

Short Communication

A Second Family with Probable CRAC (Colorectal Adenomata and Carcinoma) Syndrome — A New Familial Cancer

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INTRODUCTION

Tomlinson et al. recently described a new familial cancer syndrome CRAC-1 (colorectal adenoma and carcinoma), with a phenotype characterised by bowel carcinoma with associated large colorectal polyps with a serrated adenoma histology [1]. Other cancers including pancreatic and renal and breast were described in the original SM1311 pedigree, although the authors were not sure if these were part of the tumour spectrum. We describe a similar family with virtually identical clinical features, suggesting a wider tumour spectrum is part of the CRAC phenotype.

CASE REPORT

Different members of the same family (see Figure 1) were ascertained independently in clinics in both Belfast and Leeds. Details of affection status were derived from histological reports and surgical operation records. A male proband II.4 was identified with rectal adenocarcinoma aged 37. He subsequently developed a primary caecal adenocarcinoma aged 53. A 3cm renal cell carcinoma was described at post mortem (age 53), and he also had 0.5 cm rectal and 1.0 cm sigmoid serrated adenomatous polyps. His daughter (III.4) developed breast cancer aged 37, and his brother (II.6) had two colonic polyps removed aged 40. His mother I.2 died from breast cancer diagnosed aged 54, and another sister (II.2) died from primary pancreatic cancer aged 46. There was a further extensive history of bowel and breast cancers on the maternal side of the family but histological confirmation was not possible. All cases were identified from family history following presentation of III.1 for genetic counselling. At that time no living affected relatives were available for DNA testing. Recently III.4 has been confirmed as having breast cancer and genetic testing will be possible if a sample is received.

All at risk relatives have been offered colonoscopy screening, and females have been offered yearly mammography and regular breast examination by a specialist.

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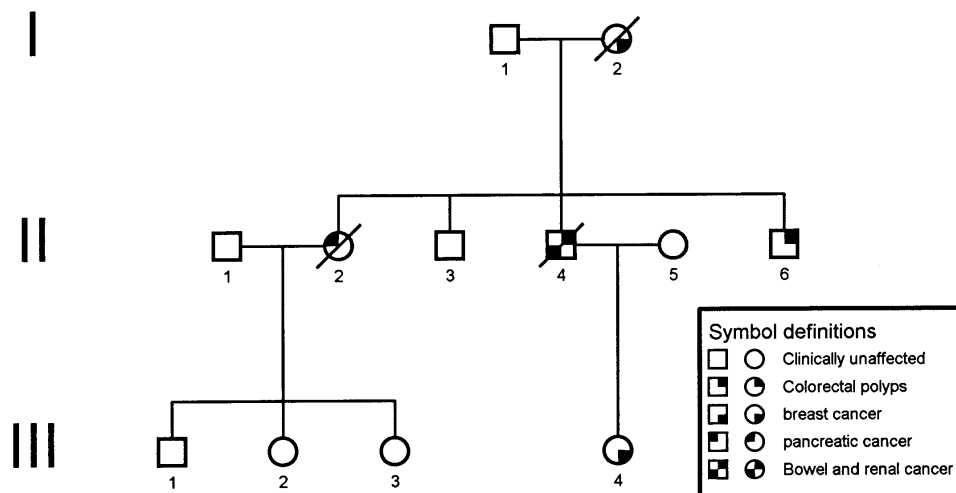


Fig. 1. Pedigree showing wide spread of tumours in addition to colorectal polyps and carcinomas.

DISCUSSION

The CRAC-1 phenotype was described in conjunction with colorectal adenomas and carcinomas with a characteristic serrated histology and associated renal and breast and pancreatic cancers. The original description in an Ashkenazi family, has shown linkage to chromosome 15q14-q22. The presence in our family of the same spectrum of extracolonic features suggest that these are part of the tumour spectrum of CRAC-1. This family, because of the tumour spectrum does not fulfill the Amsterdam criteria [2]. Although the original SM1311 family did, the clinical history in both families is not typical of HNPCC as there are more polyps than expected and the extracolonic features are not typical of the extended tumour spectrum seen in the common mismatch repair mutations [3,4].

Candidate genes in this region include *TYRO3*, *BCL8*, *FGF7*, *BUBR1* and *SMAD3* [5].

The phenotype in CRAC-1 appears to include colonic and extracolonic cancers including breast, renal and pancreatic tumours. Further studies are needed to further delineate the clinical phenotype and possible candidate genes. This will allow the true contribution of CRAC-1 in colorectal adenoma and carcinoma families to be evaluated.

CONCLUSION

CRAC1 is a new syndrome mapped to 15q14-22 with a propensity to colorectal adenomas and carcinomas. Other members in the original Ashkenazi pedigree developed pancreatic, breast, renal and caecal carcinomas. We confirm these cancers as consistent extracolonic features. Our family has no Jewish ancestry. The phenotype of CRAC syndrome includes a propensity to multiple pancreatic, bowel, renal and probable breast cancers.

Acknowledgement

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