

Thymomatous myasthenia gravis

HHW Liu¹, JWH Tsang², SYY Pang¹, SL Ho³, RTF Cheung³, ACY Chu¹, MMY Tse¹, W Mak¹, PWL Ho¹, KH Chan³

¹Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

²Department of Clinical Oncology, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

³Research Centre of Heart, Brain, Hormone and Healthy Aging, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

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 thymectomy 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

HF Liu¹, WY Zhang¹, PWL Ho¹, JWM Ho¹, DB Ramsden², ZJ Zhou³, SL Ho¹

¹Division of Neurology, Department of Medicine, The University of Hong Kong, Hong Kong

²Department of Biochemistry, The University of Hong Kong, Hong Kong

³School of Medicine, University of Birmingham, United Kingdom

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.