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MUTYH-associated colon disease: adenomatous polyposis is only one of the possible phenotypes. A family report and literature review

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ABSTRACT

Aims and background. The MutY human homologue gene (*MUTYH*) is responsible for about a quarter of attenuated familial adenomatous polyposis. Occasionally, it has been associated with hyperplastic polyps and serrated adenoma. We report a family where the same *MUTYH* mutation determined four different phenotypes, including a case of hyperplastic polyposis syndrome.

Patients and methods. A family with a history of right-sided colon cancer and multiple colonic polyposis was investigated. Genetic tests were correlated with clinical findings to define phenotypic manifestations of *MUTYH* mutations. The pertinent English-language literature was reviewed to evaluate the risk of malignancy of *MUTYH* and the role of prophylactic surgery.

Results. Three male siblings carried a biallelic *MUTYH* mutation (G382D-exon13), while the fourth was heterozygote. One developed an isolated cecal cancer at the age of 48. Another, aged 38, was diagnosed with numerous minute colonic and rectal polyps and underwent a proctocolectomy, with final pathology showing a picture of hyperplastic and lymphoid polyposis. The third biallelic brother, 46 years old, developed four hyperplastic lesions, while the heterozygote brother had a large flat serrated adenoma of the right colon removed at the age of 50.

Conclusion. Many aspects of *MUTYH* mutation still need to be clarified and one of them regards the different phenotypic expressions. Although the majority of reported cases manifested attenuated adenomatous polyposis, hyperplastic polyps and serrated adenomas appear to be more common than expected. Presenting hyperplastic polyposis syndrome is very unusual and may represent a clinical dilemma for correct management. Current evidence suggests to handle *MUTYH*-associated polyposis as typical FAP.

Key words: MutY human homologue (MUTYH), familial adenomatous polyposis, colorectal cancer, hyperplastic polyposis syndrome, serrated adenoma.

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