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Iatrogenic melanoma. Comment on: Melanoma epidemic: a midsummer night's dream?

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MADAM, We read with great interest the recent article about the controversy over the explanation of the melanoma epidemic.[1] The past decades have witnessed a substantial increase in the reported incidence of cutaneous malignant melanoma (CMM) without a proportional rise in melanoma mortality in most European countries. The paper suggests that the large increase is likely to be due to diagnostic drift which classifies benign lesions as stage 1 melanoma.[1,2]

Histology is the gold standard for the diagnosis of CMM, but the assessment of small and thin melanocytic lesions, that constitute a growing proportion of lesions submitted for histology, is problematic, and interobserver agreement is moderate at best.[3,4] Histological indicators of malignancy have largely been derived from larger lesions, and it is unknown if they are equally applicable for small lesions. As the consequences of overdiagnosis are generally limited to a small local re-excision and increased patient stress, whereas underdiagnosis results in an increased chance of recurrence and death, judgement tends to be skewed towards malignancy.[2,4] In our clinic, members of melanoma families have been under surveillance since 1981. In many of these families, a mutation (p16-Leiden) in the high-penetrance melanoma susceptibility gene CDKN2A has been identified.[5] During surveillance of 37 families with a p16-Leiden mutation, melanomas have been diagnosed in 105 genetically tested relatives, 12 of whom (11%) were noncarriers. These 12 noncarriers had a total of 13 melanomas. As part of a study on the effect of surveillance (manuscript in preparation) the slides of 126 melanomas were reviewed. These consisted of all in situ melanomas (n = 63), and invasive melanomas with missing data or of a nonsuperficial spreading histological type (n = 52) that had been diagnosed in mutation carriers within these 37 families. All melanomas of the 12 noncarriers that were available for histological review (seven in situ and four invasive melanomas from 10 patients) were added to the set. Slides were revised by a pathologist who is a member of the Dutch melanoma panel (W.J.M.). Revisions were performed blinded for the patients' mutation status. After disclosure of the mutation status a disproportionately high proportion of (in situ) melanomas reclassified as benign melanocytic lesions turned out to be cases of noncarriers. Eight (seven in situ and one invasive) of the 11 melanomas of noncarriers were reclassified as benign (73%), compared with only 13 of the other 115 cases (11%). In seven of 10 mutation-negative relatives a history of melanoma was therefore not confirmed.

These results touch on two important issues. Firstly, the value of genetic testing for CDKN2A mutations has been discredited because of a reported increased melanoma incidence among mutation-negative relatives.[6] Our data show that overdiagnosis may account for a significant proportion of this observation. Secondly, increased screening and surveillance of individuals with a low a priori melanoma risk may result in removal of increased numbers of small and histologically equivocal lesions, some of which will be overdiagnosed as cancers and (especially in the case of individuals with a single relative with melanoma) will contribute to the chance of an inappropriate picture of familial clustering.

References

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