Commentary

Parkinson’s Disease and Cancer

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The association of Parkinson’s disease and cancer had recently attracted renewed interest, and results are coming from well-designed epidemiologic studies (mainly cohort studies). In particular, the findings from Danish Parkinson’s disease patients (1, 2) showed that the association between Parkinson’s disease and melanoma was present both before and after the diagnosis of Parkinson’s disease and was not explained by levodopa treatment. The suspicion that levodopa could increase the risk of melanoma was suggested in several clinical reports, the first of which appeared soon after the drug was introduced as a new therapy for Parkinson’s disease in the early 1970s. The hypothesis seemed biologically plausible, but the evidence did not support a causal relationship (3-6). On the contrary, the increased risk of melanoma in Parkinson’s disease patients is now well established, although a clear biological explanation is still lacking. For other cancers, the cohort study of the Danish Parkinson’s disease patients confirmed an inverse association with smoking-related cancers (standardized incidence ratio: 0.38 for lung cancer and 0.47 for larynx cancer). This inverse association was first seen in 1966 (7) and in 1976 by Doll and Peto (8).

The study of Driver et al. (9) published in this issue of *Cancer Epidemiology Biomarkers & Prevention* has the merit of reinforcing the evidence of an association between Parkinson’s disease and melanoma in a prospective study with good control of confounding (and modifying) factors. A possible confounder of the association between melanoma and Parkinson’s disease is social class, as melanoma and Parkinson’s disease seem to be more frequent in higher socioeconomic status individuals with more opportunities for recreational (and thus intermittent) sun exposure. In contrast, this study clearly showed that socioeconomic factors could not be indicted as responsible for the association. Indeed, the “matching” for social class was elegantly done, recruiting both Parkinson’s disease cases and controls from the Physician’s Health Study cohort; the excess risk for melanoma remained.

Nonetheless, the findings of this study raise a even more intriguing question. First, this study confirmed the decreased risk of cancers other than melanoma and, in particular, of smoking-related cancers, previously observed not only in Parkinson’s disease patients (1, 2, 10) but also in those with other neurological diseases (11). Future studies should concentrate on an appropriately powered search for possible genetic factors that predispose to Parkinson’s disease, but decrease cancer risk, perhaps via an increased tendency to apoptosis. This approach will be facilitated by the nature of Parkinson’s disease, a disease with good survival, high incidence in western countries, and frequently affecting patients of upper socioeconomic status with a good compliance to follow-up, thus allowing cohort and nested case-control designs to provide sufficient power. However, second and more surprisingly, this study also showed that smokers among Parkinson’s disease patients had fewer tobacco-related cancers than smokers in the reference group. Thus, there is an intriguing picture of fewer smokers among Parkinson’s disease patients and even fewer tobacco-related cancers among Parkinson’s disease patients who smoked. Although the first inverse association was already known, this second finding is completely new and suggests a gene-environment interaction. The authors hypothesized a role for CYP2D6 with a less efficient polymorphism among the Parkinson’s disease patients, leading to poor toxin metabolism and to a decreased activation of pro-carcinogens present in tobacco smoke. Other factors could be involved, including other P450 enzymes or genes involved in the DNA excision-repair pathway. Certainly, further studies will help us to understand the biologic mechanisms.

It is, therefore, time for a gene-environment study of melanoma and other cancers, measuring candidate genes (or a genome-wide scan) in the setting of a study with validated histories of sun exposure and tobacco smoking. Meanwhile, the study by Driver et al. itself, as further person-years accumulate, should be able to better estimate the risk of each type of cancer among Parkinson’s disease patients.

References

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