Muir-Torre Syndrome diagnostic and screening. a single center experience

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Introduction: Muir-Torre syndrome (MTS) is a rare genetic condition that predisposes individuals to skin tumors and visceral malignancies. Because of the potentially aggressive nature of internal malignancies and sebaceous carcinoma, and the tendency to have multiple low-grade visceral cancers, close cancer surveillance is required in individuals and their families with this usually autosomal dominant disorder. Although the majority of MTS is caused by mutations in DNA repair genes resulting in microsatellite instability, a newly described subtype of MTS does not demonstrate microsatellite instability and may be inherited in an autosomal recessive pattern. Neoplasms may be subject to immunohistochemistry or both immunohistochemistry and genetic testing to confirm the diagnosis of MTS. Here, we offer an update and an approach to the diagnosis and management of MTS with a particular emphasis on the role of immunohistochemistry and genetic testing.

Currently, it is believed that there are two types of MTS. The variant of Hereditary Nonpolyposis Colorectal Cancer or Lynch Syndrome, associated with germline mutations in DNA repair genes encoders of proteins, and the other spectrum of the disease, however, has no correlation with family history and seems to involve other genes than the DNA repairing ones.

Methods: We studied two families who meet high risk criteria and Lynch syndrome suspected in Muir-Torre variant (MTS). The first case, family 1, patient was 52 years old and diagnosed of colorectal cancer with fibroadenomas and immunohistochemistry diagnosis presents no nuclear expression for MSH2 - MSH6 without family history of cancer. The second case, family 2, patient had a sebaceous tumor on right arm with MSH2 expression was not found. At the same time his brother (50 years-old) was diagnosed colorectal cancer. The genetic testing for Muir-Torre syndrome was performed in both of them.

Results: In both cases the mutation is identified in c.1345_1348delAAGT MSH2 gene. In exon 8 of the gene MSH2 germline mutation heterozygous consisting of a deletion of four nucleotides that cause a change in the reading frame and a truncated generation of protein was identified p(Lys449Phefs*4). The identified mutation is responsible for Lynch syndrome in each patient and therefore the first-degree relatives have a 50% risk of presenting the mutation.

Conclusion: The most common form of MTS is a variant of Hereditary Nonpolyposis Colorectal Cancer or Lynch Syndrome, associated with germline mutations in DNA repair genes encoders of proteins MutL Homolog (MLH1 and MSH2). Recently, mutations in genes of proteins MutS Homolog 6 (MSH6) and Postmeiotic Segregation Increased 2 (PMS2) were also implicated. Thanks to the existence of consultation hereditary cancer and genetic counseling has been possible to make the diagnosis of this syndrome. A special emphasis on the role of immunohistochemistry and genetic testing. The importance of a multidisciplinary coordination encompassing, pathologists, dermatologists, internists and oncologists, among others has possible not only diagnosis but proper monitoring and implementation of primary prevention and or secondary in those cases detected both affections as carriers.