Muir-Torre syndrome

Authors: Doctors Alexander C. Katoulis, Evangelia Bozi, Professor Nicholas G. Stavrianeas
Creation date: May 2004

Scientific Editor: Professor Thierry Philip

Abstract
Muir-Torre syndrome represents the association of multiple sebaceous tumors (i.e. hyperplasia, adenoma, epithelioma and carcinoma), or keratoacanthoma (KA) with one or more visceral carcinomas. This syndrome is very rare. Muir-Torre syndrome is dominantly inherited. It is caused by a mutation in DNA mismatch repair genes (hMLH1 at 3p21.3 or hMSH2 at 2p22-p21). Muir-Torre is therefore allelic to hereditary nonpolyposis colorectal cancer (HNPCC). Sebaceous tumors are usually multiple, with sebaceous adenomas being the commonest. KA, 3-10 in number, are usually located on the face or the trunk. Cutaneous tumors may precede or follow the first presentation of internal malignancy, which usually involves the gastrointestinal tract, the breast or the genitourinary tract. The malignancies are usually multiple, occur at an early age, but tend to be of low-grade and have a relatively low incidence of metastases. The management should be multidisciplinary including genetic counselling, regular dermatology follow-up and relevant cancer screening.

Keywords
Muir-Torre syndrome, sebaceous tumors, keratoacanthoma, hereditary non polyposis colon cancer, hMLH1, hMSH2

Disease name
Muir-Torre syndrome

Definition/Diagnostic criteria
Muir-Torre syndrome represents the association of multiple sebaceous tumors (i.e. hyperplasia, adenoma, epithelioma and carcinoma), or keratoacanthoma (KA) (a common benign epithelial tumor of pilosebaceous origin) with one or more visceral carcinomas (Schwartz and Torre, 1995).

The criteria for diagnosis are: 1. At least one sebaceous tumor; 2. At least one internal malignancy. Every patient with multiple KA should be evaluated for the presence of sebaceous neoplasms, the absence of which still requires consideration of this syndrome.

Epidemiology
Muir-Torre syndrome is very rare. Almost half of the patients have at least one KA.
Genetics
Muir-Torre syndrome is dominantly inherited. It is caused by a mutation in DNA mismatch repair genes. Mutation may arise either in the hMSH2 gene located on chromosome 2p22-p21 or in the hMLH1 gene at 3p 21.3 (Mathiak et al, 2002). Patients are heterozygous for the mutation. Normal allele inactivation results in an increased risk of malignancy. Molecular analysis in hereditary non polyposis colorectal cancer (HNPCC) demonstrated a common genetic basis, with the observation of germline mutations in the hMSH2 gene in both syndromes (Dore et al, 1999).

Histogenesis
The association of KA and sebaceous neoplasms may be explained by their common derivation from pilosebaceous glands.

Clinical description
Sebaceous tumors are usually multiple, with sebaceous adenomas being the commonest. KA, 0.5-1.0 cm in diameter, are usually located on the face or the trunk. They vary from 3 to 10 in number. Cutaneous tumors may precede or follow the first presentation of internal malignancy. Internal malignancies usually involve the gastrointestinal tract, such as colorectal, gastric or esophageal cancer. Less commonly, the breast or the genito-urinary tract may be involved. The malignancies are usually multiple, occur at an early age, but tend to be of low-grade and have a relatively low incidence of metastases (Akhtar et al, 1999). Barana et al. (2004) reported the first family with Muir-Torre syndrome harboring a large deletion within the MSH2 gene. The family had 3 affected individuals in 2 generations. The father had 2 metachronous colon cancers starting at age 53 years, a daughter had a colon and ovarian cancer starting at age 42 years, and a son was affected by an adenoma with a focus of carcinoma at age 47 years. All 3 affected members presented with cutaneous lesions characteristic of Muir-Torre syndrome.

Diagnostic methods
Histology: typical "sebaocanthoma" of Muir-Torre syndrome displays architecture of KA with well-differentiated sebaceous lobules of sebaceous adenoma (Schwartz, 1994).

Management
The management should be multidisciplinary including genetic counselling, regular dermatology follow-up and relevant cancer screening. For skin tumours, oral isotretinoin may be effective and might have a preventive role also for future malignancies.

References

http://www.orpha.net/data/patho/GB/uk-MuirTorre.pdf