INTRODUCTION

Guillain Barre syndrome (GBS) is the commonest acute predominantly motor neuropathy. It comprises of heterogeneous group of disorders of presumed autoimmune etiology. The overall incidence of Guillain Barre syndrome (GBS) is found to be 1.1/100,000/year to 1.8/100,000/year. The incidence of GBS increases with age after 50 years from 1.7/100,000/year to 3.3/100,000/year. Up to 70% cases of GBS are caused by antecedent infection. There is limited data regarding incidence of GBS in Pakistan. One series of 34 patients with GBS, described age range between 3-70 years. Up to 45% cases were caused by antecedent infection. The vast majority of cases are sporadic but occasionally clusters have been described in families.

We describe two cases of definite Guillain Barre syndrome and two probable cases occurring in a single generation of a family. To the best of our knowledge this is the first case report of Guillain Barre syndrome occurring in four siblings from Pakistan.

CASE REPORT

Case 1 (Index case): A 22 years old female student developed high grade fever with rigors and chills documented up to 106°F associated with dry cough and rhinorhoea. Three days later she gradually developed weakness of both lower limbs progressing over a period of 24-48 hours. She was unable to walk without support and had marked difficulty in getting up from sitting position. There was numbness and tingling sensations in both lower limbs but there was no difficulty in swallowing or breathing. Patient was admitted in our hospital for further evaluation. She was hemodynamically stable with pulse rate of 100/minute, blood pressure of 110/70 mm of Hg, and core tempreature of 98.6°F. Neurological abnormalities included reduced power (both lower limbs 2/5, 4/5 in both upper limbs) while the deep tendon reflexes (DTRS) were absent in lower limbs and 1+ in both upper limbs. Nerve conduction velocities were decreased in median, ulnar and lateral popliteal nerves. F-wave latencies were prolonged in all extremities. Sensory potentials were reduced or could not be elicited. Sensory conduction velocities were slowed. CBC showed Hb 12 g/dl, WBC count 5000/mm3 and platelet count 353000/mm3. Serum electrolytes, liver and kidney function were normal. ESR, HbsAg, anti-HCV antibodies, ANA and CPK were within normal. The diagnosis of GBS was made on the basis of clinical presentation further supported by nerve conduction studies. She received plasmapheresis everyday for 5 days. Her weakness gradually improved over one month. Six months later she was able to walk independently and returned back to college but still reported having occasional numbness and tingling in both lower limbs. Follow-up examination after 2 years revealed normal muscle power and 2+ DTRS. But still complains of occasional paraesthesias of lower limbs.

Case 2: Four years earlier the elder sister of index case who was 22 years of age at that time developed a short febrile illness with cold. One week later she developed difficulty in walking and tendency to fall down, associated with numbness and tingling in all four limbs. She was hospitalized in a tertiary care facility with these symptoms. On examination she was found to have pulse of 82/minute, BP of 120/80 mmHg and core temperature of 98.6°F. Neurological examination showed power of 1/5 in both lower limbs and 3/5 in both upper limbs. Deep tendon reflexes were absent in both lower limbs and 1+ in both upper limbs. Cranial nerves were intact. On the basis of clinical presentation GBS was suspected. Initial nerve conduction studies (NCS)
suggested borderline abnormal changes of early GBS. Subsequent NCS showed motor axonal neuropathy affecting lower limbs more than upper limbs. Her CSF examination showed protein was 60 mg/dl, glucose was 27 mg/dl. WBCs were 5 and RBCs were occasional. She was diagnosed as a case of GBS on the basis of clinical presentation further supported by NCS and CSF findings. She was given intravenous immunoglobulin at a dose of 0.4 g/kg/day for 5 days. After one month, her weakness improved to some extent but she was still walking with support and was unable to return to college until one year later. After a period of 5 years she is fully independent, can do her routine work but occasionally feels numbness of lower limbs.

**Case 3:** The elder brother of index case who is at present 38 years old, 15 years back developed fever with pharyngitis. Within a week of developing fever he developed weakness of both lower limbs progressing gradually over a period of 2 weeks associated with numbness and tingling which was more marked in lower limbs. The weakness gradually improved after 1 month and he was able to return back to normal routine after few months. This patient still walks with a limp but does not have any atrophy or deformity of limbs. Although no workup was done at that time as the patient was living in a remote village but history and the outcome strongly point towards probable diagnosis of GBS.

**Case 4:** The elder sister of index case, when 5 years old present 38 years old, 15 years back developed fever associated with fits. A few days later she was unable to walk and became completely bed bound. She was clinically diagnosed as a case of poliomyelitis in a rural health centre. Until the age of 11 years patient was unable to walk without support. She still walks with a limp but does not have any atrophy or wasting of the limbs as would be expected after poliomyelitis. Although no workup was done for this case but the clinical presentation and the clinical outcome suggests the probable diagnosis of GBS in this case as well.

Figure 1 shows the complete family tree for this generation of affected siblings.

![Pedigree of family.](image)

**DISCUSSION**

Mostly GBS occurs as sporadic cases. Based on indirect evidence, it is considered as group of autoimmune disorders. It has been reported to follow an infection by several organisms including cytomegalovirus (CMV), Ebstien Barr virus (EBV) and influenza vaccine. The commonest epidemiological association has been described with a preceding infection by Campylobacter jejuni.

We report the incidence of GBS in four siblings of a family, two of which were definite GBS and two had probable GBS. The diagnosis of GBS is mostly clinically supported by CSF and electrodiagnostic criteria. Two of our patients fulfilled this criterion although the other two had not been tested for supporting evidence; their clinical picture strongly resembles the ones with diagnosed GBS. Occurrence of GBS within family members has been described as case reports. Gelejins et al. described twelve families with 2-3 members with history of GBS after a systemic search in all GBS patients in Netherlands. This report is unique in that four siblings in a single generation have not been described previously. The occurrence of GBS in 3 out of 4 patients at the same age (22 years) is also unusual.

Clustering of cases of GBS has also been reported following an epidemic of waterborne diseases, and after exposure to organophosphate pesticides. But the occurrence of symptoms in these patients, each years apart, rules out these explanations. This strongly suggests genetic predisposition. The strongest indirect evidence of genetic predisposition, before our report, comes from the description by Joseph et al. of three siblings, younger than 2 years. The genetic basis of Guillain Barre syndrome (GBS) has not been elucidated so far. At least one study has described the presence of hereditary neuropathy with liability to pressure palsy (HNPP) in one family, but this is unlikely to be the explanation in the present cases.

The diagnosis of HNPP is suspected in adults with recurrent focal compression neuropathies such as carpal tunnel syndrome and peroneal palsy with foot drop that also have family history consistent with autosomal dominant inheritance. PMP 22 is the only gene known to be associated with HNPP. A contiguous gene deletion of chromosome 17p11.2 that includes PMP 22 is present approximately in 80% of affected individuals. The absence of recurrent focal compression neuropathies in these cases, rules out the suspicion of HNPP.

HLA complex based susceptibility has been implicated in many autoimmune disorders and at least one case of father and a son with GBS has been described to have complete HLA matching. Many studies have tried to identify the association between the occurrence of GBS and particular HLA type. In last three decades about
twenty studies investigating HLA distribution in GBS patients have been published including the following HLA alleles, HLA-DR3, HLADQB1*03, HLAB54 and cwl, HLADQB1*0401, HLAB-DQB1*04. A large scaled case control study failed to find an association between HLA DR and HLADQ molecules and disease susceptibility. It was concluded that HLA system did not play a general role in the susceptibility to develop GBS.

A simple Mendelian inheritance seems unlikely and the presence of preceding febrile illness in the vast majority of patients highlights the importance of environmental triggers even in patient with genetic susceptibility. More genetic, epidemiological and molecular studies will be required before we can unravel the mystery of occurrence of familial clustering in an otherwise sporadic disease.

REFERENCES


