

Oncogenetic testing for persons with familial atypical multiple mole melanoma syndrome

Familial atypical multiple mole melanoma (FAMMM) syndrome is an autosomal dominant genodermatosis characterized by multiple melanocytic nevi, usually more than 50, and a family history of melanoma. In 60% of the cases it is associated with mutations in the CDKN2A gene. Some FAMMM kindreds show an increased risk for the development of pancreatic cancer and possibly other malignancies.

Globally, 5 to 10% of malignant melanomas would occur in familial clusters but variations in penetrance and expressivity of the genes involved, regional variations and the fact that only limited data are available make it difficult to have an accurate estimate of the prevalence of FAMMM.¹

Clinical recommendations

- Consider a patient as having FAMMM if all of the following criteria apply:
 - Malignant melanoma in one or more first- or second-degree relatives
 - High total body nevi count in the order of 50 or more, including some clinically atypical nevi
- Refer to a centre for genetic counselling preferably an affected member of families with:
 - 2 first degree relatives with melanoma
 - 2 cases of melanoma (even if more distant relatives) if one or both have had multiple primary melanoma or the cases have the atypical mole syndrome (dysplastic nevi)
 - 3 or more cases of melanoma (one of these cases may be pancreatic cancer instead of melanoma)
 - a patient with 3 or more primary melanomas
- Testing should only be done after extensive counselling, including information on the limitations of genetic testing in FAMMM.

Follow-up of members of a FAMMM family

If a mutation in the family is found, carriers are considered at high risk and the following recommendations apply; non-carriers in such a family may nevertheless have an intermediate risk and should be managed as such.

If no mutation is found then all members of the family should be considered to be at intermediate risk.



The following recommendations guide the follow-up of high risk subjects and can also guide the follow-up of intermediate risk subjects, together with the clinical judgment that takes into account the personal history of melanoma, the number of nevi, the presence of atypical nevi, and the family history.

- Educate family members regarding the need for cutaneous photoprotection and the need to avoid sunburn, particularly in children;
- Educate family members regarding pigmented lesion characteristics that suggest the presence of melanoma;
- Perform a baseline, head-to-toe skin examination at age 12, and repeat every 6–12 months;
- Recommend to family members to perform monthly self-examination of the skin, seeking to identify new or changing pigmented lesions;
- Consider supplementing skin cancer surveillance with (standardized) clinical photographs to facilitate recognizing clinically important pigmented lesion changes, especially in patients with numerous clinically atypical nevi;
- Use dermoscopy (epiluminescence microscopy) and digital dermoscopy as an adjunct to evaluating pigmented lesions, particularly in high risk patients;
- Increase the frequency of skin examination during puberty and pregnancy, periods during which nevi may change rapidly;
- Excise all pigmented lesions that are clinically suggestive of melanoma as well as those that are changing in a clinically worrisome manner. Avoid wholesale, prophylactic removal of all nevi;
- In CDKN2A mutation carriers consider offering the option to screen for pancreatic cancer through endoscopic ultrasound in combination with MRI if there is a first or second degree relative with pancreatic cancer. Explain there is no proven benefit. This can start at the age of 50 or 10 years younger than the earliest family member with pancreatic cancer. As these screening tests are not currently considered standard of care, these patients should be included in clinical research screening programs if possible.

Reference:

1. Leachman SA, Carucci J, Kohlmann W, Banks KC, Asgari MM, Bergman W, et al. Selection criteria for genetic assessment of patients with familial melanoma. *J Am Acad Dermatol.* 2009;61(4):677.e1-14.

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