

Penicillamine—Associated Myasthenia Presenting as Respiratory Failure

M. Hafizullah,*

M.B., B.S., M.R.C.P.,

Postgraduate Medical Institute
Lady Reading Hospital,
Peshawar, Pakistan

J.P. Delamme,** M.B., Ch.B.,
M.D., M.R.C.P.,

G.E. Packe,*** M.B., Ch.B.,
M.R.C.P.

and

C.W.F. Clarke,**** M.B., Ch.B.,
F.R.C.P.,

Burton Road Hospital, Dudley,
West Midlands, U.K.

Summary

A classical Rheumatoid arthritis patient having Penicillamine developed severe breathlessness and generalized muscle weakness. A Ch R antibodies supported the diagnosis of Penicillamine-associated Myasthenia. The patient is reported as he had some atypical features:— (1) respiratory failure as a presenting feature is rare, (2) major clinical feature of ocular symptoms were absent, (3) no definite response to anticholinesterase agents and (4) plasma exchange resulted in a decrease in A Ch R antibodies but there was no associated clinical response.

Introduction

The development of anti-acetylcholine receptor (A Ch R) antibodies is a recognized albeit uncommon complication of Penicillamine therapy in Rheumatoid arthritis. A myasthenic syndrome, closely resembling Idiopathic Myasthenia gravis in its clinical, humoral and electrophysiological features, is an associated accompaniment of such circulating antibodies.¹ We report a case patient with Rheumatoid arthritis who developed progressive muscular weakness leading to respiratory failure.

* Senior Registrar, Department of Cardiology, Lady Reading Hospital.

** Consultant Rheumatologist.

*** Registrar, Gen. Medicine.

**** Consultant Physician and Endocrinologist,

Burton Road Hospital, Dudley, West Midlands.

Case Report

A 52-year-old Caucasian female with a five year history of classical Rheumatoid arthritis was started on Penicillamine in November 1981. Eight months later she was admitted to hospital as an emergency due to severe breathlessness which had gradually developed over the previous eight weeks. At that time she was receiving Penicillamine 750 mg./day; Prednisolone 14 mg./day and Chloroquin 250 mg./day for five days a week. She was tachypnoeic (respiratory rate 32/min.) and demonstrated generalized muscle weakness: extensors of the neck being worst affected. She had no signs of active synovitis. Examination of respiratory, cardiovascular and neurological systems was unrewarding.

Preliminary investigations including x-ray chest, E.C.G. haemogram and blood biochemistry were normal. Over the next four days, her respiratory effort deteriorated. At this time the blood gases, which were initially normal, confirmed respiratory failure (PO_2 6.76 kPa, PCO_2 10.48 kPa) and mechanical ventilation was commenced.

Edrophonium and Neostigmine tests were negative on six separate occasions. Electromyographic studies revealed non-specific low amplitude responses in the quadriceps which were unaffected by Edrophonium. A biopsy of deltoid muscle showed no evidence of myopathy. A Ch R antibodies were supporting the diagnosis of Penicillamine-associated Myasthenia. Striated muscle antibody was positive. H.L.A. typing was A 1,2 B8 - 12 DR 4.

Mechanical ventilation was stopped after nineteen days, while she was taking Pyridostigmine 300 mg./day and Prednisolone 40 mg./day. Due to persistent weakness and tachypnoea, plasma exchange was undertaken daily for five days, replacing two litres of plasma by human plasma protein fraction. Following plasma exchange, A Ch R antibodies were undetectable; however no immediate clinical response was observed. A Ch R antibodies re-appeared a month later but during the following eight months, there was a gradual fall in titre (Fig. 1.) with a return of muscle strength comparable to that prior to the myasthenic illness.

Discussion

The detection of A Ch R antibodies in a patient suffering with profound muscle weakness, which developed during Penicillamine therapy, would strongly suggest drug-induced Myasthenia. Several atypical features distinguish this patient from those previously reported. Firstly, respiratory failure as a main presenting feature is rare in idiopathic Myasthenia gravis² but previously unreported in Penicillamine-associated Myasthenia. Secondly, ocular symptoms, which were absent

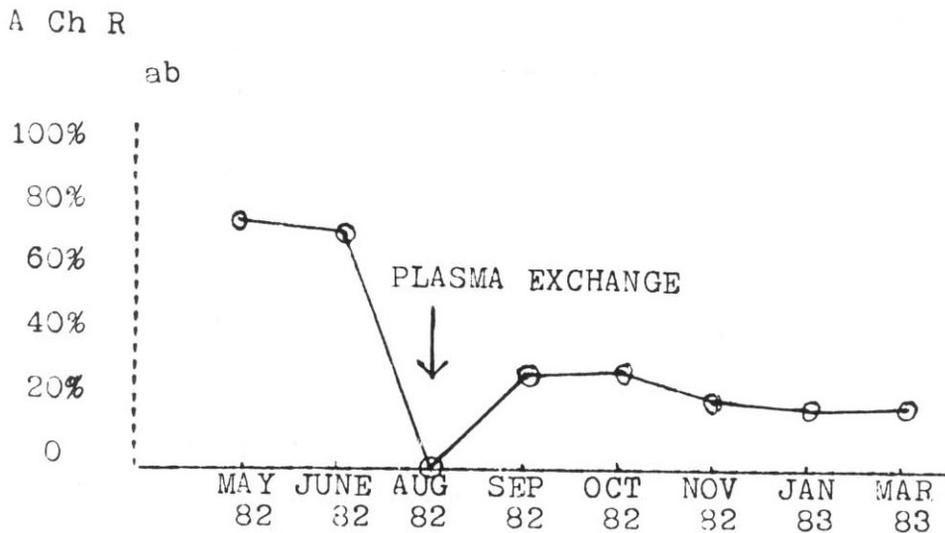


Fig. 1. Acetylcholine receptor antibodies titre.

in our patient, have previously been regarded as a major clinical feature of both Penicillamine-associated⁴ and Idiopathic Myasthenia. Thirdly, we were unable to demonstrate any clinical or electromyographic response to the use of anticholinesterase agents. Finally plasma exchange in both Idiopathic and Penicillamine-associated Myasthenia results in a decrease in A Ch R antibodies and an accompanying clinical improvement.³ In our patient although a fall in antibody levels occurred, there was no associated clinical response. These features would suggest that Myasthenia was not the sole pathological process giving rise to the patient's symptoms. It would also imply that the presence of A Ch R antibodies, even when associated with muscular weakness and Penicillamine therapy, cannot be taken as diagnostic of Penicillamine-induced Myasthenia.

References

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