Carotid dissection in Loeys-Dietz Syndrome, a case report

M. Cao, L. Chessa*, M Colombi, S. La Starza, M. Beccia. V. Ceschin, M. Rasura**
Stroke Unit, Sant' Andrea Hospital, Rome, II Faculty of Medicine and Psychology
***Genetic Department, Sant' Andrea Hospital, II Faculty of Medicine and Psychology**
**** Genetic Department, Univerity of Brescia**

Introduction

Loeys-Dietz syndrome (LDS) is an autosomal dominat disorder of connective tissue. There are more types of Loeys-Dietz syndrome, which are distinguished by their genetic assay. Signs and symptoms of LDS can become anytime in childhood or adulthood, and the their severity is variable. As defined by Loeys et al. in 2006 the disorder is characterized by the triad of arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate (1).
In addition, other features of Loeys-Dietz syndrome are: heart defects such as atrial septal defect, patent ductus arteriosis, bicuspid aortic valve, instability or malformation of cervical spine, easy bruising, wide scars, soft skin texture, and translucent skin, osteoporosis, allergies and asthma, dyspepsia and diarrhea, abdominal pain, and/or gastrointestinal bleeding and eosinophylic inflammation, rupture of the spleen or bowel, rupture of the uterus during pregnancy.
Approximately 75% of patients show craniofacial manifestations; approximately 25% have systemic manifestations of LDS but minimal or absent craniofacial features (2).
In initial reports, LDS patients, defined as those with mutations in TGFBR1 and TGFBR2, were stratified into two types, depending on severity of craniofacial features (type 1) or cutaneous features (type 2) (1).
Given that vascular disease is the major concern for this patient group, and that patients with mutations in TGFBR1, TGFBR2, SMAD3, or TGFB2 show more widespread and/or aggressive vascular disease when compared with Marfan syndrome or thoracic aortic aneurysm and dissection, irrespective of the severity of systemic features, some authors propose a revised nosology and that a mutation in any of these genes in combination with documented aneurysm or dissection should be sufficient for the diagnosis of LDS (Tab 1) (2, 3)

Case report

S.C., 45 year old woman was admitted in Stroke Unit of Sant' Andrea Hospital on the Second of February of 2013 because of onset of severe acute headache and aphasia. In the past the patient suffered from migraine, mild hypertension and used oral contrapcetives; no neck o head traumatic injury, but hypothyroidism were reported. No face and body abnormalities were shown. The neurological exam showed mild aphasia and weakness in upper right arm. The patient underwent to a brain and artery MRI that showed a small ischemic lesion in occipital left lobe and occlusion of left carotid artery (Fig 1), confirmed by carotid ultrasonography. A pulmonary CT did not show any aneurism or vascular malformation.
Blood sample showed a MTHFR homozygous mutation; trans-esophageal echocardiography showed a mild pericardium effusion, and a small passage of microballs during Valsalva maneuver. The patient started Warfarin therapy which was stopped on October 2013 in order to submit the patient to hysterectomy because of a severe metrorrhagia. So the patient started LMW heparin and, before the operation, underwent to Angiographic carotid and brain CT which showed right carotid dissection, without any new cerebral ischemic lesions (Fig 2). Because of severe anemia she underwent to hysterectomy and, 5 days after, was admitted in our Stroke Unit where underwent to a genetic assay which detected LDS, characterized by a missense mutation in SMAD3 . She started Warfarin therapy and refused other diagnostic exams in order to identify other vascular systemic lesions.

Conclusions

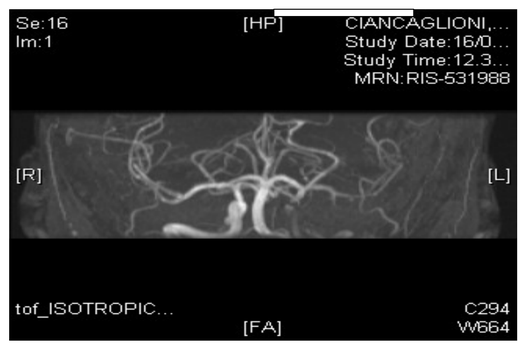
LDS is a rare connective disorder which involves young and adult patients. Clinical characteristic are aneurism, artery dissections, hypertelorism, and bifid uvula or cleft palate. Our clinical case show how patients with only few craniofacial signs can have a positive genetic test for LDS. So can be useful to submit patients with artery dissection and/or occlusion without a suggestive history of traumatic injury to genetic assays for Marfan or LDS. This paper will alert clinicians caring for these patients to the need for specialized patient counseling and management and highlight the evidence-based expansion of the clinical spectrum of LDS to include patients with minimal or no dysmorphic features. Such reasoning and practices have proven productive in the diagnosis and care of patients with Marfan and vascular Ehlers–Danlos syndromes.

Tab1, Mutations of LDS

LDS type (proposed)	Gene symbol	Other disorders reported
LDS 1	*TGFBR1*	TAAD (previously, LDS 1a, 1b, 2a, 2b)
LDS 2	*TGFBR2*	TAAD, MFS2 (previously LDS 1a, 1b, 2a, 2b)
LDS 3	*SMAD3*	Aneurysms-osteoarthritis syndrome
LDS 4	*TGFB2*	Aneurysm, aortic and cerebral, with arterial tortuosity and skeletal manifestations

LDS, Loeys–Dietz syndrome; MFS2, Marfan syndrome type 2; TAAD, thoracic aortic aneurysm and dissection; TGFBR, transforming growth factor-β receptor.
Source: http://www.omim.org.

Fig 2: Ischemic lesion and left ICA occlusion



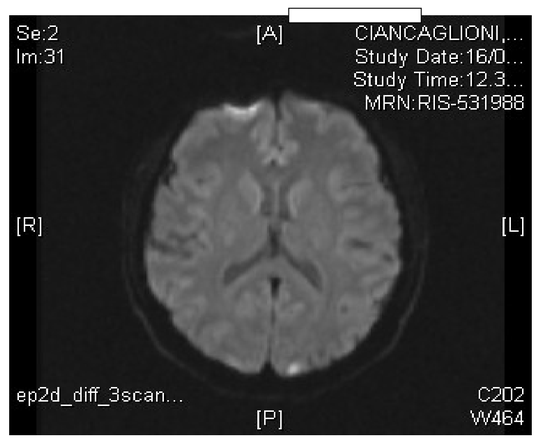
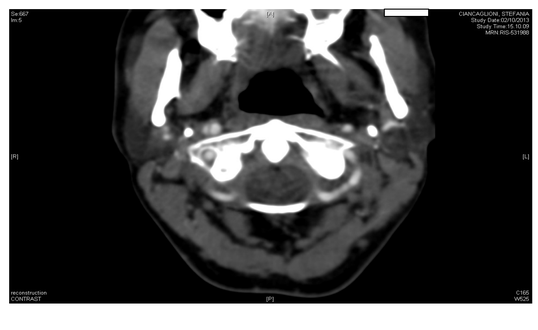


Fig 2: Dissection of right ICA



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