CLINICAL PROFILES, MANAGEMENT AND OUTCOME OF MYASTHENIC CRISIS IN A TERTIARY CARE CENTER IN KARACHI, PAKISTAN

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ABSTRACT

To determine the clinical profiles, management and outcome of myasthenic crisis (MC) in patients presenting to a tertiary care hospital in Karachi, Pakistan. This was a retrospective study of forty patients with Myasthenic crisis(MC) admitted at the Aga Khan University Hospital, Karachi between 1999 and 2014.Demographics, clinical presentation, hospital course, management and outcomes were reviewed. Ventilatory support for respiratory muscle or bulbar weakness was taken as crisis identification at arrival. Out of the total 40 patients with MC; generalized onset was seen in 28 (70%) and isolated bulbar symptoms in 12 (30%) patients. Fifteen patients (37.5%) had MC as a first presentation. In a third world country with insufficient resources and limited access to specialist care, early recognition of MC by general practitioners is important. Patient education about avoidance of possible precipitating factors and recognition of early symptoms of MC is essential.

Keywords
Myasthenic Crisis (MC), Myasthenia Gravis (MG)

INTRODUCTION

Myasthenic crisis (MC) is defined by the presence of respiratory failure and the need for invasive or noninvasive mechanical ventilation.[1] The most severe level of weakness and high mortality occurs during the first 1 to 2 years of disease onset, after which many patients experience improvement.[2] Administration of non-invasive positive pressure ventilation (NIPPV) has enabled us to treat some MC patients in the general ward without intubation[6] however, other serious MCs still require intensive care with intubation.[7] Plasma exchange (PE) and intravenous immunoglobulin (IVIG) are used to treat myasthenia gravis (MG) exacerbations and crises.[10] In-hospital mortality of MG is low. Hospital utilization of IVIG has significantly increased compared to PE and thymectomy.[11]

METHOD

Sixty one adult patients with MC or suspected MC presenting to the Aga Khan University Hospital, Karachi, Pakistan between 1999 and 2014 were studied retrospectively. The age range was between 18 to 80 years. Need for ventilatory support due to respiratory muscle or bulbar weakness was taken as crisis identification. Twenty one patients were excluded from this study due to various reasons including misdiagnosis of crisis, diagnosis of some other neuromuscular (NM) disorders or inadequate data. Ultimately data pertaining to demographics, clinical presentation, hospital course, management and outcomes of 40 cases with MC were reviewed. The Statistical Package for Social Sciences (SPSS V.19) was used for statistical analysis. Results are presented as frequency and percentages for qualitative variables and mean, and SD for quantitative variables. Analysis of variance was used to assess differences between sexes and age groups. This study was approved by the ethics review committee of the Aga Khan University Hospital.

RESULTS

Median age at presentation of MC was 50 years with 24 (60%) males and 16(40%) females .Ten patients (25%) were admitted through outpatient clinics and 30(75%) were admitted through the emergency department. Out of a total of 40 patients with MC: 28(70%) had a generalized onset and 12 (30%) had

isolated bulbar symptoms. Details of basic investigations done for the diagnosis and work-up of myasthenia gravis are listed in Table 1.

The most common triggering factor seen was infection in 19 (47.5%) including respiratory infections and gastroenterits ,while non-compliance to medications by known myasthenic patients was noted in 6 (15%). 3(7.5%) had a recent surgery as an inciting factor and 4(10%) patients either were on inadequate dosing or had poor response to medications. The mean duration of diagnosis of MG prior to presenting with crisis was 33.9 days. It was the first presentation of MG in 15 (37.5%) patients.

Thymectomy had been done prior to presentation in 9 (22.5%) with MC.

16 (40%) were admitted to the ICU requiring ventilator support, 15 (37.5%) were treated with non-invasive ventilation in the special care units and 9 (22.5%) were managed on the general neurology floor.21 (53.8%) patients had a delay in start of treatment either due to delay in recognition that the patient was in crisis, due to patient reluctance for treatment of MG or management at non specialist hospitals.

Treatment options of plasmapheresis and IVIG were offered to all patients. However choice by the patient/ family was made according to financial constraints or personal preference. Plasmapharesis was done in 18 (45%), IVIG was given to 11/40 (27.5%) and pulse steroids to 8 (20%) patients for MC. One elderly patient refused treatment and 2 patients were transferred to other facilities due to unavailability of an ICU bed. 13 (32%) patients were on immunosuppressants at presentation. The mean duration of hospitalization was 12.7 days. Some patients had other comorbidities like diabetes in 11 (27.5%) and hypertension in 7(17.5%) which may have increased complications and prolonged hospital stay, however a causal relationship could not be established.

All 38 treated (95%) patients were discharged home. At 3 months follow up post discharge 29 (72.5%) were stable on medications while 11 (27.5%) were lost to follow up specially those who had come in from distant areas of Pakistan or from Afghanistan.

DISCUSSION

All our patients were offered and treated with standard available therapy including PE, IVIG and intravenous pulse steroid therapy.

A retrospective review of hospital records of 53 patients admitted for 73 episodes of MC at the Columbia-Presbyterian Medical Center over a period of 12 years, from 1983 to 1994 showed a median age at onset of first MC to be 55 years (range: 20 to 82), with the ratio of women to men of 2:1.[4] In our study, the median age of presentation with MC was similar at 50 years, however there was a male pre-dominance with sixty percent male patients. The reason for this is unclear, since, similar to other populations; the prevalence of MG is higher in women in Pakistan.[12] Perhaps access to tertiary health care for women in critical condition is an issue.

In a large retrospective analysis from a NM diseases registry in Spain that included 648 patients with MG, out of 62 patients who presented with a life threatening event like dysphagia or respiratory weakness, it was the first manifestation of MG for 50%. [7] In comparison, in our very small sample, MC was the first presentation of MG for 15/40 (37.5%) patients. More than 50% of the patients had aggravated symptoms of MC due to late diagnosis. These are substantially high numbers and underline the importance of creating awareness amongst the general neurologists in the community of identifying MC in the absence of a previous diagnosis of MG, to ensure early access and referral to appropriate level of health care.

The most common known precipitant is infection in approximately 38% of MC patients[4] and this was similar in our study showing infection as the leading cause in 47.5% patients while 6/40 (15%) were non-compliant to medications. This highlights the importance of extensive counseling for all myasthenic patients at initial diagnosis, about the nature of disease, need for prolonged treatment, precipitating factors and identifying early signs of crisis. These simple measures can prevent a crisis in the first place and/or prevent morbidity, mortality and the cost that goes with its management. In a large study done in Iran over 17 years it was found that 18.2% of thymectomized patients (20 of 110) and 38.5% of non-thymectomized patients (42 of 109) had MC. This was significant (P = 0.001; odds ratio = 2.8 with 95% CI of 1.5 to 5.2).Likewise most of our patients with MC 31(77.5 %) had not undergone a thymectomy. Ocular myasthenia has less clinical worsening episodes and a higher chance of complete stable remission. Generalized disease has less chance of a drug free remission. The risks of episodes of worsening persist at a steady rate over a period of time, being maximum in

the first year. Risk of exacerbations is unpredictable and can occur after prolonged clinical quiescence, often related to reduction of immunosuppression[8] and 13 (32.5%) of our patients were already on some immunosuppressant when presented with MC.

Due to the retrospective nature of our study, we were unable to establish clinically relevant associations especially between MC and response to different treatment modalities. Treatment between PE and IVIG was based on affordability of the patients rather than being truly randomized. Clinical data was deficient which resulted in excluding otherwise eligible patients.

CONCLUSION

Basic education regarding MC to general practitioners in Pakistan is of profound importance as they are the ones who treat majority of such patients and precautions to diagnosed patients with MG regarding avoidance of possible precipitants may lead to early diagnosis and more efficient clinical care.

MC in this advanced era of medicine is still a significant cause of prolonged hospitalization and increased mortality and morbidity especially with limited resources in a third world country like Pakistan. Respiratory support with IVIG, plasmapheresis or intravenous pulse steroids remain the mainstays of treatments without any significant difference in outcome with either use. Patient education about avoidance of possible precipitating factors and recognizing early symptoms of MC should be part of standard care. The data available on myasthenic crisis in our region of Southeast Asia is scarce and this needs to be looked into to improve the living standards of known MG patients and those who develop MC.

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ABBREVIATIONS

MC: Myasthenic Crisis
MG: Myasthenia Gravis
RNS: Repetitive Nerve Stimulation
AChRAb: Acetyl Choline Receptor Antibody
PE: Plasma Exchange
IVIG: Intravenous Immunoglobulin
BiPAP: Bilevel positive airway pressure
NM:Neuromuscular

Table 1: Results for investigations done for the evaluation of Myasthenia Gravis (N=40)

	Positive	Negative	Not checked
1.RNS	25(62.5%)	5(12.5%)	10(25%)
2.AChRAb	22(55%)	1(2.5%)	17(42.5%)
3.Elevated CK	2(5%)	10(25%)	28(70%)
4.Thymoma on CT Chest	11(27.5%)	23(57.5%)	6(15%)

RNS: Repetitive nerve stimulation; AChRAb: Acetyl Choline Receptor Antibody
CK: Creatinine phosphokinase

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Sara Khan; Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dureshahwar Kanwar; Study concept and design, data collection, data analysis, manuscript writing, manuscript review
Sadia Nishat; Study concept and design, data collection, data analysis, manuscript writing, manuscript review