



Alimentary Tract

Increased risk of breast cancer in first-degree relatives
of Crohn's disease patients
An IG-IBD study

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Abstract

Background. Increased rates of colorectal cancer have been reported in patients with ulcerative colitis as well as with Crohn's colitis. This risk could be the result of shared genetic susceptibility and could be co-inherited rather than being just secondary to a long-standing, extensive mucosal inflammation.

Aim. To assess the prevalence of all malignancies in first-degree relatives of Crohn's disease patients in order to establish whether any association exists.

Patients and methods. A total of 632 outpatients with a diagnosis of Crohn's disease and 632 control subjects were recruited. Information concerning the presence of malignancies was collected in 3292 first-degree relatives of Crohn's disease patients and in 3303 first-degree relatives of controls.

Results. Two hundred and fourteen (6.5%) subjects were found to be affected by malignancy in the first-degree relatives of Crohn's disease patients and 180 (5.5%) in the first-degree relatives of controls. Forty-seven (7.4%) of Crohn's disease patients had a first-degree relative with IBD, but none of them had cancer. The frequency of extra-intestinal malignancies was higher in first-degree relatives of Crohn's disease patients than in those of controls ($p = 0.011$). Frequency of breast cancer in female relatives of Crohn's disease patients, mainly in mothers, was two-fold higher than that in controls (0.91% versus 0.42%; odds ratio = 2.16; 95% confidence interval = 1.14–4.08; $p = 0.015$). The presence of breast cancer showed no association with any specific phenotype of disease in Crohn's patients.

Conclusions. These results did not corroborate the hypothesis about a common genetic susceptibility between Crohn's disease and colorectal cancer. An unexpected finding was the more frequent occurrence of extra-digestive malignancies. The prevalence of breast cancer in first-degree relatives of Crohn's disease patients, in particular the mothers, was more than double than in those of controls. This

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¹ See Appendix A for the list of members.

association, if confirmed, would suggest that there may exist common genetic and/or environmental factors for Crohn's disease and breast cancer.

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1. Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are two distinct yet similar diseases that are both marked by chronic and relapsing inflammation. A series of studies have reported both UC [1,2] and CD [3–6] to be associated with an increased risk for developing precancerous dysplastic epithelial changes and colorectal cancer (CRC). Data that support as well as refute the hypothesis that CD is associated with an increased risk of CRC exist. However, increasing data demonstrate a similar risk of CRC in CD of the colon and in UC. Earlier studies did not adjust for the absence of colonic disease, a history of colonic resection, or the duration or extent of disease, and this probably resulted in the apparently lower risk of CRC in CD. Ekbom et al. [5] found that the relative risk of CRC in patients with CD irrespective of disease localisation was approximately 2.5, but in Crohn's colitis, the relative risk was 5.6, which is similar to the relative risk seen in UC.

Several studies show an excess of cancer of the small intestine [6] on the basis of only few cases [7]. Several extra-intestinal cancer types such as squamous cell skin cancer, non-Hodgkin's lymphoma, vulvar cancer and bladder cancer have been found to occur more frequently among patients with CD compared to the general population [8–10].

This cancer risk could be the result of shared genetic susceptibility and could be co-inherited rather than being just secondary to a long-standing, extensive mucosal inflammation [11]. In this case, the relatives of IBD patients should show an increased prevalence of malignancies than the general population. Earlier studies [12–14] failed to show an increased risk of CRC in first-degree relatives of patients with IBD.

Aim of the present investigation was to assess the prevalence of malignancies in first-degree relatives of CD patients in order to establish whether any statistical association exists.

2. Patients and methods

A case-control study has been carried out to examine the frequency and risk of malignancies in a large number of first-degree relatives of CD patients stratifying these rates according to age, type of disease and extent of inflammation upon diagnosis of CD.

A total of eight Italian centres, specialised in the management of IBD, were invited to provide clinical information on consecutively admitted CD patients. Patients with no evi-

dence of gastro-intestinal diseases, pair-matched for gender, age ± 5 years and living in the same geographic area as the CD patients were recruited from orthopaedic clinic as controls.

A total of 632 outpatients (53.0% males, mean age 40.3 ± 14.1 years, range 2–85 years) with a definite diagnosis of CD [15] but with no evidence of cancer and a same number of control subjects (mean age 39.7 ± 15.1 , range 3–83 years) were recruited. Clinical characteristics of the patients included in the study, according to Vienna classification, are shown in Table 1.

Data regarding first-degree relatives divided into parents, siblings and offspring focusing on their medical history (presence, age at onset and type of malignancies, age and cause of death) were obtained through a questionnaire submitted to CD patients and controls. Digestive cancers included all malignancies which were directly related to the CD or associated with sclerosing cholangitis. All the others were included as extra-intestinal malignancies. Information regarding family history for IBD among CD patients was registered as well.

Accuracy of the data was ensured by consulting medical practitioner's records of only the first-degree relatives of the CD patients. Data on smoking status of first-degree relatives of patients and controls were not collected.

Information concerning the presence of malignancies was collected in 3292 (about 93%) first-degree relatives of CD patients and in 3303 (about 95%) first-degree relatives of controls.

Statistical analyses were performed using the SPSS statistical package for Windows (release 11.0.1—SPSS Inc., Chicago, IL, USA). Descriptive statistics are provided as mean, standard deviation (S.D.) and frequencies. Univariate

Table 1
Description of CD patients

N	632
Sex	
Male	53.0%
Age at diagnosis	
<40 years	78.8%
Site of disease	
Ileum	41.4%
Ileo-colon	31.2%
Colon	25.4%
Upper GI tract	1.9%
Behaviour of disease	
Penetrating	18.4%
Strictureing	37.1%
Inflammatory	44.5%

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