Annals of Health Research
Volume 3, Issue No. 1
Jan - June 2017

CASE REPORT

Miller-Fisher syndrome in a Nigerian child: A Case Report

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Summary

Miller-Fisher syndrome is a syndrome of ataxia, areflexia and ophthalmoplegia which was first described by Miller Fisher in 1956. The disorder has an immunological basis and has been regarded as a descending form of Guillain – Barré syndrome (GBS). It is a rare clinical condition which may be confused with other common illnesses.

This report describes a nine-year-old boy who presented with a five-day history of diplopia and difficulty in walking following an upper respiratory tract infection. On examination, he had ataxia, ophthalmoplegia and areflexia with cerebrospinal fluid cytoalbuminological dissociation. This case report emphasises the need to have a high index of clinical suspicion in patients with features of cranial mononeuropathy multiplex and hyporeflexia.

Keywords: Ataxia; Cytoalbuminological dissociation; Miller-Fisher Syndrome; Mononeuropathy multiplex; Ophthalmoplegia.

Introduction

The syndrome comprising ataxia, areflexia and ophthalmoplegia was first described by Miller Fisher in 1956. [1] It has an immunological basis and has been regarded as a descending form of Guillain – Barré syndrome (GBS). [2] The clinical features include a triad of ataxia, areflexia and ophthalmoplegia. There may be descending muscular weakness, with respiratory depression. It is a rare clinical condition that can be confused with other common illnesses. This case report emphasises the need to have a high index of clinical suspicion in patients with features of cranial mononeuropathy multiplex, hyporeflexia and cerebrospinal fluid (CSF) cytoalbuminological dissociation.

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Case Description

A nine-year-old boy presented to the emergency paediatric unit with a five-day history of diplopia and difficulty in walking. He had an upper respiratory tract infection two weeks previously which was treated with Ampiclox®. The symptoms of respiratory infection had subsided within five days. He subsequently developed diplopia, dysphonia, dysphagia, generalised weakness with difficulty in walking without support. He aspirated oral contents and developed repeated unproductive cough. There was no history of rash, headache, head injury or ingestion of canned food. The history of snake bite or

exposure to toxic substances was denied. He was fully immunised according to the national recommendations and had been a healthy child.

On examination, he was afebrile, had no rash but was too weak to complete a sentence. The vital signs on admission included a body temperature of 36.8°C, pulse rate of 120/minute, blood pressure of 110/70mmHg and respiratory rate of 32cycles/minute. He was dyspnoeic with crepitations in the left lower zone of the lungs. He was fully conscious but had ptosis of the left eye, and the extraocular eye movements were limited in all directions. The pupillary size, visual acuity and fundoscopy were normal. There were dysphonia, dysarthria and lower motor neurone seventh cranial nerve palsy on the right. The gag reflex was absent suggesting cranial nerves IX and X palsy. Also, there was remarkable ataxic gait with normal muscle bulk, but the muscle power in both upper and lower limbs was Graded IV, and deep tendon reflexes were globally reduced. The plantar reflexes were flexor in type bilaterally, and the peripheral sensations were normal. The gastrointestinal tract and the ear, nose and throat examinations were normal. There were no ticks found on the skin and scalp.

Laboratory investigations showed total white cells count of 16.6×10^9/L (normal range 3-11 × 10^9/L) with an elevated erythrocyte sedimentation rate of 80mm/hour (normal range 0- 20mm/hour). The lumbar puncture showed normal opening pressure with CSF glucose of 67mg/dL (random blood glucose 88mg/dL), protein of 81mg/dL (normal range 15-40mg/dL) and chloride of 100mEq/L. There were no cells in the CSF, the CSF culture yielded no growth and was Acid-Fast-Bacilli (AFB) negative.

Bacteriological culture of blood and urine yielded no growth, but nasopharyngeal swab culture yielded *Klebsiella* species which was sensitive to ofloxacin, gentamycin and ceftazidime. Other ancillary tests such as retrovirus screening, serum electrolytes, urea and creatinine, chest radiography and electrocardiography were normal. There wereas no facilities for viral cultures or toxicological screening. The identification of *Campylobacter* species, Clostridium botulism toxin from the stool, as well as GQIB antibody assay and nerve conduction studies, were not done due to lack of appropriate facilities. Brain CT scan was not done for reasons of financial constraint.

The progression of the underlying condition was closely monitored clinically. The boy received intravenous fluids for five days, antimalarial drugs and antibiotics while efforts were made to procure intravenous immunoglobulin, which was not readily available in our centre. Nevertheless, gradual clinical recovery was noticed and the neurological deficit resolved over the next eight days, and the child was discharged home on the ninth day of hospitalisation. The ataxia gradually improved while the ophthalmoplegia completely resolved within two weeks. Based on the triad of ophthalmoplegia, areflexia, and ataxia with laboratory evidence of CSF cytoalbuminological dissociation, the diagnosis of Miller-Fisher syndrome was clinically made.

Discussion

Miller-Fisher syndrome is an uncommon variant of Guillain- Barré syndrome (GBS), and it is reportedly rare among children. [3, 4] The classical triad of symptoms in this syndrome consists of ataxia, areflexia and ophthalmoplegia while other cranial nerves can be involved as observed in the index child. [4] Close to 223 cases were reported in the published literature between 1956 and 1992, of which 32 cases were children. [1, 2]

The incidence of Guillain - Barré syndrome is 0.8/100,000, and approximately 6% of these are of the Miller-Fisher variant (MFS). [3, 5, 6] The diagnosis of MFS is usually made on clinical grounds but with laboratory supports in the form of elevated CSF protein without pleocytosis (also known as cytoalbuminolgical dissociation). This typical CSF picture is found in 65% of cases with or without Ganglioside Q 1b subtype of ganglioside autoantigen isoform (GQIb-ganglioside) antibodies which are present in about 95% of cases of MFS. [2, 7]

MFS is considered a post-infectious autoimmune

disease. In about two-thirds of cases, the immune neuropathy is provoked by an acute infectious illness. [8] As is the case in GBS, a wide range of pathogens including *Campylobacter jejuni*, *Haemophilus influenzae*, *Streptococcus aureus*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *Coxiella burnetti*, cytomegalovirus, Epstein-Barr virus, varicella –zooster and mumps virus have been reported as antecedent infections in MFS. [3] A study of antecedent infectious agents in MFS showed that 18% of patients with MFS were seropositive for *Campylobacter jejuni*, lower than 31% for GBS. [9,10]

Klebsiella species was cultured in the nasopharyngeal swab of the index patient. The diagnosis of MFS is arrived at with high index of suspicion and after excluding some common conditions. The differential diagnosis in the index child included brainstem encephalitis, tuberculous meningitis, poliomyelitis, diphtheria, botulism, envenomation, trauma, brainstem neoplasm, vascular disease, HIV and tick paralysis, although the latter is not common in our environment.

The diagnosis of MFS in the index child was based on the presence of the clinical triad of areflexia, ophthalmoplegia and ataxia and the descending weakness. This child also had the involvement of cranial nerves VII, IX and X which are observed in the oro-pharyngeal variant of the disease. This diagnosis was further supported by laboratory evidence of elevated protein in the absence of CSF pleocytosis. Though, the detection of GQIb-ganglioside antibody is more accurate (> 90%) for MFS, [3, 4] facilities for the investigation were not available for this child. In GBS, the antibodies are directed at the peripheral nerves in a distribution in keeping with the diagnosis. There is molecular mimicry between the myelin of the cranial nerves III, IV and VI and the lipo-oligopolysaccharide components of Campylobacter, which is a common cause of antecedent illness in MFS. Immuno-histochemical studies have revealed the presence of GQIb epitope staining in the paranodal regions of the extra-medullary portions of the third, fourth and sixth cranial nerves in patients with MFS. It has also been shown that ganglioside composition showed a higher percentage of GQIb in the optic nerve and all the three ocular nerves. [4] The correlation between the anti-GQIb antibody and acute ophthalmoplegia has been shown in typical cases of MFS, atypical MFS (without ataxia), in GBS with ophthalmoplegia and Bickerstaff brainstem encephalitis. [10] Therefore, the anti-GQIb antibody has been implicated in the pathogenesis of the external ophthalmoplegia. [11] Other antibodies to GTIa, GDIb, GD3 ganglioside epitopes are present to a lesser degree. [11, 12]

Dysphagia and dysarthria were very prominent in the index child with the attendant aspiration of oral contents which has a potential to worsen, further, the respiratory compromise that is consequent upon the descending muscle weakness. However, the aspiration pneumonitis was treated with the immediate use of antibiotics in the index case. Though the mainstay of treatment of different variants of GBS is immunomodulation with either immunoglobulin therapy or plasmapheresis, we wish to report that our patient made a spontaneous and good recovery without either therapy and without residual morbidities in agreement with the known self-limiting course of the disease. [3, 4]

Conclusion

Miller Fisher syndrome is an uncommon presentation with mimics that should be excluded in patients with cranial mononeuropathy multiplex especially in a resource-limited setting. The diagnosis is easily missed because of the non-specific nature of the disorder. Therefore, an exhaustive review of the patient's history, physical examination, radiological and cerebrospinal fluid findings are critical in the diagnosis of Miller-Fisher syndrome.

Consent

Written informed consent was obtained from the child's parent for the use of his biodata and clinical history in this case report.

Acknowledgement
We would like to acknowledge the supports of Dr S.A. Sotimehin, a Consultant Paediatrician at the Olabisi Onabanjo University Teaching Hospital, Sagamu in the co-management of the child.
Publication History: Submitted 20 - May 2016; Accepted 06 - November, 2016

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