Journal of Crohn's and Colitis (2014) xx, xxx–xxx

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Impact of the diagnosis and treatment of cancer on the course of inflammatory bowel disease

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Received 3 December 2013; accepted 29 December 2013

KEYWORDS:
Cancer;
Inflammatory bowel disease (IBD);
Therapeutic management;
Immunomodulators

Abstract

Background: The effects of extra-intestinal cancer on the course of inflammatory bowel disease (IBD) are poorly understood.
Aim: To evaluate the impact of cancer and its management on IBD outcomes.
Methods: A total 80 IBD patients (51 Crohn's disease, 29 ulcerative colitis; 33 men, median age at cancer diagnosis 48 yrs) diagnosed with extra-intestinal cancer were selected from a prospective database. IBD activity and therapeutic requirements (assessed year-by-year) were compared before and after cancer diagnosis, with a control group of patients without cancer matched for gender, birth date, date of IBD diagnosis and IBD phenotype.
Results: Paired comparisons of the consecutive periods before and after cancer diagnosis did not show significant changes in median (IQR) percentages of years with active disease (27% [0–50] vs. 19% [0–53]), while the proportion of patient-years on any immunosuppressant remained stable (26% vs. 28%). Chemotherapy had no significant effect on IBD activity. Compared to controls, patients with cancer had a similar IBD activity and use of anti-TNF, but less use of immunomodulators (19% vs. 25%, $p < 0{,}001$) and an increased rate of surgery (4% vs. 2.5%, $p < 0{,}05$). Individual variations in IBD activity after cancer diagnosis were not significantly different in patients with cancer and their matched controls.
Conclusion: Occurrence of extra-intestinal cancer impacts IBD therapeutic management, with a trend towards less use of immunomodulators and more surgery. In the long-term, cancer diagnoses and treatments do not modify IBD outcomes.

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1873-9946/$ - see front matter
http://dx.doi.org/10.1016/j.crohns.2013.12.022

Please cite this article as: Rajca S, et al, Impact of the diagnosis and treatment of cancer on the course of inflammatory bowel disease, *J Crohns Colitis* (2014), http://dx.doi.org/10.1016/j.crohns.2013.12.022

1. Introduction

Incidences of both inflammatory bowel disease (IBD) [1] and cancer [2] are increasing worldwide, and patients with IBD have an increased lifelong risk of intestinal and extra-intestinal malignancies.[3] Associated IBD has a negative impact on the prognosis of extra-intestinal cancer independent of TNM staging.[4] In a Danish population study, breast cancer patients with CD had a shorter survival compared to breast cancer patients without CD.[5]

Conversely, little is known about the evolution of IBD in patients diagnosed with malignancies. On one hand, oncologists usually recommend avoiding immunosuppression, taking into account the risk of relapse or the worsening of the cancer while on immunosuppressive drugs,[6,7] yet at the present time approximately 50% of IBD patients are receiving immunomodulators or anti-TNF. In addition, cancer treatment may be associated with IBD reactivation.[8] Moreover, extensive and metastatic cancers may worsen the course of IBD through activation of the inflammatory process.[9] Thus, diagnosis and treatment of extra-intestinal cancer may have significant impacts both on the therapeutic strategies and IBD activity. The aim of the present study was to assess the long-term impacts of diagnoses of extra-intestinal cancer and cancer treatments on IBD outcomes.

2. Materials and methods

2.1. Study population

Patients were enrolled from the MICISTA Registry, a clinical database of all patients with IBD evaluated by the same staff of physicians at St Antoine Hospital from 1975 to the present. This database included 7158 patients as of December 2011. Data were collected retrospectively before 1995 and prospectively afterwards. A history of cancer or current cancer was specifically noted in the database.[10] Patients with diagnoses of extra-intestinal cancer between 1990 and 2009 were selected. Exclusion criteria were a history of intestinal cancer, a follow-up duration below 6 months after cancer diagnosis, skin cancer in patients older than 90-years old, loss to follow up before 1995, and cancer in remission for more than 10 years at the date of IBD diagnosis.

Selected cancer patients were anonymously matched in a 1/3 ratio to 240 patients without cancer (1/3) that constituted a control group. Matching criteria were as follows: gender, birth date (in windows of 5 years), calendar year of diagnosis (windows of 5 years), and disease phenotype (ulcerative colitis [UC] or Crohn's disease [CD]).

2.2. Evaluation of disease evolution

IBD activity was assessed year-by-year by analysing the occurrence of flare-ups, hospitalisation, or abdominal surgery. This was codified prospectively at each visit or hospitalisation for every calendar year according to a pre-established gradation from 0 to 5.[10] Each patient-year was considered as active (activity score >1) if a flare-up requiring a therapeutic modification or a complication occurred during the year, or in the case of chronic active disease, and inactive in the other cases (activity score <2). Flares and hospitalisations were taken into account only when symptoms were related to active IBD and not therapy-related or cancer-related. Similarly, only intestinal surgical procedures performed for IBD or IBD-related complications were taken into account and codified in the hospitalisation group. Restorative procedures performed in a patient with inactive disease were not included in the grading. Disease evolution was assessed using the same criteria in matched controls, considering a caesura date corresponding to the date of cancer diagnosis of the index case.

2.3. Treatment

The principles for the treatment of CD and UC in our unit have been detailed elsewhere.[10] Briefly, disease flares were treated with mesalamine, steroids, or (after 1999) anti-TNF. Maintenance therapy used aminosalicylates, immunomodulators (azathioprine [AZA] as first line drugs, methotrexate in patients unresponsive or intolerant to AZA, or anti-TNF, according to clinical severity. The overall strategy remained mostly unchanged over time; however, there was a distinct tendency to initiate immunosuppressants earlier in the disease course after 1990.[11] Surgery was performed for stenotic complications, extra-parietal complications, neoplasia or intractable forms of CD or UC after well-conducted medical management. In patients with cancer, maintenance and type of immunosuppressants were discussed with the oncologist or the related specialty consultant.

The maximum treatment received by one patient during each calendar year was codified prospectively at each visit or hospitalisation, according to a pre-established gradation (0–5).[10] All treatment(s) were taken into account, even for treatments of short duration.

2.4. Statistical analyses

Continuous data are expressed as medians with interquartile range (IQR), and differences between the groups were tested for significance with Wilcoxon rank sum tests for paired or unpaired comparisons as appropriate. Discrete data are given as percentages, and comparisons were made with Pearson chi-squared tests. Periods before and after the diagnosis of cancer were compared both at the individual level and after pooling patient-years within the period considered. The year of diagnosis of cancer was included in the period prior to cancer when the diagnosis of cancer was made before June 30 of the calendar year, and in the subsequent period in the other cases. Inter-individual comparisons considered the period preceding cancer diagnosis and the period subsequent to cancer diagnosis. Only patients having durations of follow-up lasting more than one year both before and after diagnosis of cancer were included in this comparison. Percentages of patient-years were calculated by pooling all patient-years within each consecutive period. Subset analyses were performed in patients who received cytotoxic chemotherapy.

Comparisons with the control group first considered the total of patient-years of the period subsequent to the date of cancer diagnosis in the two groups. In addition, a paired comparison was performed considering the variations of mean individual percentages of years with active disease,

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