



Uma publicação semanal do Grupo Brasileiro de Estudos de Tumores Hereditários

Câncer de Endométrio e HNPCC (Câncer Colorretal Hereditário sem Polipose)

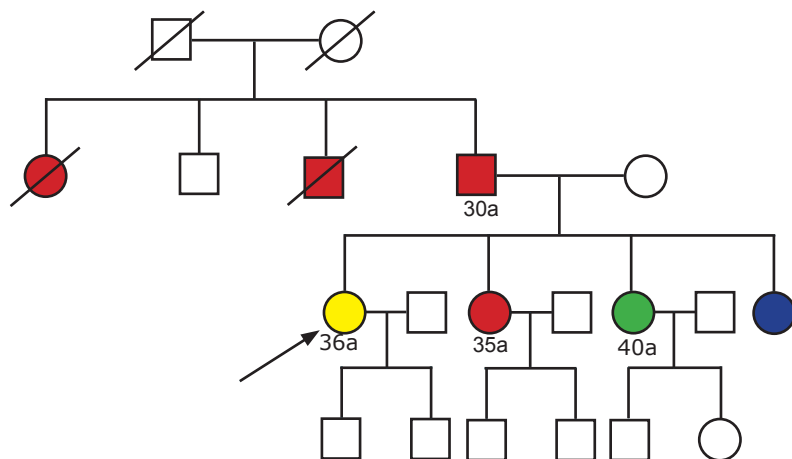
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Caso Clínico

CCT, 49 anos. Admitida no Departamento de Cirurgia Pélvica do Hospital do Câncer A.C. Camargo em 17 de agosto de 1998. Com antecedente de Adenocarcinoma de Cólon aos 36 anos, submetida a colectomia direita. Aos 46 anos foi diagnosticado Adenocarcinoma de endométrio, submetida a histerectomia e radioterapia adjuvante.

Heredograma



Legenda

- Câncer colorretal
- Câncer colorretal/Câncer de Endométrio/Adenoma
- Câncer colorretal/Adenoma
- Câncer de ovário

Idade indica a idade ao diagnóstico do primeiro tumor

A paciente pertence a uma família HNPCC pois preenche os critérios de Amsterdam. Realizou seguimento na Instituição com colonoscopias semestrais entre 1998 e fevereiro de 2003. Na colonoscopia realizada em fevereiro de 2003 foi diagnosticada uma lesão em cólon transverso, com anatomopatológico de adenocarcinoma bem diferenciado. Foi indicada totalização da colectomia com ileoreto anastomose. A paciente preferiu repetir a colonoscopia. No segundo exame foi realizada nova biópsia com anatomopatológico de colite inespecífica. Apesar de orientada quanto à necessidade da complementação da colectomia, a paciente não retorna ao hospital desde abril de 2003.

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É uma publicação semanal
distribuída aos sócios
do Grupo Brasileiro de
Estudos de
Tumores Hereditários.

Sede

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Câncer de Endométrio e HNPCC

Quadro 1. Risco de Câncer em Pacientes com Mutação nos Genes de Reparo.

Tipo de Câncer	Risco de Câncer em Pacientes com Mutação Identificada	Risco de Câncer na População Geral
Colorretal	70-82%	2%
Endométrio	42-60%	1,5%
Estômago	13%	<1%
Ovário	12%	1%
Rim/Trato Urinário	4%	<1%
Cérebro	3,7%	<1%
Via Biliar	2%	<1%
Intestino Delgado	1-4%	<1%

Fonte: Myriad. Disponível em <http://www.myriadtests.com/provider/cancerh1.htm>

Artigo: Instabilidade Microssatélite em Pacientes com Tumores de Cólon e Endométrio

High frequency of microsatellite instability and loss of mismatch-repair protein expression in patients with double primary tumors of the endometrium and colorectum.

Cancer. 2002 May 1;94(9):2502-10.

Planck M, Rambech E, Moslein G, Muller W, Olsson H, Nilbert M.

BACKGROUND: Patients with the familial syndrome hereditary nonpolyposis colorectal carcinoma (HNPCC) exhibit an increased risk for several tumor types, of which the greatest lifetime risk is for colorectal and endometrial carcinoma. HNPCC is caused by a germline mutation in one of several identified mismatch repair (MMR) genes and typically presents with microsatellite instability (MSI) and frequent loss of MMR protein expression in the tumor tissue. The objective of this study was to estimate the proportion of double primary tumors of the endometrium and colorectum that displays tumor characteristics suggestive of MMR deficiency. **METHODS:** The authors used the southern Sweden regional population-based Cancer Registry to identify women who developed double primary tumors of the endometrium and colorectum. Of the 256 women who were diagnosed with carcinoma at both of these sites during the period 1958-1998, 39 women had developed their first tumor before age 50 years. The authors successfully retrieved 67 tumors from 36 of these patients and analyzed them for MSI and immunohistochemical expression of the MMR genes, MLH1, MSH2, and MSH6. **RESULTS:** The MSI status of the 67 tumors was high MSI in 37 tumors, low MSI in 13 tumors, and microsatellite stable (MSS) in 17 tumors. Immunohistochemical loss of MMR protein expression was correlated with MSI status and was demonstrated in 29 high MSI tumors, in 1 low MSI tumor, and in 1 MSS tumor. A concordant loss of the same MMR protein in both tumors was found in 12 of 27 patients. **CONCLUSIONS:** The authors demonstrated a high frequency of MSI (75%) in tumors from women with endometrial and colorectal carcinoma who had their first tumor diagnosed before age 50 years and observed concordant immunohistochemical loss of MMR protein expression, suggestive of a possible underlying germline mutation, in 12 of 27 patients (44%). They concluded that double primary malignancies of the colorectum and endometrium at a young age should make the clinician suspect HNPCC.

Artigo: Risco de Câncer em Parentes de Primeiro Grau de Pacientes com Tumores de Cólon e Endométrio

A population based cohort study of patients with multiple colon and endometrial cancer: correlation of microsatellite instability (MSI) status, age at diagnosis and cancer risk.

Int J Cancer. 2001 Feb 15;91(4):486-91.

Cederquist K, Golovleva I, Emanuelsson M, Stenling R, Gronberg H.

Hereditary non-polyposis colorectal cancer, HNPCC, is an autosomal dominant condition predisposing to cancers of primarily the colorectum and the endometrium. The aim of our study was to identify persons at a high risk of hereditary colorectal cancer and to estimate their risk of colon and other HNPCC-associated tumours. Family histories of cancer were obtained on 89 persons with double primary (DP) cancers of the colon and the endometrium. The cancer risks in their 649 first-degree-relatives (FDR) were analysed. The microsatellite instability (MSI) status of the tumour of the proband was also analysed and the cancer risks were estimated in relation to MSI status and age at diagnosis in the proband (over or under 50 years). The overall standardised incidence ratio (SIR) was 1.69 (95% CI; 1.39-2.03). In the =50-year-old cohort the SIR was 2.67 (95% CI; 2.08-3.38). Colon, rectal and uterus cancer exhibited significantly increased risks. This risk was further increased in the =50-year-old MSI positive families. Several =50-year-old MSI negative HNPCC-like families with increased risks were also identified. In conclusion a FDR to a person with a DP cancer of the colorectum or the colon/endometrium have a significantly increased risk of having a colorectal or other HNPCC-associated cancers if the proband is diagnosed with one of the cancers before age 50. These families are candidates for genetic counselling and colorectal screening programmes. Mutations in mismatch repair genes can explain some of the increased risk in these families, but mutations in MSI negative families are probably due to other colon cancer susceptibility genes not yet described.

TABLE II - OBSERVED NUMBER OF CANCERS AND SIR IN FDR TO PROBANDS WITH DIFFERENT MSI STATUS IN PROBANDS WHO GOT THEIR FIRST CANCER DIAGNOSIS BEFORE OR AFTER THE AGE OF 50 YEARS

Site (ICD 7)	Probands \leq 50 n = 33			Probands $>$ 50 n = 46		
	Obs	SIR	95%-CI	Obs	SIR	95%-CI
MSI negative						
All	36	2.34	1.64-3.24	23	0.87	0.55-1.31
Stomach (151)	4	3.74	1.01-9.57	0	0.00	0.00-1.76
Colon (153)	8	7.27	3.13-14.33	2	1.10	0.12-3.97
Rectum (154)	2	3.13	0.35-11.28	2	1.83	0.21-6.62
Uterus (172)	3	6.41	1.29-18.72	2	3.02	0.34-10.89
Ovary (175)	2	3.72	0.42-13.42	0	0.00	0.00-4.75
MSI positive						
All	33	3.17	2.18-4.45	18	1.36	0.81-2.15
Stomach (151)	1	1.45	0.02-8.06	0	0.00	0.00-3.56
Colon (153)	15	21.13	11.82-34.85	3	3.30	0.66-9.63
Rectum (154)	1	2.33	0.03-12.94	3	5.66	1.14-16.54
Uterus (172)	1	3.00	0.04-16.68	4	11.07	2.98-28.34
Ovary (175)	2	5.24	0.59-18.93	0	0.00	0.00-8.44

Atenção: No dia 5 de agosto não haverá reunião científica.

Programação das Próximas Reuniões

Dia/Horário: Terças-feiras das 9 às 10 horas

Local: Sala de Reuniões da Pediatria

Data	Tema	Coordenador
12/08/2003	Retinoblastoma	Célia Antonneli