



ATYPICAL VARIANT OF MOTOR NEURON DISEASE (VULPIAN BERNHARDT/ FLAIL ARM) – A CASE SERIES

Neurology

Dr. Dinesh Chaudhari

Associate Consultant, Institute of Neurosciences, Indraprastha Apollo Hospitals – 110076

Pushendra N Renjen*

Sr. Consultant Neurologist & Academic Coordinator, Institute of Neurosciences, Indraprastha Apollo Hospitals *Corresponding Author

Dr Anjali Mishra

FNB Critical Care, Max Super speciality Hospital, New Delhi

Dr Abhas Kumar

DNB Neurology, Institute of Neurosciences, Indraprastha Apollo Hospitals – 110076

ABSTRACT

Flail arm syndrome (FAS) has a similar clinical course and pathological findings as amyotrophic lateral sclerosis (ALS). It is important to distinguish the two diseases because FAS patients have significantly better survival rates compared with other typical ALS variants. Patients with FAS present with predominantly proximal, progressive and symmetric wasting and paresis of the upper limb (UL) muscles, while lower limbs (LL) and bulbar muscles are spared. FAS patients seem to show a prolonged survival compared to other ALS subtypes. In this article we will discuss about two such cases of Flail arm syndrome (FAS), who had better prognosis.

KEYWORDS

Motor neuron disease (MND) Vulpian Bernhardt Flail Arm Edaravone

INTRODUCTION-

Motor neuron disease (MND) encompasses a group of rapidly progressive and universally fatal neurodegenerative disorders of the human motor system, first described in the mid-19th century by the French Neurologist Jean Martin Charcot [1]. Amyotrophic lateral sclerosis (ALS) is the commonest MND phenotype, clinically characterized by progressive neurological deterioration and co-existence of upper and lower motor neuron signs [2]. In addition, the varied clinical presentations of MND also include (i) progressive muscle atrophy (PMA, ~ 10% of MND cases), a clinically pure lower motor neuron (LMN) phenotype, (ii) primary lateral sclerosis (PLS, 1-3% of MND cases), a clinically pure upper motor neuron (UMN) phenotype and (iii) progressive bulbar palsy (PBP, 1-2% of MND cases), an isolated bulbar phenotype with relative preservation of spinal motor neurons. More recently, an association between ALS and frontotemporal degeneration (FTD) has been established, suggesting that ALS forms a continuum with primary neurodegenerative disorders, a notion underscored by the identification of the c9orf72 hexanucleotide expansion [3,4].

Vulpian-Bernhardt syndrome / Flail arm syndrome (FAS) –

Flail arm syndrome (FAS) has a similar clinical course and pathological findings as amyotrophic lateral sclerosis (ALS) [5,6]. It is important to distinguish the two diseases because FAS patients have significantly better survival rates compared with other typical ALS variants [7,8]. MND has been reported to have multiple variants, one of those atypical variants of MND is the so-called flail arm syndrome (FAS), sometimes also referred to as Vulpian-Bernhardt syndrome, man-in-the barrel syndrome, or brachial amyotrophic diplegia [8–10]. Patients with FAS present with predominantly proximal, progressive and symmetric wasting and paresis of the upper limb (UL) muscles, while lower limbs (LL) and bulbar muscles are spared [11]. Only few studies about this variant exist and little is known about its epidemiologic characteristics. Hu et al. [12] and Couratier et al. [11] report a male to female ratio of around 4–9:1, which is much different from that in "classical" ALS, where ratios of 1.2:1 to 1.5:1 [5] are reported. In addition, FAS patients seem to show a prolonged survival compared to other ALS subtypes [5,11].

Case Presentation -1:

A 61 years old pleasant gentleman from Assam with history of Type 2 Diabetes Mellitus for past 5-6 years, presented with progressively worsening, symmetrical weakness of bilateral upper limbs for 3 years. It was associated with slowly progressive wasting of his arms but no significant functional involvement of other regions. No other family members were affected. Past history was unremarkable. Neurological examination at the time of presentation revealed symmetric, predominantly proximal wasting and weakness of both arms (especially of the infra-, supraspinatus and deltoideus) leading to

severe functional disability (Figure - 1). The upper limbs adopted a characteristic position, with the shoulders slumped, and the arms, forearms, and hands pronated. Bulbar and leg muscles were not affected. Fasciculations were noted in the upper limbs. Deep tendon reflexes were absent in the upper and hyperactive without clonus in the lower limbs. The jaw jerk and abdominal reflexes were normal. Plantar responses were flexor bilaterally. Sensory functions were normal. In view of progressive diplegia without lower limb involvement, Nerve Conduction Velocity (NCV) and Electromyography (EMG) of all 4 limbs was done. It revealed progressive multi-segmental denervation with atrophy of muscles of upper limbs leading to flail upper limbs and slow progression in lower limbs with normal NCV. With these NCV-EMG findings and clinical examination, diagnosis of Vulpian Bernhardt Syndrome / Flail Arm Syndrome was made. Patient was started on Riluzole and Intravenous Edaravone therapy. Upon 2 years of follow up patient has not deteriorated further.

Case Presentation -2:

A 73 years old male patient known case of Hypertension, came with complaints of progressive weakness of bilateral upper limbs for last 12 years. No bulbar symptoms, sensory symptoms or pain was there. He did not have any sensory or motor symptoms of lower limbs. No other family members were affected. Past history was unremarkable. Neurological examination at the time of presentation revealed symmetric, predominantly proximal wasting and weakness of both arms. Plantar responses were flexor bilaterally. Sensory functions were normal. NCV/EMG of all four limbs showed pure motor, severe, bilateral progressive preganglionic lesion at anterior horn cell level of cervical segments leading to flail upper limbs with showed normal bulbar muscles. Hence diagnosis of Vulpian Bernhardt Syndrome / Flail Arm Syndrome was made and patient was started on IV Edaravone and Oral Riluzole treatment. Patient has been doing good in 2 years of follow up with no further progression of his symptoms so far.

Discussion and Review of Literature –

In 2009, Wijesekera et al. [5] proposed for the first time operational definitions with standardized inclusion and exclusion criteria for FAS and the less frequent flail leg syndrome (FLS), based on a large multicenter study including 135 FAS and 75 FLS cases. Patients are usually classified according to the revised El Escorial research diagnostic criteria [13], and categorized according to site of onset (bulbar or limb onset ALS). The operational definitions of the Flail Arm (FAS) and Flail Leg (FLS) syndromes are summarized in Table 1 [5]. To differentiate these conditions from early limb onset ALS or PMA, it specified that functional involvement must be confined to the flail limb for at least 12 months after onset of symptoms [5].

ALS-FA form accounts for 2% to 11.4% of the overall ALS patients, with a mean onset similar to ALS, i.e. at 53.3–57.3 years, being males

more frequently affected (male/female ratio of 1.5-5 to 1) [14]. ALS-FA diagnosis requires a proper clinical history, and diagnostic neurophysiological and neuroradiological testing, with the exclusion of other central nervous system diseases mimicking ALS-FA [15]. As in the classic spinal ALS, there are no sensory symptoms and signs, with normal spinal cord MRI; unlike the classic spinal ALS which affects lower limbs starting with a distal weakness, the ALS-FA variant presents with proximal weakness and reduced/absent deep tendon reflexes and a better prognosis with a 5-10 years of increased survival. Symptoms are usually confined to one spinal region for at least 12–18 months [16]. Electromyography shows denervation in the cervical region [1].

Table 1 : Operational definitions for the flail arm and flail leg syndromes [5]

Table 1 Operational definitions for the flail arm and flail leg syndromes [5]		
Inclusion Criteria	Flail arm syndrome	Flail leg syndrome
	LMN disorder of upper limbs	LMN disorder of lower limbs
	Characterized by progressive, predominantly proximal weakness and wasting	Characterized by progressive distal onset weakness and wasting
	Also included in this category were patients who had typical pattern of wasting for flail arm, but also had pathologic DTRs or other pathologic reflexes in the upper limbs at some point during the disease (without hypertonia or clonus)	Also included in this category were patients who had typical pattern of wasting for flail leg but also had pathologic DTRs or other pathologic reflexes† in the lower limbs at some point during the disease (without hypertonia or clonus)
Exclusion criteria	Functionally significant weakness or wasting in lower limbs and bulbar musculature within 12 months of onset of upper limb symptoms	Functionally significant weakness or wasting in upper limbs, bulbar and respiratory musculature within 12 months after onset of lower limb symptoms
	Hypertonia in upper limbs	Hypertonia or clonus in lower limbs
	Distal upper limb weakness or wasting without proximal involvement at presentation	Wasting or weakness beginning proximally in legs without distal involvement at presentation.

Unlike ALS patients, it is well known that respiratory muscle weakness and bulbar weakness are relatively less frequent in FAS as in the case of this patient. And considering that OSA is relatively prevalent among 50-70-year-old men, it could not be regarded as the same as ALS. For these reasons, it is unclear whether OSA was concurrent and unrelated to FAS or an early symptom of FAS as in ALS [17].

CONCLUSION –

- It is important to distinguish the two diseases because FAS patients have significantly better survival rates compared with other typical ALS variants
- Patients with FAS present with predominantly proximal, progressive and symmetric wasting and paresis of the upper limb (UL) muscles, while lower limbs (LL) and bulbar muscles are spared.
- Detailed clinical history with neurological examination aid in the diagnosis.

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