Lambl's excrescences in a woman with recurrent changes of consciousness

Excrescências de Lambl em mulher com alterações recorrentes da consciência

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Resumo

Excrescências de Lambl são estruturas filiformes longas hipermóveis que ocorrem em superfícies de fechamento de válvula cardíaca. Elas podem ter origem a partir de depósitos de fibrina sobre o endotélio lesionado, mas falta evidência definitiva de associação com acidente vascular cerebral embólico. O caso de uma mulher de 56 anos com cirrose hepática e episódios recorrentes de alterações no nível de consciência é descrito. Pouco tempo após a realização de transplante de fígado, ela apresentou um acidente vascular cerebral isquêmico agudo e excrescências de Lambl não suspeitadas foram detectadas na válvula aórtica por imagens de ecocardiograma transesofágico. A paciente teve manifestações neurológicas inicialmente atribuídas à encefalopatia hepática, e mais tarde definidas como acidentes vasculares cerebrais, com base em estudos de ressonância magnética. Embora a anormalidade valvular possa ser considerada de baixo potencial de risco embólico, a possibilidade de relação causal não foi totalmente descartada no caso aqui descrito. Causas insuspeitas de embolia cerebral só podem ser totalmente descartadas por exame histopatológico ou necropsia. O objetivo deste relato é analisar as principais características de excrescências de Lambl, enfatizando desafios diagnósticos no contexto de embolia cerebral e encefalopatia hepática sintomática.

Palavras chave: excrescências de Lambl, diagnóstico, acidente vascular cerebral cardioembólico, encefalopatia hepática

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Abstract

Lambl's excrescences are hypermobile long threadlike structures that occur in heart valve closing surfaces. They may originate from fibrin deposits on the injured endothelium, but there is no definitive evidence of association with embolic cerebral stroke. The case of a 56 year-old-woman with liver cirrhosis and recurrent episodes of changes in the consciousness level is described. Shortly after performing liver transplant, she presented an acute ischemic stroke and Lambl's excrescences were incidentally suspected in the aortic valve by transesophageal echocardiography images. The patient had neurological manifestations initially attributed to hepatic encephalopathy, and later defined to be cerebral attacks, with base on studies of magnetic resonance imaging. Although the valvular abnormality can be considered of low embolic potential risk, the possibility of causal relationship was not entirely ruled out in the case herein described. Unsuspected causes of brain embolism may only be cleared by histopathology or necropsy. The aim of this report is to review major features of Lambl's excrescences, emphasizing diagnostic challenges in the context of cerebral embolism and overt hepatic encephalopathy.

Key words: Lambl's excrescences, diagnosis, cardioembolic stroke, hepatic encephalopathy

Introduction

Lambl's excrescences (LE) are rare threadlike structures occurring in closure lines of heart valves, usually without functional disorder.[1-8] They originate as small tears, with or without thrombus formation, on endocardial surface of contact in the valve margins and have fibrous acellular axes.[1-4,9,11] This case study describes a 56-year-old woman with recurrent changes in the level of consciousness attributed to hepatic encephalopathy (HE), but the relationship with repeated ischemic strokes was later established. Suspected images of LE were incidentally found in the aortic valve during the investigation of the ischemic episodes. Although without robust evidence,[6] this rare cardiac change have been associated with acute ischemic stroke (AIS) and other neurological disorders.[1,4,8-11] The purpose is to comment additional diagnostic challenges, involving LE, in a patient with hepatic cirrhosis.

Case report

A 56-year-old Brazilian woman was referred to liver transplantation clinic in November 2013 due to cirrhosis by autoimmune hepatitis, and repeated episodes compatible with EH for about 10 months and

requiring intensive care unit (ICU) support. In addition, she had obesity, arterial hypertension and type 2 diabetes mellitus. In October 2012 she underwent cerebral aneurysm embolization and, since then, she presented clinical signs of encephalopathy. She denied smoking or alcoholism, ascites, jaundice or gastrointestinal bleeding. Physical examination revealed no significant abnormalities. Laboratory tests showed moderate anemia, low platelets, and mild changes of the liver function tests as well as of metabolic profile; the rest of routine determinations were unremarkable. The case was approved for liver transplant due to recurrent neurological manifestations compatible with hepatic encephalopathy, poorly controlled by adequate clinical and nutritional management. In October 17th 2014 she underwent a liver transplantation. On the 20th day post-transplant, the patient developed lowering level of consciousness, unresponsive to verbal or painful stimuli, and anisocoria. She was transferred to the ICU and a magnetic resonance imaging (MRI) study showed reduced brain volume and leukoaraiosis; hyperintense signal in T1 on the globus pallidus, probably due to deposition of manganese; as well as hyperintense signal in T2/ FLAIR on the right occipital lobe with restriction to diffusion extending to the mesial area of the ipsilateral temporal lobe, which would be associated with acute ischemia; and chronic lacunar infarctions in cerebellar hemispheres (Figure 1).

Culture of tracheal secretion revealed *Pseudomonas aeruginosa* and *Staphylococcus epidermidis* was found in blood cultures, and were treated with meropenem, polymyxin B, linezolid, and ceftaroline, but episodes of fever persisted. As new culture of tracheal aspirate showed *Pseudomonas* and blood cultures were positive for *Candida albicans*, ceftaroline was maintained in addition to levofloxacin, and micafungin. Because of persistent fever, a transesophageal echocardiogram (TEE) was done, disclosing thickened aortic valve with a hypermobile mass, measuring 4 mm and adhered to the aortic surface of the right coronary leaflet, resembling vegetation. Additionally, a filiform image measuring 0.26 cm was observed on the ventricular side of the same leaflet, considered suggestive of LE (Figure 2).

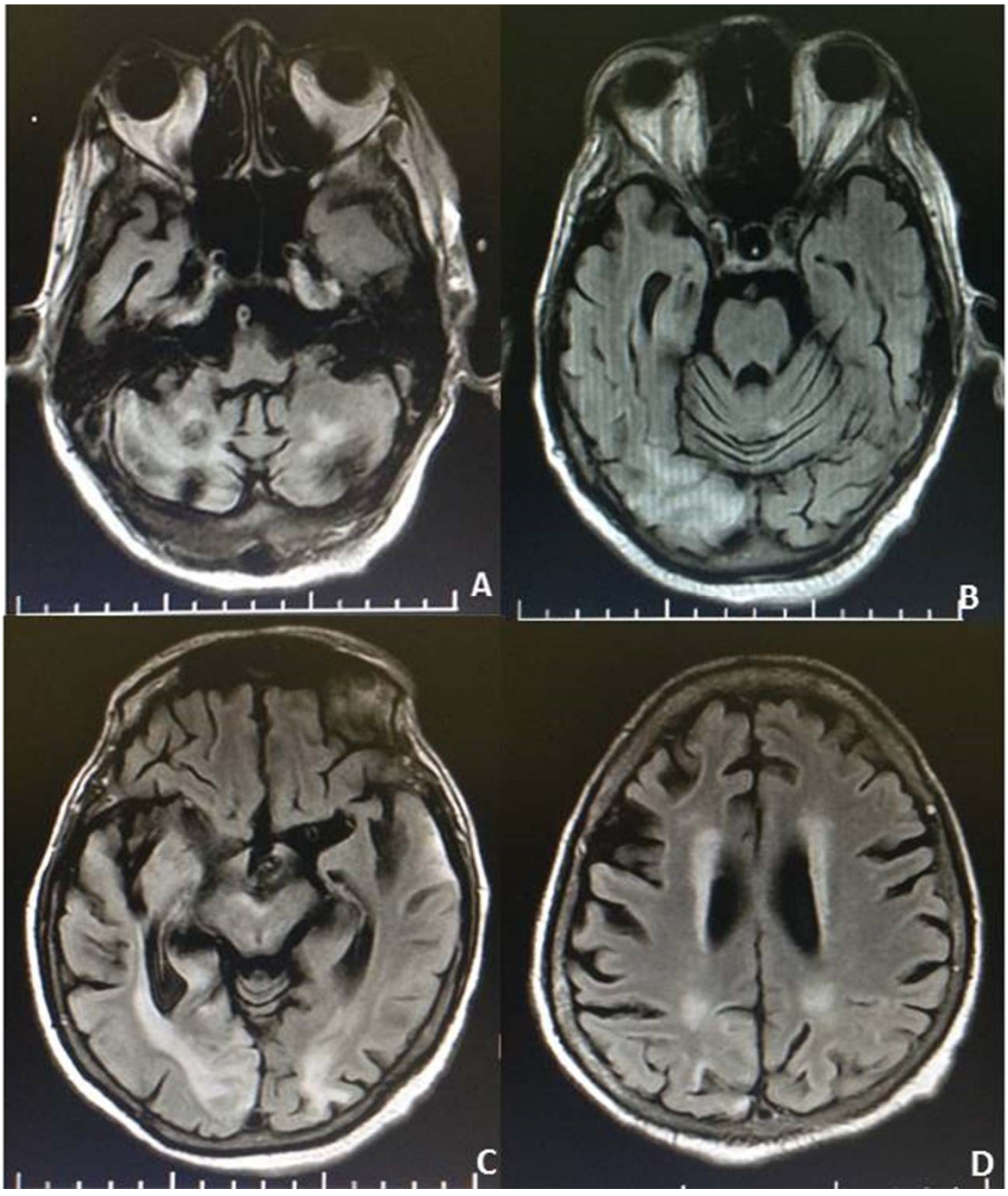

Figure 1 (Magnetic resonance imaging of the brain without contrast). **A**: images compatible with chronic infarctions in cerebellar hemispheres; **B** and **C**: T2/FLAIR hyperintense signal and diffusion restriction involving the cortex and white matter in the right occipital lobe, extending to the temporal lobe, associated with cortical T1 hyperintense signal indicative of subacute ischemic injury; and **D**: T1 hyperintense signal in the area of globus pallidus probably due to manganese deposits associated with hepatic impairment.

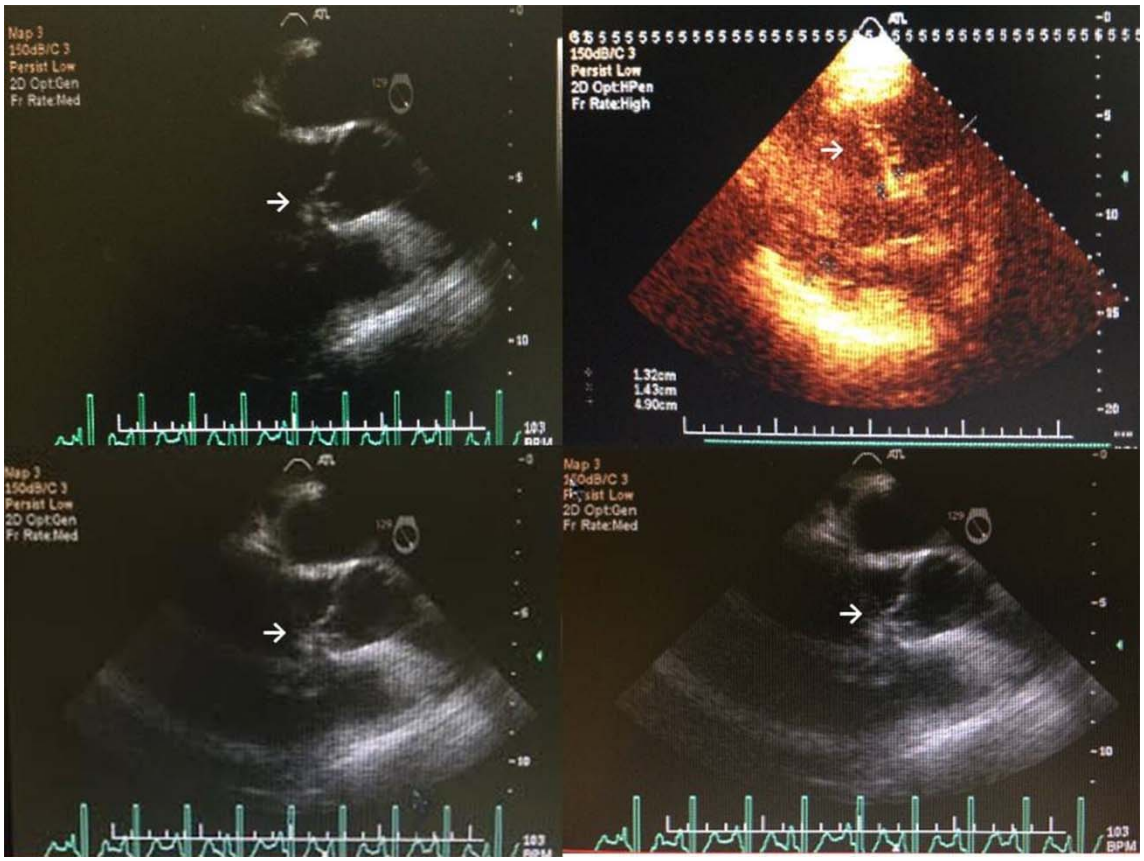

Figure 2 (Transesophageal echocardiography with color Doppler): view of hypermobile strands attached to the right coronary leaflet of the aortic valve, with characteristic of Lambl's excrescences.

With the suspicion of LE, it was hypothesized that this condition might had caused brain microembolism, which mimicked her episodes of HE before the liver transplant, because apparently well compensated patient repeatedly evolved with severe episodes of "hepatic encephalopathy". She was evaluated by cardiologists and rivaroxaban (20mg daily) was used. There was clinical and laboratory improvement and no episodes of consciousness change. TEEs of control were performed during her admission and confirmed the unchanged presence of images both of the mass and the filiform structures, and absence of new changes. The discharge occurred approximately 100 days after liver transplant and she was referred to the Home Care team. Currently, the patient remains in regular follow-up at liver transplant clinic, and with progressive neurological improvement under use of oral anticoagulants.

Discussion

LE, also known as valve excrescences or valve strands, were first described in 1856 by Vilém Dušan Lambl.[1,3-5] They are fine and filiform fibrous strands that arise in heart

valve closure sites. These formations have less than 1 mm thick and at least 10mm in length and may present as single strands, in raw or in clusters.[3] The classical structure is composed of a core of hypocellular and avascular fibroelastic tissue coated by a layer of endothelial cells.[1,3-5,10] The diagnosis of LE is suspected by findings of TEE, which has more sensitivity and specificity than transthoracic echocardiography (TTE), in special to detection of aortic or mitral valve damages. Definitive diagnosis of LE has been established with base on imaging studies, but histopathological data should be necessary if the differential hypotheses of fibroma, fibroelastoma, myxoma or thrombus cannot be ruled out.[1,3-5,11,13]

LE are described in association with chronic rheumatic heart disease, pulmonary or systemic hypertension and endocarditis, but can occur without concomitant cardiovascular disease.[5,8,12] Although with pathogenesis not entirely cleared, the initial event could be discrete lesions on the endothelial surface in areas of high stress and trauma, such as closing lines of the mitral and aortic valves. Fibrin deposition on the injured endothelium, would cause excrescences; the strands may also result from fibrosis related to the aging process that can lead to thickening in areas of heart valve closure.[1,4,10,12] Other authors admit that the growths could be protective anatomic variants, resulting from mechanisms related to frequent impacts of flow overload and constant movements of the leaflets of the valves that might give origin to transitional injuries followed by normal repair, including the endothelial lining.[5]

The alleged mechanism of AIS in patients with LE remains unclear; but it is possible that a portion of the formed excrescence or thrombus on the surface of the lesion may tear, causing embolus to the brain, eye and spleen.[1,3,4,8] Liu et al. described the association between migraine head pain (which did not completely meet the criteria of a specific primary headache) and AIS in two patients with LE.[4] The authors hypothesized that LE originated microemboli which caused areas of cerebral ischemia, manifesting as migraine headache.[4] The risk of ischemic events is higher among the youngest people.[14] Some authors suggest that LE should be discarded in case of cryptogenic stroke.[4] The consensual treatment was not established due to scarce controlled studies.[5,13,14] Case reports suggest conservative follow-up for asymptomatic patients with incidental finding of LE.[1,10] For patients with AIS there are several treatment options, including antithrombotic therapy with antiplatelet drugs, anticoagulation and cardiac surgery.[1,3,4,8-13] However, in a double-blind randomized study of treated AIS, LE did not increase adverse events; nor aspirin or warfarin had advantage on treatment.[14] Case studies about stroke

recurrences on antithrombotic treatment indicated that surgical removal of LE may be effective to prevent AIS.[1,4,8,11-13]

The differential diagnosis of LE based on TEE images includes benign and malignant heart conditions such as papillary fibroma and fibroelastoma, myxoma, metastasis, primary malignancy, thrombosis and endocarditis vegetation.[1,3,8,10,12,13] Primary cardiac tumors are very uncommon (5%) and are usually intracavitary, originating from the endocardium, valve, or myocardium; about 75% are benign, and myxomas are the most common followed by fibromas, lipomas, rhabdomyomas, hemangiomas, teratomas, papillary fibroelastomas, pericardial cysts, and cysts of atrioventricular node area.[15-18] Importantly, metastatic cardiac tumors are about 20 times more common than primary tumors of this organ.[17] Baikoussis et al. evaluated 117 patients from 16 to 82 years of age operated by cardiac tumor; and found myxomas (77.78%), other primary tumors (12.82%), infradiaphragmatic tumors (5.98%), and thrombi (3.42%); and in three cases there were neurological complications.[15] Papillary fibroelastoma is the main differential diagnosis of LE, the second most prevalent (10%) of the primary tumors, and in over than 75% of cases is found in valves.[16,18] They are often asymptomatic, but classic manifestations include transient ischemic attack, stroke, angina, myocardial infarction, sudden death, heart failure, syncope, or visual impairment.[16] Taha et al. reported a patient with an exceeding rare phenomenon, a papillary fibroelastoma affecting the chordae of mitral valve and two aortic LE.[18] This association may pose more difficulties for control and diagnostic challenges among non-specialist health care workers.

In the present report the patient was categorized as MELD 11 and CHILD-PUGH B 9, carrier of autoimmune hepatitis and liver cirrhosis and presented episodes compatible with HE before the successful liver transplantation. Her recurrent changes of consciousness level ceased shortly after the administration of oral anticoagulants. A major concern was about the possible diagnostic confusion between clinical manifestations of cerebral ischemia and the common symptoms of HE. Additionally, the presence of aortic LE was incidentally suspected during the imaging studies performed to investigate the etiology of cerebral embolic episodes.

In conclusion, the patient had neurological manifestations and images of ischemic stroke coexistent with TEE images highly suspected of LE, but the hypothesis of etiologic relationship between these conditions was not confirmed. Notwithstanding, the possibility of positive correlation of causality was not entirely ruled out. Unsuspected causes of brain embolism can be established by histopathology of

samples, or complete necropsy studies as reported in a woman with gastric cancer by dos Santos et al.[19] They evaluated microscopic features of thrombi into meningeal vessels and found tumor cell clumps plus fibrin clots.[19] Worthy of note, in most of the articles, strands and LE are considered synonymous at least in part because of similarity on echocardiography, but the histological features are different.[6] The Guidelines for the use of echocardiography in the evaluation of a cardiac source of embolism consider that even giant LE are valvular conditions with low embolic potential.[6] Controlled studies about pathophysiology of LE with great number of patients are lacking, but case studies have suggested that LE detected by TEE may be associated with embolic events.

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