Letter to the Editor

Neuro
epidemiology

Received: July 16, 2010
Accepted: September 2, 2010
Published online: October 21, 2010

Neuroepidemiology 2010;35:303–304
DOI: 10.1159/000321177

No Role for Melanoma Treatment in the Association between Melanoma and Amyotrophic Lateral Sclerosis or Parkinson's Disease

Peter D. Baade[a, b], *Elena Herrero Hernández*[g], *D. Michal Freedman*[f], *B. Mark Smithers*[c, d], *Lin Fritschi*[e]

[a]Viertel Centre for Research in Cancer Control, Cancer Council Queensland, [b]School of Public Health, Queensland University of Technology, and [c]Department of Surgery and [d]Queensland Melanoma Project, Princess Alexandra Hospital, University of Queensland, Brisbane, Qld., and [e]Western Australian Institute for Medical Research, University of Western Australia, Perth, W.A., Australia; [f]Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, Md., and [g]Center for Research on Occupational and Environmental Toxicology, Oregon Health and Science University, Portland, Oreg., USA

In 2007 we published the results of our study of all people diagnosed as having melanoma in Australia between 1982 and 2001, and compared their mortality risk of amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD) to the general population [1]. Although the absolute risk was small, the melanoma cohort had a 70% higher risk of death due to ALS and a nearly 3-fold higher risk of death due to PD than the general population, consistent with a US study [2], strengthening the evidence for an association between melanoma and each of the 2 neurodegenerative diseases.

In Australia, surgical excision is the preferred treatment for melanoma, with no patient receiving adjuvant therapy after resection of a primary lesion. Patients with stage III disease rarely receive interferon, with most being watched or treated in clinical trials. The only melanoma patients who receive chemotherapy are those diagnosed as having a stage IV melanoma.

We suggested that it was unlikely that treatment was an explanation for the observed association [3]. However, in the absence of definitive data about the thickness of melanomas in the study cohort, it was possible that a large proportion of melanoma patients who died of either ALS or PD had thicker melanomas. Thus this treatment hypothesis remained a possibility, particularly when several chemotherapeutics that could be used in the treatment of more advanced melanoma have neurotoxic effects [4, 5].

While specific treatment data are not available, we sought additional information about the thickness of the melanoma among our original melanoma cohort. In the absence of stage information, thickness is the strongest predictor of survival [6]. This information was provided by the Australian Institute of Health and Welfare, who matched the melanoma cohort information with the melanoma thickness details collected by each of the state and territory cancer registries. Before 1990 there was a relatively large proportion of melanoma cases with missing thickness data (~27%), so we have presented thickness data for the full period and the restricted 1990–2001 period (~9% missing thickness).

Table 1. Melanoma thickness for persons diagnosed as having melanoma in Australia between 1982 and 2001

Melanoma thickness	Melanoma patients who died from ALS[1]	Melanoma patients who died from PD[2, 3]	All melanoma patients
Diagnoses in 1982–2001			
≤1.00 mm	28 (53)	59 (46)	73,819 (58)
1.01–2.00 mm	8 (15)	16 (13)	17,429 (14)
2.01–4.00 mm	6 (11)	19 (15)	10,889 (9)
>4.00 mm	1 (2)	16 (13)	6,035 (5)
Unknown	10 (19)	18 (14)	18,086 (14)
Total	53 (100)	128 (100)	126,258 (100)
Diagnoses in 1990–2001			
≤1.00 mm	13 (57)	29 (47)	56,246 (63)
1.01–2.00 mm	6 (26)	10 (16)	12,398 (14)
2.01–4.00 mm	3 (13)	9 (15)	7,658 (9)
>4.00 mm	1 (4)	7 (11)	4,389 (5)
Unknown	0 (0)	7 (11)	8,058 (9)
Total	23 (100)	62 (100)	88,749 (100)

Melanoma includes cancers coded in ICD-10 as C43. Source: Australian Cancer Database, AIHW. Figures in parentheses are percentages.

[1] Indicates those who died >12 months after their diagnosis of melanoma, up to the end of 2001, with the underlying cause of death coded as 335.2 (ICD-9) or G12.2 (ICD-10).

[2] Indicates those who died >12 months after their diagnosis of melanoma, up to the end of 2001, with the underlying cause of death coded as 332 (ICD-9) or G20 (ICD-10).

[3] Of the original case group of 129 melanoma patients who died of PD, 1 patient could not be matched and has been excluded from this analysis.

These results (table 1) show that of the 53 melanoma patients who died of ALS, only 1 (2%) was known to have melanoma diagnosed >4 mm thickness. The corresponding percentage among the 128 melanoma patients who died of PD was 13% (n = 16).

While not definitive, the thickness distribution for the melanoma patients who died of ALS or PD provides greater weight to

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

Accessible online at:
www.karger.com/ned

the hypothesis that chemotherapeutics have played minimal or no role in the previously reported association. As such we felt it was important to disseminate this information in order to more appropriately focus future research efforts in understanding the biological bases of the co-occurrence of both diseases. Alternative mechanisms to explain the co-occurrence could include genetic variants and gene expression changes in pigmentation genes occurring in PD [7] and in ALS [8]; shared embryological origin for melanocytes and neurons, commonalities between melanin and dopamine synthesis and variants of melastatins (TRPMs) [9, 10], due to the involvement of selected TRPMs in this cancer and in neuronal cell death.

Acknowledgements

We acknowledge the assistance of staff from the Cancer and Screening Unit, Australian Institute of Health and Welfare, who conducted the data extraction required for this study.

References

1 Baade PD, Fritschi L, Freedman DM: Mortality due to amyotrophic lateral sclerosis and Parkinson's disease among melanoma patients. Neuroepidemiology 2007;28:16–20.
2 Freedman DM, Travis LB, Gridley G, Kuncl RW: Amyotrophic lateral sclerosis mortality in 1.9 million US cancer survivors. Neuroepidemiology 2005;25:176–180.
3 Coory M, Smithers M, Aitken J, Baade P, Ring I: Urban-rural differences in survival from cutaneous melanoma in Queensland. Aust NZ J Public Health 2006;30:71–74.
4 Schiff D, Wen PY, van den Bent MJ: Neurological adverse effects caused by cytotoxic and targeted therapies. Nat Rev Clin Oncol 2009;6:596–603.
5 Sul JK, Deangelis LM: Neurologic complications of cancer chemotherapy. Semin Oncol 2006;33:324–332.
6 Balch CM, Gershenwald JE, Soong SJ, Thompson JF, Atkins MB, Byrd DR, Buzaid AC, Cochran AJ, Coit DG, Ding S, Eggermont AM, Flaherty KT, Gimotty PA, Kirkwood JM, McMasters KM, Mihm MC Jr, Morton DL, Ross MI, Sober AJ, Sondak VK: Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol 2009;27:6199–6206.
7 Gao X, Simon KC, Han J, Schwarzschild MA, Ascherio A: Genetic determinants of hair color and Parkinson's disease risk. Ann Neurol 2009;65:76–82.
8 Jiang YM, Yamamoto M, Kobayashi Y, Yoshihara T, Liang Y, Terao S, Takeuchi H, Ishigaki S, Katsuno M, Adachi H, Niwa J, Tanaka F, Doyu M, Yoshida M, Hashizume Y, Sobue G: Gene expression profile of spinal motor neurons in sporadic amyotrophic lateral sclerosis. Ann Neurol 2005;57:236–251.
9 Hermosura MC, Garruto RM: TRPM7 and TRPM2 – Candidate susceptibility genes for Western Pacific ALS and PD? Biochim Biophys Acta 2007;1772:822–835.
10 Hermosura MC, Nayakanti H, Dorovkov MV, Calderon FR, Ryazanov AG, Haymer DS, Garruto RM: A TRPM7 variant shows altered sensitivity to magnesium that may contribute to the pathogenesis of two Guamanian neurodegenerative disorders. Proc Natl Acad Sci USA 2005;102:11510–11515.

A/Prof. Peter D. Baade, Senior Research Fellow
Viertel Centre for Research in Cancer Control
Cancer Council Queensland, PO Box 201
Spring Hill, QLD 4001 (Australia)
Tel. +61 73 634 5317, Fax +61 73 259 8257
E-Mail peterbaade@cancerqld.org.au