifocality, and embolism of tumor fragments.

Since most myxomas are located in the left atrium, systemic embolism can occur mainly associated with brain symptoms (caused by brain and/or cerebellar strokes).

Brain metastases of cardiac tumors are rare, and that is why there are few cases reported in the literature. In documented cases, the occurrence of these tumors is usually more frequent in middle-aged women. (2)

We describe a case of cerebral metastasis caused by CM in a 52-year-old female patient with no cardiovascular risk factors or relevant personal or family history. She presented with prolonged fever syndrome, palpitations, asthenia and 2-month history of weight loss, associated to two presyncopal episodes. Physical examination at the cardiovascular level revealed increased R1, a tumor-plop sound, and mid-diastolic mitral valve rumbling murmur.

Transthoracic echocardiography revealed a 4.52 x 2.25 cm heterogeneous, ovoid, hyperechoic mass attached to the atrial septum, prolapsing in diastole to the left ventricle (Figure1 A).

A complete excision of the tumor was performed

and anatomical pathology confirmed the presence of a myxoid neoplasm with hemorrhagic disaggregation consistent with CM (Figure 1 B).

Two years after CM resection, the patient consulted for amaurosis fugax and photopsia interpreted as partial convulsions. A MRI of the brain showed multiple target-like cortical and subcortical lesions, reinforced with the contrast agent, which might be consistent with arteriovenous (AV) malformations, cavernomas, neoplasm, or cysticercosis (Figure 2).

Arteriovenous malformations and aneurysms were ruled out by cerebral angiography. Serologic test for cysticercosis was negative. A CT scan of the entire body showed no other tumors.

Bilateral tumor excision was performed and its histological sections showed fragments of brain tissue with architectural distortion, blood extravasation, marked edema, hemosiderin deposits, and small lymphocytes around the vessels and pseudo-vascular structures with hemosiderin deposits. Brain tissue with perivascular lymphocyte infiltration was found in some sections; others presented fragmentation of the media and myxoid change; fusiform or stellate cells with ovoid nuclei of filiform, eosinophilic cytoplasm and myxoid matrix were identified. These findings suggested metastasis of CM as probable diagnosis. An immunohistochemistry test was requested to confirm the diagnosis, which was focal positive for vimentin and diffuse for CD34, and negative for the remaining markers (Figure 3). These results, together with our patient's history and her clinical and radiological status, are consistent with metastatic CNS involvement due to CM.

Metastasis associated with CM is extremely rare given the benign nature of the tumor. By 2016, only 20 cases of brain metastases developed by CM have been published. (3) Metastases have even been reported in tissues other than the CNS. We have found no previous reports in Argentina.

Neurological complications of CM occur in 20-30% of cases. Cerebral embolism is the most common which may occur concomitantly with the cardiac tumor or even appear years later after complete resection.

The pathophysiological mechanism of metastases is still unclear. It is believed that CM is embolic during surgery or due to turbulent blood flow and it is speculated that these cellular fragments can infiltrate the wall of a vessel, weaken the endothelial layer developing an aneurysm, or initiate the growth of a metastatic lesion. (4)

The clinic of brain metastases is extremely variable and depends on the location of the lesions, which may be stable for years or show neurological deficit.

Metastases present a significant release of endothelin-1 (ET-1) from cultured CM cells, supporting the hypothesis that myxoma cells originate from primitive mesenchymal cells capable of endothe-

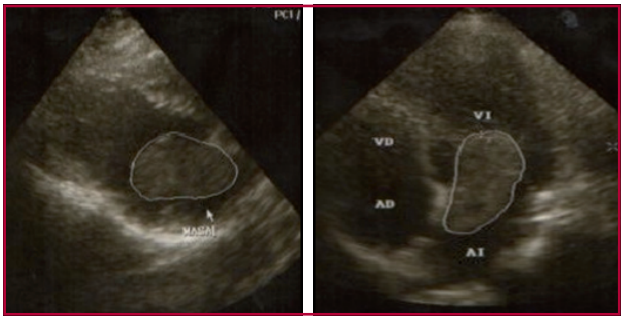

Fig. 1. A. Echocardiography showing tumor image.

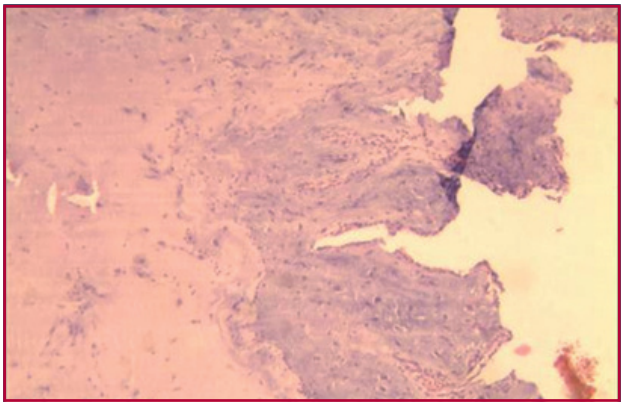

Fig. 1. B. Anatomical pathology consistent with myxoma.

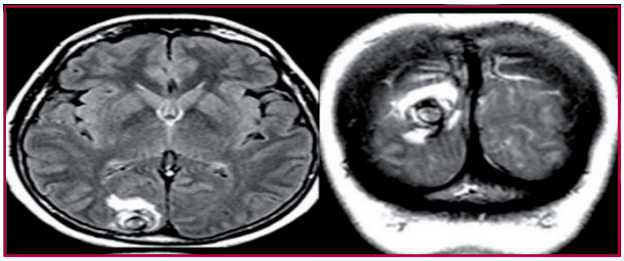

Fig. 2. Brain MRI showing cortical and subcortical lesions.

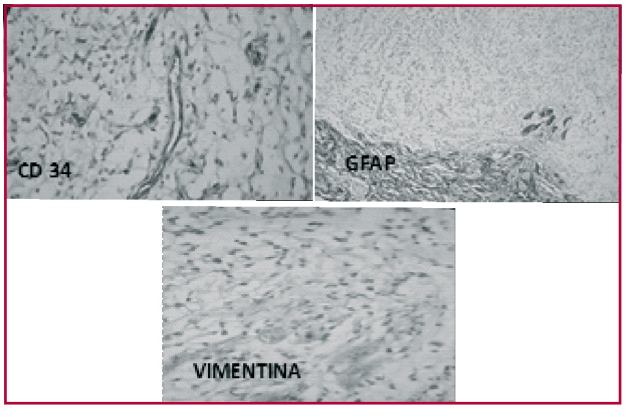

Fig. 3. Immunolabeling of metastatic tissue consistent with myxoma.

lial differentiation. Besides, they produce IL-8 and oncogene-a, CXC chemokines associated with tumor growth, as well as a significant tendency to metastasize. This theory partially explains the potential malignancy of this tumor. (5)

We found no standard treatment for cerebral metastases of CM in the literature; radiotherapy has been used for multiple lesions, and surgery for 1 or 2 brain lesions. As for the follow-up of this disease, it is recommended to follow a conservative approach monitoring with initial brain MRI and cardiac imaging at three months, followed by yearly scans for two years, and then biennially for a total follow up of 10-years. (6)

Today, our patient courses asymptomatic; follow-up brain CT-scan showed no evidence of growth or increased number of pre-existing lesions and transthoracic echocardiography revealed no recurrence of CM.

Cerebral metastases of CM are a rare and complex complication, difficult to diagnose in case of late clinical manifestation. Therefore, it is important to know that patients with CM require continuous, careful, and prolonged cardiac and neurological monitoring. In the case of our patient, two years had gone by after her cardiac surgery.

We thus conclude that this is a benign tumor but with a potential malignant behavior due to its metastatic capacity.

Conflicts of interest

None declared.

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Cavoatrial bypass due to suprahepatic vena cava occlusion in a patient with Budd-Chiari syndrome

The Budd-Chiari syndrome is defined as a chronic, congestive hepatic disorder secondary to the obstruction of the hepatic veins and/or the retrohepatic vena cava. Portal hypertension causes cirrhosis with ascites and severe lower limb edema. In the Western hemisphere, this syndrome usually occurs as a result of hereditary or acquired thrombophilic disorders, and rarely as a result of a membranous obstruction of the inferior vena cava. (1) The interventional treatment of choice to relieve portal hypertension in case of obstruction of retrohepatic vena cava is vena cava transluminal angioplasty with potential stent implantation. This procedure is long-lasting and effective in 92% of patients, (3) while in the rest of the cases, various surgical techniques can be used, such as cavoatrial bypass through a thoraco-laparotomy. (4) This surgery is rarely performed in our setting, and given that these are patients with severe ascites and metabolic and nutritional deterioration, the combined approach through the chest and abdomen is associated with thoracic and pulmonary complications. (5) In this work we report the clinical case of a female patient with obstruction of the retrohepatic inferior vena cava in whom intravascular treatment failed twice and required a cavoatrial bypass through a non-traditional approach consisting of laparotomy and minimal proximal sternotomy.

The patient was a 33-year-old woman with history of systemic lupus erythematosus, antiphospholipidic syndrome, and portal hypertension secondary to a 9-year history of Budd-Chiari syndrome. The humoral profile showed positive anti native DNA and extractable antinuclear antibodies, and complement C4 fraction, and the patient was treated with prednisone, hydroxychloroquine, diuretics and acenocoumarol. In

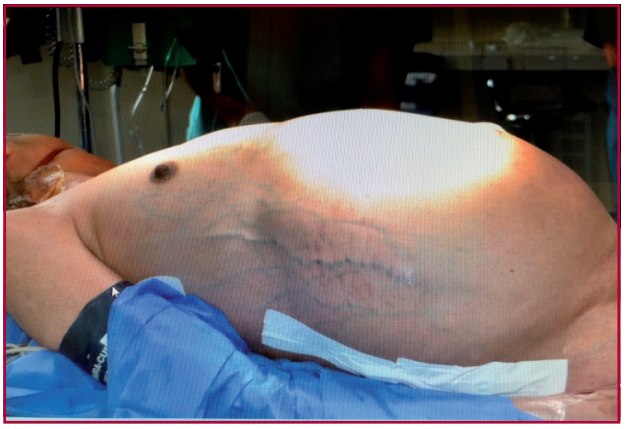

Fig. 1. Preoperative image of the patient's abdomen showing marked ascites and collateral circulation secondary to Budd Chiari syndrome.

Fig. 2. Cavography with retrohepatic inferior vena cava stenosis. The arrow shows the right hemidiaphragm.

2006, a bare-metal stent was implanted in the retrohepatic inferior vena cava with good clinical course and significant improvement of the ascites syndrome. In 2013, the patient presented with stent occlusion, with several attempts of partial repermeabilization and new thrombosis. The patient was assessed for liver transplantation, which was not performed due to her socioeconomic situation. In 2014, due to worsening of the liver congestion and refractory ascites, a cavoatrial bypass was performed (Figure 1). Figure 2 shows the cavography with inferior vena cava stenosis, extending for 4-5 cm. Through a combined and separate approach with median laparotomy and a 10 cm mini proximal sternotomy, a bridge was made between the infrahepatic inferior vena cava and the right atrial appendage using a 20 mm x 25 cm Dacron prosthesis that crossed the diaphragm (Figure 3). The patient had good immediate postoperative outcome and was discharged under anticoagulation with acenocoumarol. The two-year follow-up showed marked improvement in ascites and liver function, with reduced hypersplenism.

The Budd-Chiari syndrome refers to posthepatic portal hypertension and/or hypertension of the inferior vena cava due to outflow obstruction of the portal system. The highest incidence of this syndrome is found in China, Japan, India, and South Africa, reaching 1 out of 10.000 individuals in these countries. Surgical treatment includes direct resection of the thrombus or membrane –if present–, cavocaval or cavoatrial bypass to the right atrium, or portal bypass procedures to relieve the hypertension of the circuit, such

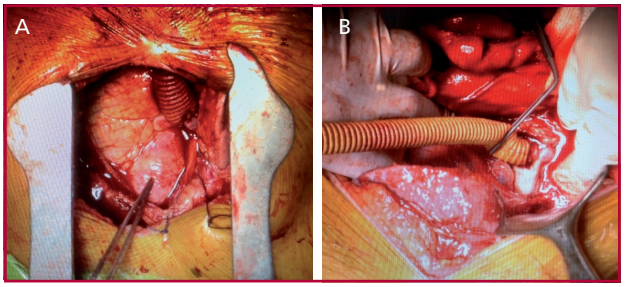

Fig. 3. Intra-operative images showing (a) anastomosis of the prosthesis in the right atrial appendage through a 10 cm long mini-proximal sternotomy, and (b) anastomosis of the prosthesis in the infrahepatic inferior vena cava through laparotomy. The arrows show the anastomosis sites.

as mesenteric-caval, splenic-caval, splenic-atrial, or splenic-jugular bypasses. With these procedures, the largest series by Dang et al. (6) reported a complication rate of 9%, an in-hospital death rate of 2.3%, and a recurrence rate of 9% and 14% (13/96) after 1- and 5-year follow-up, respectively. Another uncommon surgical technique is the Y bypass between the superior mesenteric artery, the inferior vena cava and the right atrium. Although this is a combined thoraco-abdominal surgical approach that requires a cardiac surgeon, in general these cavoatrial bypasses have better long-term patency, reduce hypersplenism, and achieve greater portal system decompression than mesenteric or splenic-cava shunts performed only within the abdominal cavity.

Thrombophilia is an inherited or acquired risk factor associated with abdominal vein thrombosis and Budd-Chiari syndrome. In contrast to the membranous obstruction of the inferior vena cava observed mainly in East Asia, the occurrence of Budd-Chiari in the Western hemisphere is usually associated to thrombophilia, as was the case of our patient.

In conclusion, the combined approach with laparotomy to access the suprarenal portion of the inferior vena cava, and the median mini proximal sternotomy to expose the right atrial appendage, could be an alternative to cavoatrial bypass in Budd-Chiari syndrome after intravascular treatment failure.

Conflicts of interest

None declared.

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Thyroid Hormone Therapy to Reverse Severe Heart Failure from Dilated Cardiomyopathy

We describe the case of an 18-year-old woman, awaiting cardiac transplantation (with left ventricular ejection fraction [LVEF] of 9%) in the ICU, fully monitored, on ventilator and inotropic support, and on diuretic therapy. The patient had systolic blood pressure of 90 mmHg, pulse rate of 95 bpm, low O2 saturation (89%), and mixed venous oxygen saturation in the pulmonary artery (SvO2) of 50%; the patient also had poor response to insulin. Although a donor heart became available, the transplantation was canceled as the patient was diagnosed with pneumonia (consolidation evidenced on chest x-ray and Gram stain of sputum showing cocci in clusters). Antibiotic therapy was initiated, but the prognosis was extremely poor; the patient started to develop progressive inhibition of aerobic metabolism, and increased plasma lactate and hyperkalemia, despite the increasing inotropic support and the high doses of insulin. The administration of thyroid hormone was discussed and approved by the senior heart transplant surgeon. A written consent for this experimental therapy was provided by the patient's family. Progressive inhibition of the aerobic metabolism was confirmed by indirect measurements of plasma potassium (K+) levels, progressive increase of lactic acidosis, and insulin resistance. Thyroid hormone was administered intravenously; the first dose of T4 (100μg) was delivered over 10 min, repeated after 30 min, and then hourly for 6 hours; the remaining medications were unchanged. Within 4 hours, there was a reduction of K+ from 7.0 mEq/L to 5.5 mEq/L, and within 6 hours plasma K+ was 5.2 mEq/L. These changes indicated that ATP was being produced, and that metabolism was improving. It would be assumed that, once the cellular metabolism was restored, an improvement of the mechanical work of the heart would follow. The patient received >1,000 μg of T4 within the first 24 hours, and some hemodynamic improvement, increased SvO2, normalization of plasma K+, reduction in plasma lactate, and mild improvement of insulin response were observed. Taking all this into account, it was clear that there was a major beneficial metabolic impact on the entire body. The restoration of aerobic metabolism and active ATP production became available as energy substrate for multiple ATPases. Within about 36 hours, systolic blood pressure remained >100 mm Hg, allowing for reduction of the inotropic support. Within 48 hrs., the patient was no longer dependent on ventilation, and the inotropic support was discontinued; LVEF improved by 15-20%. After 4 days, the patient had an episode of atrial fibrillation requiring cardioversion, to which she responded well. The only complication was that she developed exophthalmos. The patient was discharged with LVEF of 45-50%, and no evidence of clinical heart failure, and was removed from the heart-transplant waiting list. For 6 months the patient remained stable, LVEF remained at 50%, and she was referred to her primary care cardiologist (and unfortunately we were unable to follow her up).

Neuroendocrine interactions –in which the hypothalamic-thyroid axis plays a key role in the regulation of metabolism and energy balance– are described below. During a disease event, there is a significant reduction of plasma free thyroid hormone concentrations (triiodothyronine [T3] and levothyroxine [T4]), and increase of the reverse triiodothyronine (rT3), with no known metabolic effects or significant changes in thyroid-stimulating hormone. Multiple interactions between the thyroid hormones and the cardiovascular system have been described. (2) Thyroid hormones (i) stimulate aerobic metabolism within the mitochondria, (ii) have a direct inotropic effect, (iii) facilitate myocardial

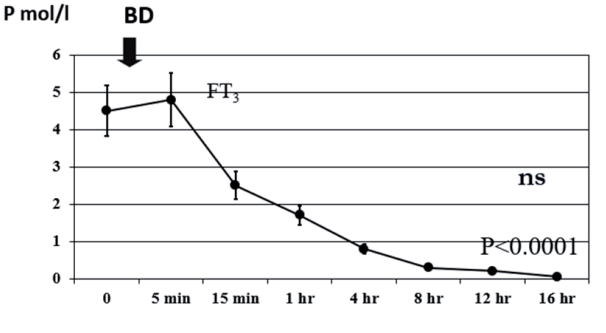

Fig. 1. Plasma levels of free triiodothyronine (FT3), following induction of brain death (BD) in the experimental animal. There was significant FT3 reduction, and no FT3 was detected at 16 hours. The arrow shows the time when the intracranial balloon was inflated with saline solution, causing intracranial hypertension.

relaxation, (iv) increase coronary artery and systemic vasodilation, (v) increase protein synthesis of multiple ATPases, and (vi) increase the synthesis of actin and myosin by stimulating nuclear cell receptors. Other important functions are (vii) enhanced synthesis and upregulation of sarcolemma beta-receptors, (viii) maintenance of the Na+/K+ pump, and (ix) the Ca2+-ATPase at the sarcoplasmic reticulum, which play a significant role in the contractility and relaxation of myocytes. (2)

The plasma free thyroid hormone concentrations vary during health and disease. A major decline has been observed in the brain-dead organ donor, which is an irreversible condition. During brain death, the systemic arterial hypertension –resulting from significant arterial vasoconstriction– causes further ischemic injury to all organs. This has been well-documented both in the laboratory and in clinical practice. (Figure 1) After the recovery from a disease event, the value of FT3 traces back to pre-disease level. Therefore, for endocrinologists, thyroid hormone replacement therapy should not be indicated in the presence of a non-thyroid illness syndrome (NTIS) event. Thyroid hormones play a significant role on cardiac hemostasis. The advanced stages of NTIS are always associated to a varying degree of depressed myocardial function, sometimes referred to as 'stunned myocardium'. (4) Its clinical effects may vary from minimal hemodynamic impairment to cardiogenic shock. Medical management may range from aspirin alone to implantation of a left ventricular assist device. With adequate supportive therapy, recovery usually occurs within days or weeks.

The effect of T3/T4 therapy during a NTIS has been well documented in three laboratory and clinical conditions, in which the depressed myocardial function was fully recovered to a normal systolic contractility and diastolic relaxation. It has been observed in: (i) transient regional myocardial ischemia of 15 min duration followed by reperfusion (stunned myocardium) (4), (ii) transient global myocardial ischemia in patients undergoing open heart surgery on cardiopulmonary bypass (5), and (iii) inadequate global myocardial function in brain-dead potential organ donors. (3) New experimental and clinical data indicate that T3 has been used in (iv) the ICU in patients who were hemodynamically compromised, and experimental studies have confirmed that thyroid hormones can have an (v) important therapeutic role in reducing infarct size and improving myocardial function after an acute MI. It is well known that critically ill patients, whose aerobic metabolism has been progressively inhibited: 1) present progressive increase of lactic acidosis, 2) require higher doses of inotropic support, and 3) show poor response to insulin therapy and develop hyperkalemia, all of which lead to cardiovascular instability. Death usually follows rapidly. Once aerobic metabolism has been restored, the ATP pool is normalized, lactic acid is no longer produced, the Na+/K+ pump function is recovered, and ionic levels are restored to normal values. The upregulation and activation of beta-adrenergic receptors allow for a rapid reduction of inotropic support. Insulin response also recovers, allowing the cell to metabolize glucose aerobically. Patients receiving T3 show rapid normalization of hemodynamic function. (6)

In our experience with all three conditions, myocardial dysfunction rapidly reversed with the administration of T3/T4. Therefore, we advocate thyroid hormone therapy for patients with NTIS and hemodynamic instability.

Conflicts of interest
None declared.
(See authors' conflicts of interest forms on the web/Supplementary material).

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