Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Impact on Clinical Presentations and Response to Different Modalities of Treatment

Summary

This study included 60 patients (42 male and 18 females) with a mean age 46.77 years ranging from 14 to 81 years old who fulfilled the clinical criteria and the first three electrodiagnostic criteria of the EFNS/PNS guidelines on management of CIDP ***(Hughes RA,2006).*** The study was conducted in Ain Shams University Hospitals**.**

The study was designed aiming to:

1. Focus on clinical presentations, neurological disabilities and associated concurrent illnesses among CIDP Egyptian patients.
2. Determine the effectiveness of oral prednisone, plasma exchange and intravenous immunoglobulins in comparison to each other as available therapeutic agents.
3. To investigate the role of TNFα and MMP9 as markers for the diagnosis of CIDP patients which may be of help in the planning for future new models of treatment .

All patients were submitted to:

1. Full general and neurological history and examination.
2. Neuropathy Impairment Score (NIS) and Modified Rankin Scale (MRS) were performed for each patient before the start of treatment.
3. Laboratory investigations including routine immunological tests and serum level of TNFα (in all the patients and 20 controls).
4. CSF analysis.
5. Neurophysiological assessment: electromyography and nerve conduction studies.
6. Sural nerve biopsy for electron microscopy study and immunohistochemical assessment for MMP9 expression.

The patients were divided into 3 groups:

-Group (1) receiving full dose oral prednisone in a dose of 2mg/kg/day for 2 months then gradual tapering of the dose was done guided by the clinical improvement of the patient.

-Group (2) undergoing PE in the following regimen: 2 sessions per week for 4 weeks (8 sessions).

-Group (3) receiving IVIg in a dose of 0.4mg/kg/day for 5 successive days.

The choice of treatment was made according to the clinical presentation of the patients as well as the affordability and the accessibility of the modality of treatment.

Follow up of the patients was performed after 2 months from the start of treatment with both NIS and MRS.

The main results of our study were as follow:

- There was cranial nerve affection in 16.7% of the cases. Upper limb weakness was present in 80% while lower limb weakness was present in 93.3% of the patients. Sensory affection was present in 83.3% of the patients.
- Mixed sensorimotor affection was present in the majority of patients (76.6%) while the minority had either pure motor affection (16.6%) or pure sensory affection (6.6%).
- DM as a concurrent disease with CIDP represented the higher percentage of patients (30%) compared to others: CIDP with hepatitis (16.7%), collagen diseases (16.7%), or malignancy (3.3%).
- The mean values of NIS and MRS in the presence of DM, hepatitis and collagen diseases were higher but didn't reach a statistical significant difference when compared to those with CIDP alone before treatment while after the treatment (whatever its modality) those mean values were higher in the presence of concurrent diseases.
- Nerve biopsy of our patients revealed mild to moderate degree of demyelination in 86.7% of the cases while severe demyelination was detected in the remaining 13.3% of them. Edema was present in the majority (76.7%) while inflammatory cells were present in a minority (13.3%) of cases. Axonal degeneration was observed in 96.7% of the patients.

- There was statistically significant higher mean of TNFα levels in cases compared to that of controls.
- TNFα levels in CIDP patients were not statistically correlated to the clinical scores while statistically higher in DM and collagen diseases as concurrent diseases. Also, there was a positive correlation between TNFα levels and distal latency and negative correlation with conduction velocity of one nerve.
- Positive immunohistochemical staining of epineurial blood vessels for MMP9 were observed in almost all the cases (58/60) although no statistically significant correlations could be detected as regard the clinical scores, NCS as well as the concurrent diseases.
- CIDP patients respond well to the three modalities of treatment irrelevant to their type as expressed by the statistical significant decrease of the MRS and the total NIS and its subscores from before to after treatment.
- Plasma exchange is the most effective treatment followed by IVIg followed by oral prednisone.

Conclusion and Recommendations

1. CIDP is an acquired immune mediated polyneuropathy. Its early diagnosis is important as it is potentially treatable.
2. The Neuropathy impairment score is a standardized objective reliable and detailed score which evaluated properly the clinical presentations of our CIDP patients and their response to treatment. We recommend it to be applied as an available tool for assessment and also for evaluating the response to treatment in all peripheral neuropathy patients.
3. The presence of either demyelination and edema in sural nerve biopsy confirm the diagnosis of CIDP and accordingly we recommend the nerve biopsy as a confirmative diagnostic tool for CIDP patients.
4. TNFα in CIDP patients is considered a sensitive marker for the presence of active immune system diseases. We recommend controlled therapeutic trials on anti TNFα (Etanercept) on a large group of patients to be properly evaluated as a new model of treatment.
5. MMP9 is a specific marker for CIDP and may be a helpful additional parameter for its diagnosis. MMP9 inhibitors may be considered as a novel therapeutic approach in the future.

6. We recommend further trials on a large group of patients with CIDP and concurrent diseases to study their specific findings in neurophysiology and nerve biopsy. The choice of treatment for those patients should be tailored according to the individual condition.
7. CIDP patients respond well to prednisone, plasma exhange and intravenous immunglobulins.
8. Plasma exchange is more effective than prednisone and we would encourage it as the first line of treatment when it is available. Concerning IVIg, it needs further clinical trials on a larger group of patients to evaluate its effectiveness compared to other modalities of treatment.
9. We recommend long-term trials on CIDP patients with different modalities of treatment to determine the most effective treatment which can reduce the frequency of relapses with the least side effects.
10. The available modalities of treatment are effective in the presence of demyelination on nerve conduction studies but the axonal affection remain a problem of management which needs a solution by further researches.
11. Further clinical therapeutic trials are needed to evaluate the effectivenss of other immuosuppressive drugs as Rituximab, methotrexate, cyclphosphamide and cyclosporin.
12. We need to build a well equipped and specialized center for the neuromuscular diseases to be a referral point for all patients presenting with peripheral nervous system affection in our society in which a qualified team-work of neurologists, physiotherapists, pathologists, immunologists and genetic researchers can work together. The specialized neurologists can properly examine those patients and perform for them a detailed neurophysilogical studies. The neuropathologists will provide the clinicians with a proper diagnosis by Electron Microscopy aiming for the best management. Regular system of follow-up with special protocoles for each case will be provided by the neurologists. Immunological and genetic researches will help in the planning for future models of treatment.