

TO THE EDITOR

IL6-Gene Variation in Parkinson's Disease

I have read with interest the recent report on the putative impact of chemokine polymorphisms in Parkinson's Disease¹. Based on a meta-analysis of case-control investigations for *IL-6* and several other candidate genes, the authors concluded protective effects of an *IL-6* promoter variant, rs1800795 or IL-6 G[-174]C. However, key issues appear to have been overlooked. Firstly, the study by Infante et al² used a TaqMan genotyping procedure with unknown primers. It is therefore impossible to tell in retrospect whether the transcribed or the antiparallel DNA strand served for allele calling and whether the risk allele was "G", or "C". As rs1800795 stands for a canonical substitution that can be read as "G" or as "C" depending on the template, strand information is essential to define genetic exposure. A second study³ used sequence-specific oligo probes that do not differentiate between "G" and "C" but rather call only the "C" allele on the transcribed strand. A third study⁴ genotyped the non-transcribed strand as can be verified by consulting the original pyrosequencing protocol. Chu et al failed to correct for the alternate strand and have mistaken "G" for "C". In other words, two of the three studies in question are non-informative and the third gives results that were misinterpreted. Finally, the authors have muddled IL-6 studies in Table 2 and have omitted additional studies⁵.

The confusion of risk and protective alleles emphasizes further the need for strand-sensitive meta-analyses of G:C and A:T transversions. It is unfortunate that this procedure is not routinely implemented in PDGene (URL: <http://www.pdgene.org>), a database that was consulted by the authors and that also offers meta-analyses of case-control investigations. Having

reviewed all PDGene entries for rs1800795, I note that as of September 2012, data from multiple studies²⁻⁴ have been misassigned to rs13447446, a G:T substitution 63bp downstream from rs1800795. Other studies that did not investigate rs1800795 are included in PDGene's meta-analysis of this variant. While Chu et al must be given credit for identifying these errors, the information available is insufficient to support a protective role of rs1800795 in Parkinson's disease.

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REFERENCES

1. Chu K, Zhou X, Luo BY. Cytokine gene polymorphisms and Parkinson's disease: a meta-analysis. *Can J Neurol Sci.* 2012; 39(1):58-64.
2. Infante J, García-Gorostiaga I, Sánchez-Juan P, et al. Inflammation-related genes and the risk of Parkinson's disease: a multilocus approach. *Eur J Neurol.* 2008;15(4):431-3.
3. Ross OA, O'Neill C, Rea IM, et al. Functional promoter region polymorphism of the proinflammatory chemokine IL-8 gene associates with Parkinson's disease in the Irish. *Hum Immunol.* 2004;65(4):340-6.
4. Håkansson A, Westberg L, Nilsson S, et al. Interaction of polymorphisms in the genes encoding interleukin-6 and estrogen receptor beta on the susceptibility to Parkinson's disease. *Am J Med Genet B Neuropsychiatr Genet.* 2005;133B(1):88-92.
5. Maraganore DM, de Andrade M, Lesnick TG, et al. High-resolution whole-genome association study of Parkinson disease. *Am J Hum Genet.* 2005;77(5):685-93.

TO THE EDITOR

A Case of Collet-Sicard Syndrome Caused by Necrotizing Otitis Externa

Collet-Sicard syndrome (CSS), palsy of cranial nerves nine, ten, eleven, and twelve, can be caused by a diverse set of disorders. Collet-Sicard syndrome is distinguished from Villaret syndrome by the lack of sympathetic nerve fibre involvement. The most common cause of CSS is otologic tumour¹. Other causes include non-otologic neoplasia (primary or secondary): parotid tumours, skull base tumours, prostate metastases, kidney metastases, breast metastases, and melanoma metastases. Multiple myeloma and schwannomas of the hypoglossal nerve, and Hodgkin's disease have been reported as causes. Vascular lesions including carotid aneurysms and jugular vein phlebitis can cause CSS. Other rare causes of CSS have been reported¹.

Herewith, we report a patient with Collet-Sicard syndrome resulting from malignant otitis externa (OE) and subsequent abscess formation. To the best of our knowledge, this is only the second reported case of infectious CSS.

CASE REPORT

A 67-year-old man presented with a three week history of progressive dysphagia to solids and liquids accompanied by episodic regurgitation and emesis of partially digested food. His past history was significant for type 2 diabetes mellitus, hypertension, erectile dysfunction, obesity, osteoarthritis, and hypothyroidism. He had been diagnosed with left sensorineural hearing loss and left OE five months prior. Ear culture was positive for *Pseudomonas aeruginosa*. Despite an aggressive antibiotic regimen and frequent debridement and microcleaning, the OE had persisted.

A swallowing assessment prior to neurologic consultation suggested severely impaired oral and pharyngeal phases of swallowing with a high risk of aspiration on all textures. This necessitated a G-tube placement. The patient was admitted to hospital. Examination by a neurologist showed a deviated tongue to the left, failure of the left soft palate to rise, severe left sternocleidomastoid (SCM) and upper trapezius weakness and atrophy, and mild dysarthria. The initial differential diagnosis included bulbar-onset amyotrophic lateral sclerosis (ALS). Subsequent examination 3.5 months later revealed persistent