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Case Report

Omental transplantation in a patient with mild ALS

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Abstract: To demonstrate that amyotrophic lateral sclerosis (ALS) is not a neurodegenerative disease. The patient, a 33-year-old man began with symptoms of the bulbar form of ALS, characterized by burning pain in both feet during two months and then, he presented right crural monoparesis, fasciculations, slight dysarthria and he walked with help of orthopedic devices. A preoperative MRI scans showed atherosclerosis at the V4 segment of the left vertebral artery. On May 2012, he received an omental transplantation on the anterior, left lateral and posterior surface of the medulla oblongata. About 48 hours after surgery, the dysarthria disappeared and the voluntary movement of the right foot improved. Three days later, he walked without aid of orthopedic device. At present, four years after operation he present complete reversal of symptoms. In conclusión, this patient confirms that bulbar ALS is of ischemic origin and therefore, mild ALS can be cured.

Keywords: Amyotrophic lateral sclerosis, vertebral atherosclerosis, bulbar ischemia, omental transplantation, mild ALS

Introduction

Although to date Amyotrophic lateral sclerosis (ALS) is still recognized as a neurodegenerative disease [1]; my colleagues and I believe that this neurological disorder is of ischemic origin in the intraparenchymal territory of the anterior-ventral spinal arteries (AVSs) and/or anterior spinal artery, caused by atherosclerosis and associated to anatomical anomalies [2-4].

I report to a patient with mild ALS who received an omental transplantation on the anterior surface of the medulla oblongata. At present, four years after surgery, the patient present complete reversal of symptoms and signs.

Case report

A 33-year-old man was admitted to a local hospital in Lima, Peru, by difficulty walking. On February 2011, he began with pricking and/or burning pain in both feet, which was insidious and progressive, but to predominance in the right foot. Two months later, a magnetic resonance imaging (MRI) scans revealed a herniated disc in the lumbar column. However the pain in the right foot and leg diminished until disappear, and by contrast, he presented weakness and spasticity in the right lower limb. An electrodiagnostic test revealed doubtful signs of ALS. Besides this, on June 2011, he presented fasciculations in trunk and thighs;and. others MRI scans of skull and cervical column were reported as normal.

Since August 2011, he used orthopedic device in the right foot and leg, as well as he walked with help of a cane. Likewise, other electrodiagnostic study revealed clinical signs of ALS. During these 15 months of disease, the patient was attended by orthopedists, neurologists and later on, in the Instituto Nacional de Ciencias Neurologicas (Peru). As treatment, he received only analgesics, acupuncture and rehabilitation.

Examination

The patient was admitted to the hospital walking with help of a cane. He presented slight dysarthria, and moderate impairment of gag reflex. Right crural monoparesis of distal predominance [grade 2-4], patellar hyperreflexia, right Babinski sign and presence of fasciculations in upper and lower limbs. The superficial and deep sensory signs were normal. Preoperative MRI scans showed atherosclerosis at the V4 seg-

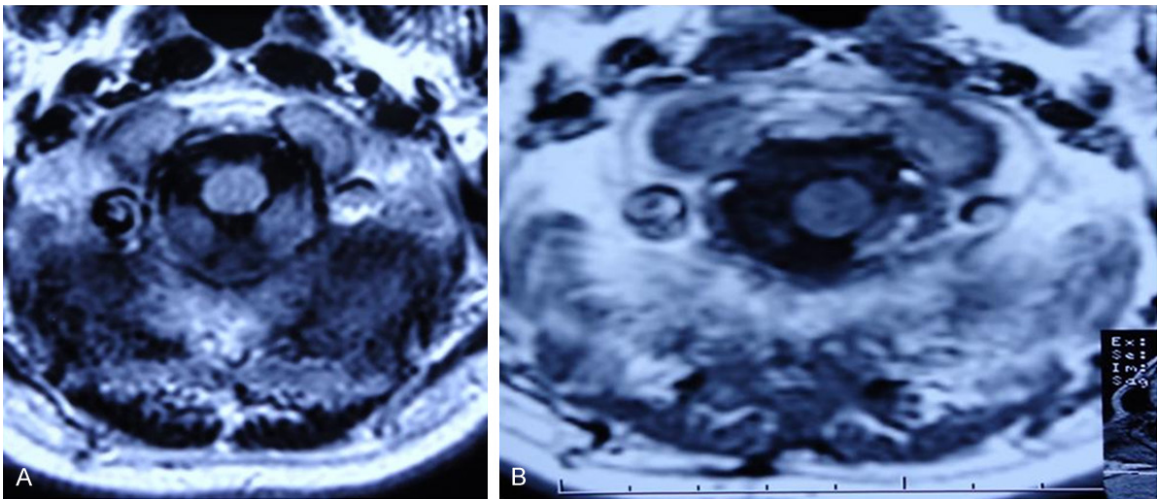

Figure 1. A. Preoperative MRI scan without contrast, showing the medulla oblongata, cerebellar tonsil and atherosclerosis at the V4 segment of the left vertebral artery. B. Postoperative MRI scan without contrast, showing omental tissue on the anterior, left lateral and posterior surface of the medulla oblongata, eight months after surgery.

ment of the left vertebral artery (**Figure 1**). A omental transplantation was proposed to the patient and his family, and before surgery, the patient's status was recorded on videotape.

Operation

With the diagnosis of bulbar ALS due to progressive ischemia in the intraparenchymal territory of the AVSAs [5-8], an omental transplantation was performed in May 5 2012, in two stages under general anesthesia [3, 9-11]. Briefly, by means of laparotomy, a 5 × 20 cm segment of omentum was obtained, which contained vascular elements good caliber. The omentum was of good quality, ie, the omentum was smooth, malleable, moderate thick and with abundant bood vessels. Second, the upper cervical cord and medulla oblongata were located through a laminectomy at the C1-C2 level. During surgery we found: 1) moderate hypoplasia at the V4 segment of the right vertebral artery; 2) slight to moderate atherosclerosis in the V4 segment of the left vertebral artery and 3) several circumferential and perforating arteries without changes in its blood flow on the lateral and posterior surface of the medulla oblongata. An end-to-end anastomoses by invagination between left occipital vessels and the gastroepiploic vessels were performed. Afterwards, a small segment of omentum was placed on the anterior, left lateral and posterior surface of the medulla oblongata. The surgery was performed without complications.

Postoperative course

About 48 hours after surgery, the dysarthria disappeared, and the intensity of voice were normalized, spasticity diminished and voluntary movement of the right foot improved. Three days later, the voluntary movement in the right lower limb was evident and he walked without aid of orthopedic device or cane. Postoperative MRI scans [January 2013] showed omentum at the lower portion of the pontine cistern, in the magna cistern and on the left lateral surface of the medulla oblongata (**Figure 1B**). This postoperative picture was recorded on two videotape.

At present, four years after operation, the motor evaluation in the right lower limb is of degree 5 and his gait is normal. Occasionally, he report fasciculations in the right thigh. He is working in the manufacture of furniture. He receive aspirin 500 mg biweekly.

Discussion

Since August 2009 and to date, we have transplanted omental tissue into 35 patients with ALS: bulbar (26 cases) and spinal (9 cases) forms of ALS. The age ranges were 33-77 years old with mean age of 52.6 (manuscript in preparation). All of them had different clinical and surgical findings. Clinically, most patients with bulbar ALS were admitted with moderate or severe degree of disease, and during surgery we found: 1) omentum poor to fair quality (thick-

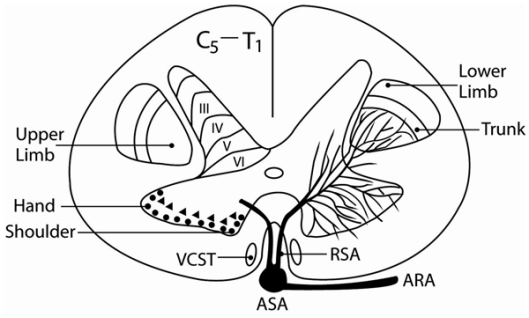

Figure 2. Schematic diagram of the cross-sectional vascular anatomy of the cervical cord. ASA, anterior spinal artery. ARA, anterior radicular artery. RSA, right sulcal artery. VCST, ventral corticospinal tract. Adapted from reference [8].

ened, pale and greasy (milky spots), ovoid, rounded and poorly vascularized); 2) moderate or severe degenerative changes in the cervical spine; 3) anatomical anomalies in the V4 segments of the vertebral arteries; 4) moderate or severe atherosclerosis in both V4 segments and 5) several exsanguinated circumferential and perforating arteries exsangues over the surface of the medulla oblongata.

I wish to comment about the onset of the symptoms in our patient report here. The central pain in both feet suggested ischemic injury in the neospinothalamic (A-delta fibers) pathways originated from IV to VI segments in the posterior horns, and by contrast, liberation of the paleospinothalamic (C-fibers) pathways [8, 12, 13], in the intraparenchymal territory from the anterior spinal artery. In the **Figure 2**, I show the normal vascularization of the anterior horns, IV to VI segments of the posterior horns, and ventral and lateral (upper limb and trunk) corticospinal tracts [8, 13, 14]. Two months later, central pain disappeared by functional recovery of the A-delta fibers [12, 15] and a new ischemic zone appeared in the anterior surface of the pyramidal decussation, especially in the antero-lateral portion of the left pyramidal tract (**Figure 3**), which caused weakness and spasticity in the right lower limb.

Likewise I believe that the appearance of dysarthria was due to an ischemic process in the lower half of one (or both) nucleus ambiguus. Because normally, the nucleus ambiguus is a vertical column, almost fusiform, of 15-mm of height and it is constituted by 1836 neurons in the right and 1942 in the left. The motoneurons

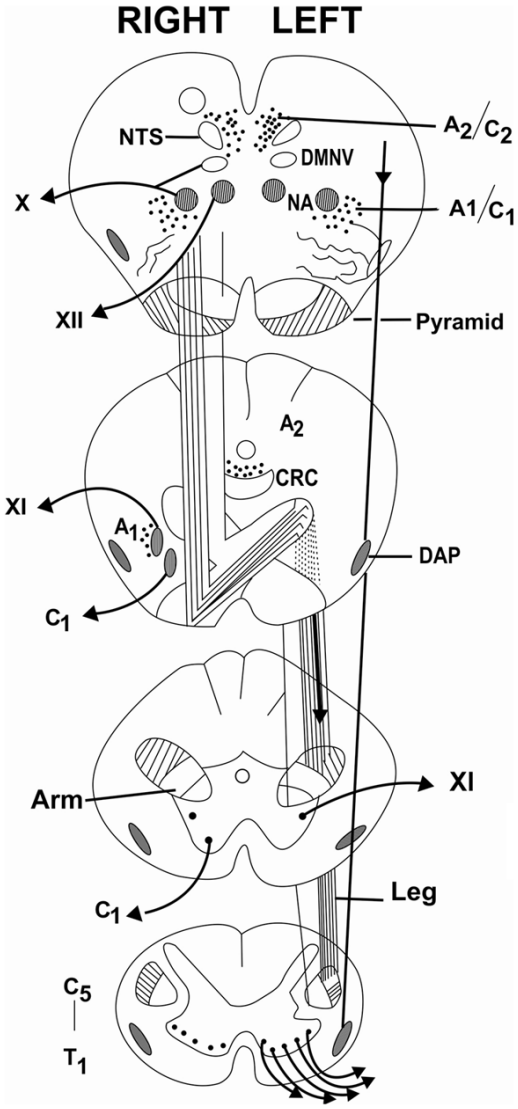

Figure 3. Schematic diagram ilustrating the pyramidal decussation and tracts, as well as the bulbar nuclei and anterior horns of the cervical spinal cord. A1/C1 and A2/C2 cell groups. NTS, nucleus tractus solitarii. NA, nucleus ambiguus. DMNV, dorsal motor nuclei of the vagus. DAP, descending autonomic pathways. CRC, cardiovascular réflex center (or commissural portion of the NST). Adapted from reference [3].

of the upper half inervate to the muscles of esophagus, pharynx and soft palate; while the lower half inervate to the muscles of larynx [13]. Moreover, in antero-laterall possession to each nucleus ambiguus are located the A1/C1 cell groups (related with the arterial pressure) and the ventral respiratory groups (VRG) or nucleus retro-ambiguus, known as expiratory centers. The ventro-lateral portions of the

nucleus tractus solitarii represents, the dorsal respiratory groups (DRG), also known as the inspiratory centers [13, 16]. Both groups send bulbospinal axons to the cervical and dorsal cord. The DRG stimulates to neurons of the phrenic nerves and external intercostal muscles, while the VRG stimulate to neurons of the accessory respiratory muscles and internal intercostal muscles [11, 16, 17]. Therefore, ischemic injury in these VRG and DRG produce respiratory worsening and different degrees of weak voice. In almost all patients with bulbar ALS, the dysarthria is the first symptom or sign. That is, an ischemic injury in the intraparenchymal territory of minute arteries less than 0.10 mm in diameter perforating the pyramids directly, and short and long branches from the AVSAs [6, 7, 18]. The presence of fasciculations in the trunk and limbs was secondary to degenerative changes in the pyramids and lower motoneurons in the anterior horns, ie, due to progressive ischemia in the intraparenchymal territory of the AVSAs and anterior spinal artery [7, 8, 14]. Therefore, the symptoms of bulbar ALS are directly related with atherosclerosis, and anatomical variants in the V4 segments of the vertebral arteries [4, 5, 7, 19]. In advanced-stage ALS, the degenerative changes in the cervical spine worsen the disease by stenosis in the V1, and V2 segments of the vertebral arteries, even after omental transplantation on the medulla oblongata.

For these reasons, we transplanted omental tissue on the anterior, left lateral and posterior surface of the medulla oblongata in our patient; because the omentum is the best tissue for developing vascular connections with underlying and adjacent zones to the omental tissue. So that, the pyramids and surrounding areas receives an increase in blood flow, oxygen, neurotransmitters, neurotrophic factors, adipocytokines and omental stem cells [2, 3, 11, 20]. So, I believe that the complete reversal of the symptoms and signs in this patient with mild ALS was due to revascularization of the pyramids and bulbar nuclei within the medulla oblongata. Finally, based in our surgical findings in patients with ALS, I think that the cervical or lumbar intraspinal injection of stem cells [21] do not penetrate into the parenchyma bulbar, due to atherosclerosis in the branches of the V4 segments in the vertebral arteries.

Conclusions

These results indicate that with this surgical modality we can cure or improve the mild ALS, because the omentum revascularize and provides stem cells in the ischemic zone. Besides, this patient also demonstrate that early-stage ALS was initiated in the anterior surface of the medulla oblongata, secondary to atherosclerosis and anatomical variants of the V4 segment of the vertebral arteries.

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