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Citation	The 15th Medical Research Conference (MRC 2010), Hong Kong, 16 January 2010. In Hong Kong Medical Journal, 2010, v. 16 n. 1, suppl. 1, p. 40, abstract no. 63
Issued Date	2010
URL	http://hdl.handle.net/10722/105551
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Thymomatous myasthenia gravis

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Background: Myasthenia gravis (MG) is an autoimmune disorder targeting skeletal muscle acetylcholine receptor. Thymoma is associated with MG in some patients, the majority of whom present with symptoms of MG before detection of underlying thymoma. This study aimed to study clinical and serological characteristics of Chinese thymomatous MG patients.

Methods: Autoimmune MG patients with thymomectomy and histologically confirmed thymoma followed up in our hospital for at least 12 months were studied.

Results: A total of 37 Chinese MG patients with histology-proven thymoma were retrospectively studied. The mean MG symptom onset age was 48.5 (range, 25-81) years; 25 (68%) were female. The mean follow-up duration was 4.9 (range, 1-15) years. Symptoms of MG preceded detection of thymoma in the majority (31 patients, 84%), in six patients thymoma detection preceded MG symptoms onset by 1 to 8 years. Nineteen (51%) patients had early-onset MG (before 50 years of age). All patients were seropositive for acetylcholine receptor antibodies and 30 (81%) patients seropositive for striated muscle antibodies. Eleven (30%) patients had experienced myasthenic crisis and the worst MGFA clinical severity grade were class I (6 patients), class II (3), class III (8), class IV (9), and class V (11); hence 31 (84%) had generalised MG and six (16%) had ocular MG. Twenty-seven (73%) patients had a history of corticosteroid therapy, 22 (60%) required azathioprine, two required other immunosuppressant (1 mycophenolate mofetil, 1 cyclosporin A). All 37 patients had good or satisfactory MG clinical outcome measured by MGFA post-intervention status (2 pharmacological remission, 23 minimal manifestation, 12 improved) though one patient died from metastatic thymoma.

Conclusion: Thymoma MG was clinically severe with frequent myasthenic crises, but responses to conventional immunosuppressive therapies are satisfactory.

Understanding molecular mechanisms underlying Lrrk2-related Parkinson's disease in mouse

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Parkinson's disease (PD) is the second most common neurodegenerative movement disorder, characterised by slow movement, resting tremor, and postural instability. *Lrrk2* has been added to the list of genes that are implicated in PD. LRRK2 is a very large gene, which has over 2527 amino acid and 51 exons. LRRK2 is a complex protein consisting of five domains, which is expressed throughout the brain and the whole body. More than 20 mutations have been reported in LRRK2 in PD patients in different races. More importantly, 5 to 6% of familial PD patients have these mutations. Some in these mutations, R1441C, R1441G, Y1699C and G2019S, are amino acids conserved across vertebrates. Some patients with LRRK2 mutations have loss dopamine neuron in substantia nigra and Lewy body, which are typical features of PD. Initial studies proved these mutations increased LRRK2 kinase activity with autophosphorylation. Tauopathy and hyperphosphorylated tau are also found in Lrrk2 in vitro models. All these indicated its important role in PD pathogenesis. The importance of the R1441 residue in the pathogenesis is highlighted by the identification of three distinct missense mutations. We generated R1441G KI mice, did molecular characterisation of it, and analysed normal DA neurons change in R1441G KI mice after MPTP injection. Furthermore, we compared the mitochondrial parameters difference between wild type and single mutation proteins (R1441G R1441C and G2019S) in HEK293 and Sh-Sy5y cell lines.

Acknowledgements: I am grateful to my Supervisor Prof Ho and Co-Supervisor Dr Zhou. I thank all my Labmates for their many valuable suggestions.