Legacy and current understanding of the often-misunderstood Foix-Alajouanine syndrome

Historical vignette

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Foix-Alajouanine syndrome has become a well-known entity since its initial report in 1926. The traditional understanding of this clinical syndrome is as a progressive spinal cord venous thrombosis related to a spinal vascular lesion, resulting in necrotic myelopathy. However, spinal venous thrombosis is extremely rare and not a feature of any common spinal vascular syndrome. A translation and review of the original 42-page French report revealed 2 young men who had presented with progressive and unrelenting myelopathy ultimately leading to their deaths. Pathological analysis demonstrated endomesovasculitis of unknown origin, including vessel wall thickening without evidence of luminal narrowing, obliteration of cord vessels, or thrombosis. Foix and Alajouanine also excluded the presence of intramedullary arteriovenous malformations. At the time, dural arteriovenous fistulas (dAVFs) had not been described, and therefore this type of lesion was not specifically sought. In retrospect, it seems possible that both patients had progressive myelopathy due to Type I dAVFs. In the decades since that original report, numerous authors have included spinal cord venous thrombosis as a central feature of Foix-Alajouanine syndrome. The inclusion of thrombosis in the clinical picture of this syndrome is not only incorrect but may leave one with the impression of therapeutic futility, thus possibly preventing successful surgical or endovascular therapy.

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Abbreviation used in this paper: dAVF = dural arteriovenous fistula.

Summary of Cases

The original 1926 French paper was a 42-page report of 2 cases of progressive myelopathy consisting primarily of an ascending paralysis from the sacral to midthoracic cord.31 Both patients suffered continued clinical decline and ultimately death. The report provided a detailed clinical description and an extensive pathological analysis of each patient. The following are summaries of the key features of each case.

Case 1

This 29-year-old man presented with a 7-month history of progressive, mild weakness in the lower extremities. The weakness was exacerbated by activities such as walking and climbing stairs. The patient’s medical history was notable only for a brief episode of low-back pain associated with albuminuria at the age of 16 years. On examination, he was noted to “walk with a very light step” and have marked atrophy of the gluteal and poste-
srori thigh muscles. Reflex examination showed “clonus at the foot” and absence of the inferior abdominal reflexes. Myelitis due to syphilis was suspected, and although blood and CSF Wasserman reactions were negative for syphilis, empirical antisyphilitic medications were initiated. The patient’s condition continued to worsen over the ensuing year. A little over a year after the onset of symptoms, he was densely paraparetic with considerable wasting of the muscles of the lower extremities. Patellar and Achilles tendon reflexes were absent. Light touch sensation was preserved, but there was diminished pain and temperature sensation in the lower lumbar and sacral dermatomes. “Electrical examination” (presumably electromyelography) showed “degenerative reactions with considerable sporadic excitability.” Cerebrospinal fluid analysis showed significant albuminocytological dissociation with massive hyperalbuminosis and mild lymphocytosis.

Slightly more than a year and a half after the appearance of his symptoms, the patient was completely paraplegic, incontinent, and suffering from cystitis. Sensory abnormalities progressed to include disturbances in light touch extending to the T-12 dermatome, and cutaneous reflex findings suggested involvement up to the T-10 level. Decubitus ulcers began to appear, and the patient suffered multiple bouts of intestinal obstruction, with pyuria and high-grade fevers. The ulcers progressed toward the sacrum, and the patient died 2 years and 9 months after the onset of symptoms.

Case 2

This 27-year-old man presented with a 3-month history of waxing and waning and progressively worsening lower-extremity weakness exacerbated by ambulation. On examination, he was found to have a dense paraparesis with the most significant diminishment in the lower-extremity flexor muscle groups. Patellar reflexes were intact, but Achilles tendon reflexes and plantar cutaneous reflexes were absent. Sensory function was intact. Cerebrospinal fluid analysis showed albuminocytological dissociation with xanthochromia, massive hyperalbuminosis, moderate lymphocytosis, and a negative Wassermann test. The patient experienced a remission in his symptoms over the ensuing 2 months, with improvement in lower-extremity motor function and gait. After another 3 months (8 months after the beginning of his symptoms), however, his condition worsened to a greater degree than ever. Complete flaccid paraplegia progressively developed, with significant muscle atrophy, impotence, and the loss of all lower-extremity reflexes as well as cremasteric and abdominal reflexes. “Electrical examination” (again, presumably electromyelography) showed complete denervation of muscles in the right leg, partial denervation of muscles in the left leg, and complete denervation of the thighs bilaterally. Sensory disturbances included loss of temperature sensation to the level of the umbilicus as well as light touch disturbances involving the right leg and foot. The overall situation progressively worsened with the appearance of decubitus ulcers and anesthesia extending to the level of the umbilicus. The patient died 11 months after the onset of his symptoms.

What Was the Actual Diagnosis?

Several lines of evidence suggest that both patients had progressive myelopathy due to Type I dAVFs, an entity that had not yet been recognized at the time of the original report. These fistulas are now known to be the most common variety of spinal vascular lesions, representing ~70% of all spinal vascular malformations. They are an abnormal communication between the radicular artery in the nerve root sleeve and the intradural venous system and are subclassified into Type Ia and Ib lesions. Normal radicular veins have a constriction point where they pass through the dura mater preventing the transmission of episodic increased pressure from the epidural and paraspinal veins into the valveless coronal venous plexus. Fistulas are usually located at this point or within the nerve root sleeve, which allows the transmission of arterial pressure into the valveless intrathecal spinal venous system and thus causing venous hypertension, congestion, and impairment of the spinal cord and nerve root microcirculation.

Type I spinal dural fistulas affect the function of the spinal cord and produce symptoms due to venous hypertension. Their exact origin is uncertain, but they are generally considered to be an acquired condition, unlike arteriovenous malformations. Growing experimental evidence has suggested that intra- and extracranial AVFs can develop spontaneously in the setting of venous hypertension produced by thrombosis or other causes. However, radiographically or pathologically evident acute thrombosis in the spinal venous system is only seen very

Pathological Findings in Both Cases

Extensive pathological analysis in both cases revealed myelitis and spinal cord necrosis, which were most prominent at the level of the lumbosacral prominence. The spinal cord abnormalities primarily involved the gray matter but also included the white matter. These findings progressively diminished in a rostral direction and disappeared in the region of the midthoracic cord. Extensive hypertrophy of the intradural vessels predominantly involved veins on the surface of the cord as well as both extra- and intramedullary veins, and to a lesser extent some arteries. Histological analysis of the affected vessels showed “endo-meso-vasculitis with necrotizing tendencies” and considerable hypertrophy of the media. The vessel lumens were widely patent.

Foix and Alajouanine excluded the presence of vascular malformations within the cord (page 31). They also stated that no thrombosis was identified: “Nous avons enfin que . . . il n’y a pas thrombose dans nos cas” (page 12). Furthermore, they noted that these pathological findings were distinctly different from other known varieties of acute and subacute myelitis of the time, such as poliomyelitis, multiple sclerosis, syphilitic myelitis, acute myelitis, Landry disease, optic neuromyelitis, myelomalacia, and congenital malformations. The authors were left without a clear diagnosis and speculated that a viral or toxic agent was involved.
rarely, and more often than not the existence of thrombosis is assumed rather than objectively visualized. Thus, although thrombosis may play a role in the development of spinal dAVFs, by the time the disease is far advanced and the patient displays progressive stages of myelopathy, a thrombus may not be evident pathologically.

The clinical presentation and course of the 2 men fit well with those typically seen in patients with Type I dAVFs. Steadily progressive thoracolumbar paraparesis, sensory impairment of the lower extremities and bowel, and bladder and sexual dysfunction with a relapsing and remitting course—features nearly identical to those seen in the original report—are indeed characteristic of patients with Type I lesions. Both patients in the original report were male, and Type I lesions primarily affect men. A factor disputing the hypothesis that patients in the original report had Type I lesions is their age: they were both younger (27 and 29 years of age) than most patients with Type I lesions. Most patients are more than 50 years old, although some as young as 28 years of age have been described.

In retrospect, it seems that the pathological descriptions of Foix and Alajouanine are consistent with many of the known changes due to the venous hypertension in Type I dAVFs. Engorgement and enlargement of the perimedullary venous plexus, caused by arterial-pressure flow within the veins, is a typical feature of Type I lesions. Hypertrophy of the media and intima with marked fibrous intimal thickening and destruction of the internal elastic lamina (so-called arterialized veins) also occur due to chronic venous congestion. These pathological changes are essentially what Foix and Alajouanine described as “endo-meso-vasculitis” with considerable hypertrophy of the media. Features of the original cases that are not completely consistent with Type I lesion pathology are the changes in both the arteries and veins, although the authors noted preferential involvement of the venous system. The focal, discrete fistula generally found in patients with Type I lesions—in the dural sleeve around the nerve root—could easily have been overlooked by the original pathologists given that it was an unknown entity and not specifically sought.

Legacy of Foix-Alajouanine Syndrome

The proliferative endomesovasculitis and venous dilation described by Foix and Alajouanine have been subsequently and similarly identified in more recent pathological descriptions of the syndrome, supporting their original findings. Although the cause of the vascular lesions was unclear to the authors, they believed that the disease was toxic or viral in origin, noting that they excluded known causes of myelitis at the time. In the decades since that original report, numerous authors have included spinal cord venous thrombosis as a central feature of the Foix-Alajouanine syndrome. Traditional teaching over the years has maintained that the clinical entity is largely attributable to progressive spinal cord venous thrombosis related to a spinal arteriovenous malformation resulting in necrotic myelopathy. Note, however, that several pathological reports have failed to consistently demonstrate

Thrombosis as a feature of Foix-Alajouanine syndrome is a myth that has been perpetuated most likely because the original report was written in French. It is possible, in fact, that several vaguely related diseases or perhaps variants of the same disease involving the spinal cord with similar clinical pictures have all been labeled Foix-Alajouanine syndrome. The traditional view of this syndrome as including progressive, fatal venous thrombosis is incorrect and may invoke a sense of therapeutic futility. This view may delay prompt diagnosis and surgical and/or endovascular treatment. Venous congestive myelopathy associated with dAVF is indeed a treatable disorder without sequelae if it is diagnosed in the early stages. The diagnosis of a Type I lesion should be con-
Foix-Alajouanine syndrome

Charles Foix and Théophile A. J. Alajouanine

Charles Foix (Fig. 1) was born on February 1, 1882, in Salies-de-Béarn in southwestern France. He was an internist and neurologist who studied medicine at the University of Paris and was a pupil of Pierre Marie at the Salpêtrière. He was an intern in 1906, working at the Médecin des Hôpitaux in 1919, and became professeur agré-gé in 1923. Foix's main contributions involved his ability to relate thromboses of specific arteries observed during autopsy procedures to symptoms and signs that he had established in his patients. Along with Jean Nicolesco, he contributed significantly to the description of the vascular anatomy of the midbrain. A most impressive teacher and clinician, Foix was at home with general medicine almost as much as he was with neurology; during the First World War, he was put in charge of a tuberculosis service. Foix died at the age of 43 years on March 22, 1927.

Théophile A. J. Alajouanine (Fig. 2) was born on June 12, 1890, in Verneix. This French neurologist was a pupil of Joseph Jules Dejerine and worked with Georges Charles Guillain and Charles Foix. He was a prolific writer on many topics, although he was especially interested in aphasia. The Laboratoire Théophile-Alajouanine, Centre hospitalier Côte-des-Neiges, Montréal, Canada, is named for him. Alajouanine died in 1980.5,21

Disclaimer
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Fig. 2. Photograph of Théophile A. J. Alajouanine (1890–1980).
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