

Development of Two Malignant Melanomas during Administration of Levodopa

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Przybilla B, Schwab U, Landthaler M, Braun-Falco O. Development of two malignant melanomas during administration of levodopa. *Acta Derm Venereol (Stockh)* 1985; 65: 556-557.

In a 72-year-old man two malignant melanomas had developed simultaneously during long-term treatment with levodopa. Although a causal relationship between tumour growth and administration of levodopa can only be suspected, such a possibility should be considered when using this drug. (Received April 19, 1985.)

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The incidence of malignant melanoma is rising, and environmental factors are discussed among others as contributing to this development (1). So in a few cases treatment with levodopa, a drug for Parkinson's disease, has been suspected to induce, to promote, or to stimulate the growth of malignant melanoma (2-6). We have seen a patient presenting with two primary malignant melanomas, which had become clinically apparent after therapy of parkinsonism with levodopa for about five years.

CASE REPORT

A 72-year-old man was admitted to our hospital with a history of two »moles» which had been present without a change for about 15-20 years on his chest and on his back. However, in the course of the last year the lesions had enlarged and become partially nodular. As the »mole» on the back had begun to cause some discomfort, it had been excised by the local physician with narrow margins. On histological examination this lesion turned out to be a primary nodular malignant melanoma (level IV, tumour thickness 3.7 mm), and the patient was referred to us eight days after excision. On clinical examination the second »mole» on the chest was suspected to be a superficial spreading melanoma with partially nodular growth. Wide excision of this lesion and, to preclude local recurrence, of the scar area on the back was performed. Histologically the lesion on the chest was a malignant melanoma (level IV, tumour thickness 1.3 mm) arising on a melanocytic naevus. No evidence of metastatic disease could be found. For the treatment of parkinsonism during the previous five years the patient had applied a mixture of 200 mg of levodopa and 50 mg of benserazide (Madopar®) up to three times a day. In addition 100 mg of amantadine hydrochloride (Symmetrel®) or amantadine sulfate (PK-Merz®) and 5 mg of methixene (Tremarit®) had been administered about once a day since five and three years, respectively. Further systemic treatment comprised some cardiovascular drugs.

DISCUSSION

Levodopa is an effective compound widely used in the treatment of parkinsonism. Usually it is administered in combination with a peripheral decarboxylase inhibitor such as benserazide or carbidopa. After crossing the blood brain barrier levodopa is decarboxylated to dopamine, thus partially compensating the lack of this neurotransmitter in the basal ganglia. On the other hand, as a precursor of melanin, levodopa is taken up by pigment cells. The incorporation into experimental melanoma is enhanced by decarboxylase inhibition, and levodopa has been shown to be toxic to these tumour cells (7). However, regarding apprehensively the interference with melanogenesis and bearing in mind the ambiguous carcinogenic potential of cytotoxic agents, concern has been raised about the

possibility that levodopa may induce, promote or stimulate the growth of malignant melanoma under certain circumstances (2–6). Yet as the natural course of malignant melanoma is highly variable, the evidence of a causal association remains tenuous. Furthermore, in 1099 melanoma patients no increased use of levodopa was found (8).

Nevertheless, it cannot be excluded that in an individual patient levodopa may precipitate tumour growth, especially when long-term treatment (4, 5, 8) or occurrence of multiple primary malignant melanomas are encountered. Such features were present in our patient, who in two long-standing “moles” had developed nodular tumour growth starting coincidentally after five years of levodopa therapy. Although this does not prove a causal relationship—even multiple primary tumours are found in about 4% of patients with malignant melanoma (9)—precautions are advisable when treatment of parkinsonism with levodopa is performed: patients receiving this compound should be monitored regularly for development or changes of pigmented skin lesions, and the drug should not be administered in individuals suffering from malignant melanoma.

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