Original Article

Monomelic amyotrophy with clinico-radiological and electrophysiological evaluation: A study from Eastern India

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Abstract

Background: Monomelic amyotrophy (MMA) is a benign, rare, sporadic disorder of adolescent and young adults with male predominance, where neurogenic amyotrophy is restricted to an upper or lower limb. It is a variant of lower motor neuron disorder with insidious onset and slow progression for 2-4 years. Paucity of cohort studies as well as relative unawareness among physicians in eastern India stimulated us to do this work. **Material and Methods:** Prospective observational study involving 140 cases of MMA from 2012 to 2016 ,conducted at S.C.B.Medical College, cuttack, Odisha to evaluate clinical profile, electrophysiology and radiological features. All the data were analysed & subjected to statistical analysis through SPSS software version 24. **Results:** Mean age at onset and presentation were 19.6yrs and 21.7yrs respectively and the average duration 3.2yrs. Upper limb involvement was more common (91.4%) with distal affection (83%) more than proximal (7%). Isolated Leg amyotrophy found in 12 cases (~9%) and 10 cases were having thigh weakness & atrophy. B/L Upper Limb distal involvement was present in 18.5% cases asymmetrically. Family history found in~2.8%. Autonomic symptoms were present in affected and bilateral homologous Limb in 21%, 5.8%(~6%) patients . Changes in electromyography (EMG) were present in affected limb (100%) and clinically unaffected limb (15%). **Conclusion:** MMA is a benign disease of young males with weakness and atrophy confined to unilateral limb or asymmetrical homologous limb and areflexia without sensory loss. It progresses variably for 2-3 years followed by stabilization without progression to Motor neuron disease.

Keywords: Electromyography, Monomelic amyotrophy, Motor neuron disease

Introduction

Hirayama *et al.*,[1] from Japan, first reported entity of "Juvenile muscular atrophy of unilateral upper extremity" in (1959). Gourie-Devi M. Suresh TG *et al.* reported (1984) MonomelicAmyotrophy (MMA) from south India.[2] Prabhakar *et al.*[3] (1981), from India, reported atrophy of one lower Limb as Wasted Leg Syndrome.[3] Several large studies on MMA are enlisted in [Table 1].[2-7] The characteristic features of this disease are young age at onset, sporadic occurrence, male preponderance, wasting & weakness confined to a single limb without the involvement of cranial nerves, pyramidal, sensory, cerebellar, and extrapyramidal systems & cortical function.[8] Less common features are coldness of hands, hyper-hydrosis, Cold Paresis.[1,2]

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Materials and Methods

After obtaining permission from Institutional Ethical Committee (IEC), a prospective observational study was designed in the Department of Neurology, Sriram Chandra Bhanja Medical College & Hospital, Odisha, a large tertiary care centre of eastern India from Aug 2017 to July 2020.

Patient selection

All cases of MMA attending OPD of Dept. of Neurology, S.C.B.Medical College & Hospital, Odisha included the study.

Inclusion criteria

- Adolescents or adults presenting to neurology OPD with a history of slowly progressive atrophy involving unilateral or asymmetrical upper limb or lower limb for at least 1-year duration were included in the study.

Exclusion criteria

- Patients with a history of poliomyelitis, significant trauma to the spine or extremities, exposure to toxins, vaccination in the past 6 months, signs of pyramidal, extrapyramidal or sensory involvement, abnormal motor or sensory nerve conduction studies other than reduced amplitude or absent compound muscle action potential (CMAP) and an abnormal cervical or lumbosacral spine MRI (except mild cord atrophy).

A detailed history was noted. Detailed general, clinical and neurological examinations have been carried out in all selected patients. Every patient was subjected to routine investigations. Motor (median nerve, ulnar nerve, tibial & peroneal) and sensory conduction studies (Upper limb-median & ulnar nerve, Lower limb-sural nerve) of the affected limb and unaffected limb nerves were performed. Electromyography (EMG) of distal and proximal muscles in affected limbs & unaffected limbs and paraspinal muscles were performed in all cases. For the paraspinal thoracic muscles EMG, the patient is asked to lie prone, with a soft cushion under the abdomen and to relax the head, shoulders and arms towards the floor. Denervation was defined as the occurrence of spontaneous muscle fibre activity like fibrillations, positive sharp waves or complex repetitive discharges in at least one insertion site.[4] Reinnervation was defined as the occurrence of large amplitude and long duration, polyphasic motor unit potentials.[4] Every patient had undergone an MRI of the spine (by 1.5-tesla intensity) in both Neutral & Hyperflexion positions (plain and gadolinium-enhanced). A predesigned Performa was filled with epidemiological (age of onset, age of presentation, sex preponderance, occupation, family h/o), clinical (Limb involvement, progression, Deep tendon reflex, fasciculation, tremor, Autonomic symptoms) and diagnostic details.

Statistical analysis

Data were analysed by using both qualitative and quantitative methods using SPSS Software version 24. The descriptive statistics of the study population were reported as counts and percentages for categorical variables and mean ± standard deviation for continuous with normal distribution.

Results

[Table 2]: A total of 140 cases were taken into the account depending upon the clinical features of the disease. As all these patients presented to our neurology OPD, the incidence of MMA was calculated to be 1 in 1000 among all the neurology outpatients. However, it was cumbersome to calculate the exact incidence in the general population. Out of 140 cases studied 138 were males, making the disease is a predominant condition of males. Mean age at onset and presentation were 19.6 years and 21.77 years, respectively. The maximum age of presentation was 39 years whereas the minimum was 14 years in our series. The average duration of illness was 3.2 years (0.7–5.3) with 24 (17%) patients were in the stationary phase. The mean duration of progression of disease was 2.4 years. The male to female ratio was 34:1. Three patients 4 (2.8%) had a positive family history (1 case-father & son, 3 cases- elder & younger brother). The majority of the patients were students. History of Fasciculation was present in 16 patients (11%) & mainly over the affected muscle (Deltoid, Bicep). Unilateral upper Limb involvement was seen in 102 (73%) patients whereas bilateral involvement was found in 26 patients (18.5%). Lower limb involvement was seen in 12 (8.5%) patients with right 8 (6%) more than left 4 (3%). Presences of autonomic symptoms

Table 1 (several previous studies)

Study	Numbers of cases	Salient features
Gouri devi *et al*[2,4]	44	mean age at onset 19.8 years with a range of 13-32 years Male : Female ratio of 10:1 Acute denervation 20 (45.5%) patients
Atchayaram Nalini *et al*[5]	279	Mean age of onset was 19.5±4.18 asymmetrical lower cervical cord atrophy in 44.6% in MRI male: female, 9:1
Freitas MR *et al*[6]	21	age of onset ranged from 4 to 41 13 males and 8 females Cervical cord MRI normal in all patients
Khandelwal D *et al*[7]	35	mean age 24.17 (+/-6.8) years All the patients, bilateral chronic reinnervative changes and 50% had chronic reinnervative changes in three limbs

like sweating & cold skin were found in 30 patients (21.35%) on the affected limb and 4 (2.84%) patients bilaterally. Nerve conduction study showed a decrease in CMAP (compound motor action potential) in affected Limb 140 (100%) without sensory conduction abnormality and EMG showed fasciculation, chronic neurogenic changes in the affected limb (100%) as well as clinically unaffected limb 24 (17%). MRI Spine was done in all patients (Neutral, Hyper Flexion Position- plain and gadolinium-enhanced) showed focal cord atrophy in 7 (5%) cases with widening & homogenous enhancement of posterior epidural space in 13 (9%) cases.

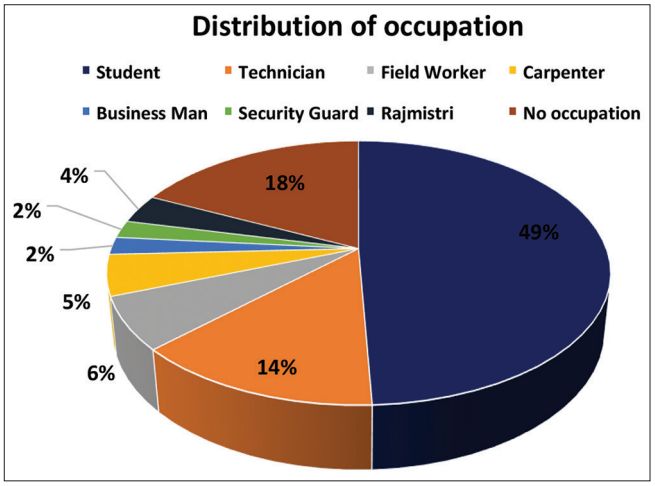
Discussion

The term "Monomelic Amyotrophy" was first coined in 1984 by Gourie-Devi *et al.*[2] who had observed either upper or lower limb atrophy, stressing the fact that the atrophy was always restricted to a single limb. However, such a term is blamed to be ambiguous by some authors due to reports of bilateral involvement.[9] The exact incidence of this disease is unknown owing to its rarity. In the series of Gourie Devi *et al.*,[2] MMA constituted 11% of the total MND cases. The mean age of onset was 19.6 years (12-31), Mean age of presentation was 21.77 years (14-39) in our study, which is similar to other studies within India as well as outside.[2,4,8,9] This little variation in the presentation can be explained by the paucity of health education in patients as well as relative unawareness among physicians of this region of the nation. Gender difference with males outnumbering females in 34:1 ratio makes our study wide different from previous reports where M: F ratio varying from 3:1 to 20:1.[4] But our study coincides with the fact that MMA is a predominant disease of males. We explain the gender discrepancy by the self-neglect as well as familial neglect and paucity of health education in Indian families. Apart from that the insidious onset and benign nature of the disease can be the cause. As the women and the caretakers don't realize it to be an emergency, they don't usually consult a neurologist. Two women in this study were from affluent society still they thought the disease to be quite physiological for 2 years. Reports of familial cases of MMA are extremely rare, though there is the possibility of an autosomal recessive or dominant trait.[4] Our study has shown a total of 4 familiar cases (1-father-son, 3-brothers) in the background of a total of 15 familiar cases reported worldwide.[4] On analysis of occupational history maximum affected are students [Graph 1] which did not show any relation between occupation and disease. MMA of the upper limb is most commonly reported in the literature,[2,4,9-12] which is concordant with our study. In our case series upper limb distal muscle involvement (82.8%), was common than proximal 10 (7%) and isolated Leg involvement in 12 (~9%) patients, which is comparable to other studies.[2,4,9-12] Bilateral Upper Limb distal involvement was a significant finding which was present in 26 (18.5%) cases asymmetrically and similar reports were described by J.Y. Kim *et al.* and Hassan Kaukab, SahniHirdesh *et al.*[9,10] In MMA of the upper limb, weakness and atrophy are known to affect the hand and forearm muscles to a greater extent, with sparing of the brachioradialis, thus giving the impression of an oblique amyotrophy.[2,4,9] Similar involvements were seen in the present study [Graph 2, Photos 1, 2]. The isolated involvement of the arm and shoulder muscles, especially the biceps and deltoid, is usually rare,[4] and our analysis also agrees to that hypothesis [Graph 2, Photo 3]. Lower limb quadriceps, calf muscles were commonly affected in the indexed cohort [Graph 3, Photo 4] which was similar to works done by Gourie Devi, Nalini A *et al.*[4,5] and J.Y. Kim *et al.*[10] Hand tremor was present in61% of cases in affected limb in comparison to 13.5% in both homogenous Upper limbs. This is less than described by Gourie-Devi, A. Nalini *et al.*[2,4] This might be due to the rampant use of beta-blockers in patients in peripheral hospitals as well as geospatial variation of presentation. Other features like Coldness

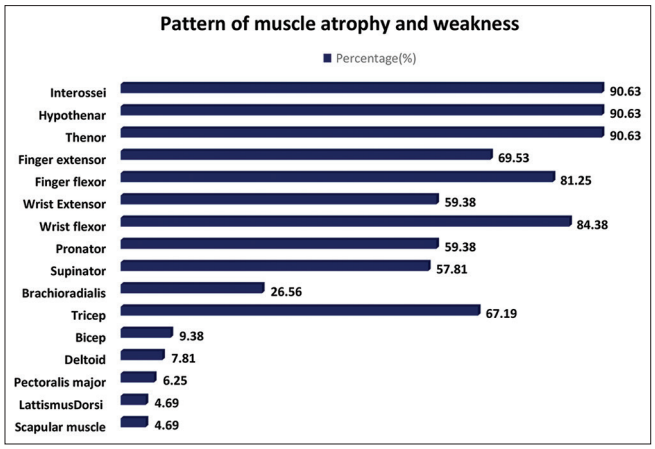
Table no: 2 (Epidemiological and clinical pictures of MMA in this study)

FEATURES OF MMA IN PRESENT STUDY			*n*=140 (%)
Mean age of presentation (years)			21.77 (14-39)
Mean age of onset (years)			19.6 (12-31)
M: F			34:1
Familial involvement			4 (2.8)
Mean duration of progression of disease (yrs)			2.4
Course of disease	Progressive	Progressive – stationary phase	100 (71.4)
		Late progressive (beyond 3 yr)	16 (11.4%)
	stationary		24 (17%)
Upper Limb (U/L involvement)			90 (62.2%)
Upper Limb (B/L involvement)			26 (18.5)
Lower Limb (U/L involvement)			12 (8.5)
Wasting Distal only (UL &LL)			118 (84.2)
Wasting Proximal only (UL &LL)			20 (14.2)
Wasting Global only (Whole Limb)			2 (1.4)
Bilateral Upper Limb distal wasting			26 (18.5)
Areflexia in affected limb			96 (69)
Areflexia in contralateral limb			21 (15)
Hyper-reflexia affected limb			8 (5.7)
Fasciculation of affected muscle			16 (11)
Tremor in only affected Limb			86 (61)
Tremor in both limb (affected & contralateral)			19 (13.5)
Autonomic features	Affected limb		30 (21.3)
	B/L Homologous limbs		4 (2.8)
Motor symptoms (On cold exposure) : Cold paresis			6 (4)

B/L : BILATERAL, U/L: UNILATERAL, UL: UPPER LIMB, LL: LOWER LIMB M: Male, F: Female



Graph 1: Showing distribution of occupation



Graph 2: Showing pattern of muscle atrophy and weakness of upper limb

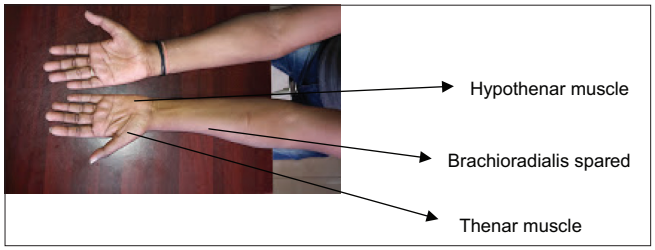


Photo 1: Showing wasting of muscles of left hand & left forearm with sparing brachioradialis

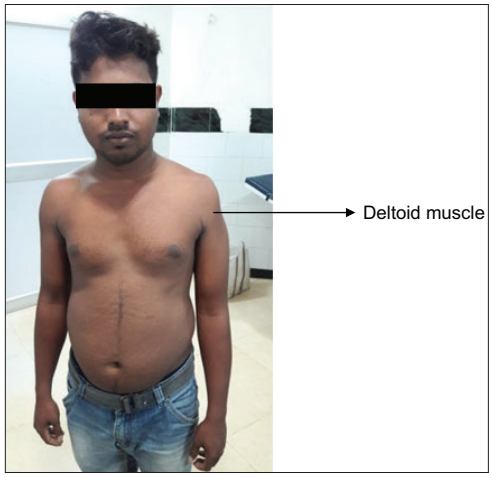
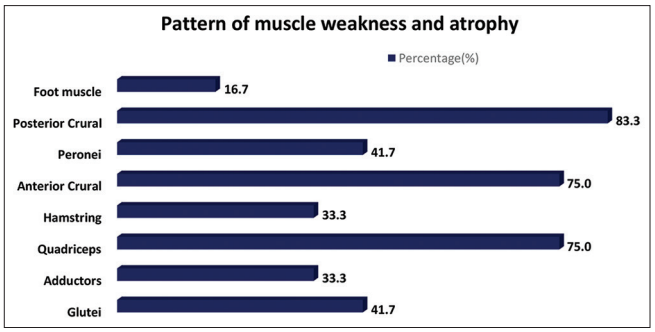


Photo 3: Showing wasting of left shoulder girdle muscles

of hands, fasciculation over deltoid and biceps, worsening of motor symptoms on exposure to cold were present in 21%, 11%, 4% cases in our series whereas it was slightly higher in previous reports.[8] This might be an incidental variation due to geographical differences in our study. Although most of our patients demonstrated hypoactive to normal stretch reflexes, a small number (5.7%) had hyperactive reflexes with distinctly absent Babinski as described by old studies.[8] EMG of all weak muscles showed varying degrees of fibrillation/fasciculation and neurogenic changes [Figure 1]. Neurogenic changes were present bilaterally in 17% cases (Upper Limb -22 cases, Lower Limb-2 case) out of 91 cases of unilateral upper limb involvement



Graph 3: Showing pattern of muscle atrophy and weakness of lower limb

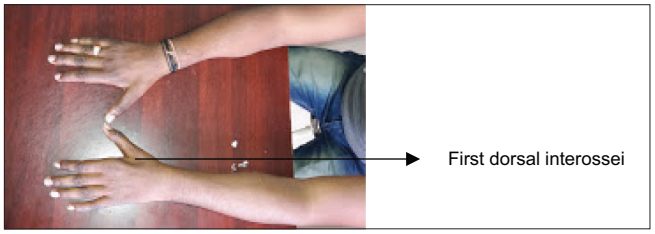


Photo 2: Showing wasting of small muscles of left hand

Photo 4: Showing atrophy of left thigh muscles

and 12 cases of unilateral lower limb involvement. MRI Changes of cervical cord showed focal cord atrophy in 7 (5%) cases with widening & homogenous enhancement of posterior epidural space in 13 (9%) cases [Figure 2] which is less than reported by Kausab Maqbool Hassanetal.[9] This may be due to less sample size. We divided the course of disease into two parts progressive and stationary phases. In our study, 17% of patients were static from the beginning of the study period is contrary to the rest 83% which showed progression followed by stabilization. The late presentation in the stationary phase in our area is due to delay in diagnosis and subjective unawareness of primary care physicians. The poor consciousness of patients about the disease can be blamed for the late presentation. No one in our study did evolve into ALS during the study period of 3 year even though 5.7% of cases had hyperactive reflexes. This depicts the relative inertness and benign course of the disease.

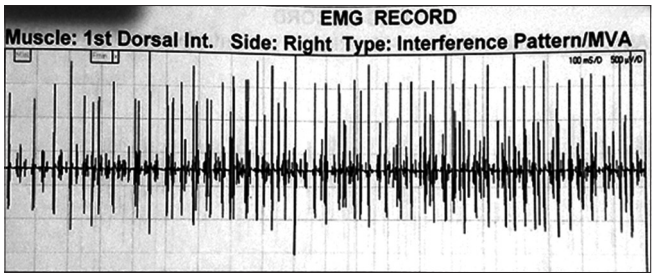


Figure 1: EMG Report showing incomplete Interference Pattern

Conclusion

The diagnosis of MMA should be considered in any case of unilateral or bilateral asymmetrical homologous limb weakness and atrophy in young adults with areflexia, without pyramidal signs and sensory loss even though it needs rapid evaluation for exclusion of structural lesion of cord. Diagnosis mainly depends on clinical presentation and electrophysiological study. Electrophysiological affection of homologous clinically unaffected limb is also found in some cases. The study did not show any correlation between occupation and disease. The condition is a benign variation of motor neuron disease with insidious onset, slow progression followed by stabilization and never evolves to Amyotrophic lateral sclerosis, even though hyper- reflexia is found in some cases. Most of the times the primary care physicians think it as a case of leprosy or amyotrophic lateral sclerosis. This causes unnecessary treatment and panic. The physicians and health workers must be aware of its benign nature, which can save many patients from huge mental agony of Motor neuron disease. The study is unique in eastern India because of paucity of literature about this despite its wide prevalence. Further studies must be undertaken to observe different variations of MMA in our area.

Summary

MMA is a benign variant of anterior horn cell disease.

The diagnosis of MMA should be considered in any case of unilateral or bilateral asymmetrical homologous limb weakness with atrophy and areflexia.

It's a disease of young people. Its progression is mostly limited to same segment.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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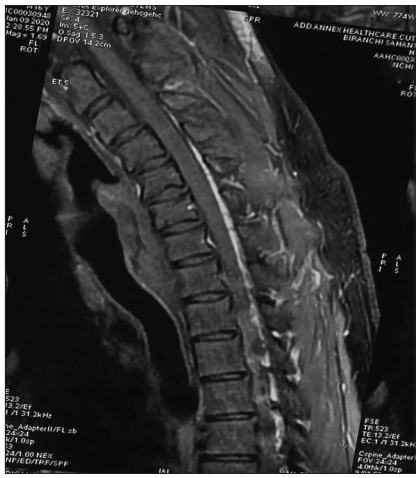

Figure 2: MRI Cervical spine showing contrast enhancement of post. epidural space