Management and follow-up of a patient with Familial Atypical Multiple Mole-Melanoma (FAMMM) Syndrome

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Introduction

Melanoma is a fast-growing malignant tumor of melanocytes. Familial Atypical Multiple Mole-Melanoma Syndrome (FAMMM) is an autosomal dominant genodermatosis characterized by the presence of a high number of dysplastic nevi and family history of melanoma or pancreatic cancer. It is currently estimated that nearly 8-12% of melanoma patients have a first- or second-degree relative with the same disease (1). This fact has been demonstrated for the first time in 1978 by Clark et al. in a study enrolling families whose members presented a higher number of atypical moles than the general population, suggesting a genetic link between the presence of atypical multiple moles and familial melanoma (2,3-5). Germline mutations associated with FAMMM concern regions encoding pro-
patients than in the general population, therefore high-risk plasm; its incidence in generally higher in FAMMM pa-

Case report

A 45 year-old woman was admitted to our Department of Dermatology and Plastic Surgery in March 2008. She reported a family history of melanoma and expressed concern over a change in the appearance of several existing moles. At physical examination the patient presented a type II phototype and numerous nevi (>100) (Fig. 1). Over the past years, the patient underwent several operations to remove pigmented lesions, most of which were benign, although two lesions, one in the sacral region and one in the left paraumbilical region, resulted as dysplastic nevi at the histopathological exam. In 1995 the excision of a pigmented lesion in the left gluteal area was performed; histological findings revealed a superficial spreading melanoma, Clark level III and Breslow depth 0.5 mm. In accordance with current guidelines on the management of melanoma patients, the patient underwent a wider margin excision (1 cm margin). Histological examination was negative for neoplastic infiltration. In 2009 a pigmented lesion in the left posterior deltoid area was excised; its histological examination revealed that the first lesion was a superficial spreading melanoma, Clark level II and Breslow depth 0.3 mm (Fig. 2). The wider margin excision revealed no neoplastic infiltration. Later, two pigmented lesions, in the right scapular area, respectively superior and inferior, were excised; their histological examination revealed that the first lesion was a superficial spreading melanoma, Clark level II, Breslow depth 0.8 mm and the second one was a superficial spreading melanoma, Clark level III, Breslow depth 0.7 mm. Therefore, wider margin excisions were performed; both were negative for neoplastic infiltrations. She is followed for skin examinations including dermoscopy.

Discussion

Melanoma is a high morbidity and high mortality neoplasm; its incidence in generally higher in FAMMM patients than in the general population, therefore high-risk members of familial melanoma families should undergo an accurate screening for this disease. However, because of the lack of concordance data on the correlation between CDKN2A gene mutations and oncogenic risk, genetic screening is not currently recommended to identify high-risk population and for risk stratification. Genetic testing for mutations in CDKN2A is of no value outside the context of clinical research and is not performed to screen FAMMM patients.

The identification of a patient as a member of a high-risk FAMMM family may be suspected by performing a complete cutaneous examination revealing numerous atypical nevi and may be determined by performing a meticulous personal and family history of melanoma and pancreatic cancer in first- and second-degree relatives. The incidence of CDKN2A mutations is indeed higher in individuals with three or more melanomas and/or in families with at least one melanoma and two or more other diagnoses of melanoma and/or pancreatic cancer in first- and second-degree relatives in one side of the family (8). However, in clinical practice it may be difficult to identify, on the sole anamnestic basis, patients from high-risk pedigrees. In fact, family history is often reported in a partial, incomplete or imprecise manner and it is seldom confirmed by pathology reports. Moreover, these patients are not always aware of the added risk to them and may leave out important information. As such, general practitioners play a central role in the follow-up of these individuals and their families and cooperate with the specialists for the management of these patients.

Patients with a suspected FAMMM syndrome must undergo frequent skin examinations, even with the use of dermoscopy, that allows an accurate and non invasive evaluation of pigmented lesion, for the prevention and early detection of melanoma. FAMMM patients, as well
as their first- and second-degree relatives, should undergo complete cutaneous examinations every 6-12 months. Skin examination must be performed on the whole skin surface, including the scalp, the oral mucosa and the genital area. Pigmented lesions are examined according to the “ABCD score” (11,12), that allows a thorough evaluation in terms of morphology and dermoscopic findings: asymmetry, borders, color, different dermoscopic patterns.

The dermoscope is an important diagnostic instrument as it combines the magnification and the elimination of the corneal/air interface, thus allowing a more accurate and objective evaluation of the pigmented lesions and enabling the diagnosis or avoiding useless surgical excisions, that are already very frequent in FAMMM patients (13).

In our case, the pattern asymmetry (Fig. 2) and the starbust aspect (Fig. 3) represent the main dermoscopic criteria for the diagnosis of melanoma.

The specialist has the task to inform the patient and to teach him how to perform skin self-examinations. Monthly self-examinations allow the evaluation of the lesions during the time intervals between check-ups, with the possibility, whenever the patient notices changes, to bring the dermatologic check forward and to proceed for the surgical operation, if it is necessary (14). In patients with personal history of melanoma, follow-up modalities vary according to the histological findings of the neoplasm, anyway they should last no less than 10 years. As regards the management of melanoma patients, periodic check-ups should be scheduled every 3-12 months, according to the initial stage and potential evolution of melanoma. If necessary, hematological and instrumental examinations may be repeated over time.

Conclusions

Identifying high-risk patients for melanoma represents a primary objective for the specialists that are involved in the management of this disease, especially in order to enact all the necessary surveillance and follow-up strategies, and, if possible, to detect the disease at the initial stage. The dermoscopy increases diagnostic abilities and proves FAMMM syndrome.

References

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