

Crohn's disease in adult from Maringá region: case report and review

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Abstract

Crohn's disease and ulcerative colitis are the main chronic disorders related to inflammatory bowel disease. The reasons are not yet clarified, but epidemiological studies suggest the involvement of immunology, genetics and environmental causes. In addition, Crohn's disease can affect any part of the gastrointestinal tract, and it is characterized for being a granulomatous, fibred and segmental disorder, preferentially of the ileum terminal region and the colon. Due to the difficult to understand its etiology and lack of information to obtain a precise number of its incidence, sometimes the treatment is not always adequate. Thus, the present work had as objective to report a Crohn's disease case in adult, and also to expand the knowledge about this pathology.

***Keywords:* Crohn's disease – Epidemiology; Inflammatory bowel disease.**

INTRODUCTION

Crohn's disease, also denominated as ileitis, is a granulomatous, fibrous and segmental affection of any part of gastrointestinal tract, but principally affects the ileum terminal region (regional or segmental enteritis) and the colon.

In 1932, Crohn reported 14 cases of inflammatory bowel disease named as terminal ileitis (CROHN; GINZBURG; OPPENHEIMER, 1932). Beyond that, in the same year, Ginzburg and Oppenheimer had published a series of case reports, designating them as regional enteritis, since in an initial vision they believed that only the terminal ileum would be involved (ANDERÍ JÚNIOR; LARANJEIRA; PESSOTI JÚNIOR, 2001). However, the involvement of colonic region by this pathology was firstly described by Lockhart-Mummery and Morson (1960). Therefore, the authors concluded that the same

disease could compromise all gastrointestinal tract, as well extradigestive tissular regions

Crohn's disease and ulcerative colitis are the mainly disorders that promote inflammatory bowel diseases (ESZTER, 2004). The inflammatory cause of bowel diseases remains unknown, but epidemiological genetic studies suggest that inherited factors, as well as immunologic susceptibility, environment and life styles, might contribute in part for individual susceptibility variation, and consequently, result in its development. Further, according to Associação Brasileira de Colite Ulcerativa e Doença de Crohn (ABCD), there are not precise estimative of this pathology in Brazil. Normally, the ABCD presents representatives in the main capitals of Brazil, but Maringá is the only non-capital city, until the present moment, to host one of them.

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Therefore, due to the worldwide increasing incidence of Crohn's disease and also to the difficulty to understand its aetiology, the present work had as objective to report and to amplify the knowledge about this pathology.

CASE REPORT

A male patient from rural zone, Caucasian, at age of 29 years was admitted in the clinic as carrier of Crohn's disease in the ileal region, after medical confirmation. According to the patient, the clinical features that made him to look for medical assistance was the presence of chronic diarrhea (recurrent situation for more than six weeks), intestinal cramps, abdominal mass and weight loss. After a combination of symptoms and radiology exams, as well as endoscopy, the disease was diagnosed and also verified the presence of stenosis. In February of 2007, the patient was submitted to ileal-colonic surgery. The medical treatment adopted was based on combination of one aminosalicilate (mesalazine) and one immunomodulator (azathioprine). Due to that, the only side effect related by the patient was the swelling. Even though, there is not family history of inflammatory bowel disease, he presents a combination of Italian and Japanese descent. The patient had suffered three hospitalizations and even presenting O positive blood type, blood transfusion was never needed. Even though he does not fit into the smoker group, he did not exercise and until now, his sedentary habit is maintained. The diet of cereals, vegetables, fruits, dairy foods, red meat, oils (fried foods) and fish consumption, before diagnosis of Crohn's disease was considered regular. However, changes had occurred in his diet, and now it presents more restrictions to cereals, vegetable, dairy food, and also oils. The quality of life was measured according to Pontes and others (2004) survey, whose low scores correspond to low quality whereas the high ones are related to great quality. The patient had a balance among all the evaluated aspects to determine quality of life, although the emotional aspect is a little lower than the average (TABLE 1). Furthermore, he claimed to present stress and depression features, but did not look for psychological-medical assistance. Today, at the age

of 30 years old, the patient is married, an administrator of a small store, from which he makes a monthly salary of approximately 5 minimum salaries (from R\$700.00 to R\$1,749.00).

Table 1 – Quality of life score

Variables	Score	Minimum	Maximum
Intestinal symptoms	58	10	70
Systemic symptoms	30	5	35
Social aspects	35	5	35
Emotional aspects	14	7	21

Fonte: PONTES et al., 2004.

DISCUSSION

According to studies carried out by Molinié and others (2004), the mean incidence of Crohn's disease (CD) in the North region of France was 6:100.000, being more common in group of 20-29 years age. Further, it was observed an increase and predominance of the ileal-colonic affection. However, United States and most of West European countries demonstrated an average of 6-7:100.000 (GASCHE; GRUNDTNER, 2005). On the other hand, a study about the occurrence of Crohn's disease during the period from 1980 to 1999 in Ribeirão Preto - Brazil, pointed out an increase of incidence from 17 to 30 cases:10.000 attended (SOUZA et al., 2002). Beyond that, the authors concluded that due to the scarcity of registered data, it turns out to be difficult to estimate the incidence of Crohn's disease not only in Brazil, but also in the developing countries.

Generally, this pathology affects compromised individuals at the age from 20 to 30 (MOLINIÉ et al., 2004; STEPHEN et al., 2001), also being possible a predominance in the fourth and fifth decade (SOUZA et al., 2002). In addition, most patients are considered Caucasian and belong to female gender (MOLINIÉ et al., 2004; STEPHEN et al., 2001; SOUZA et al., 2002). Nonetheless, in this case report, only the gender does not fit in the standard described by national and international studies.

Chronic diarrhea, a reduction of stool consistency for more than six weeks, is the most common symptoms of Crohn's disease (STANGE et al., 2006). Additional, abdominal cramps, abdominal mass, weight loss, perianal fistulas and

abscesses are also symptoms that characterize this pathology (STEPHEN *et al.*, 2001; FIOCCHI, 1998). According to Fiocchi (1998), weight loss, chronic and/or nocturnal diarrhea, abdominal pain and anal bleeding reflect the evolution of the inflammatory process. Furthermore, approximately 70% of patients have abdominal pain, whereas 60% of them exhibit signals of weight loss even before of medical diagnosis (STANGE *et al.*, 2006). In contrary to the reported case, normally the smokers are more susceptible to the development of fistulas or stenoses (LOUIS *et al.*, 2001).

In general, the involvement of extra-intestinal manifestations is related to children (ANDERÍ JÚNIOR; LARANJEIRA; PESSOTI JÚNIOR, 2001). Thus, articular, ophthalmologic, skin, thromboembolic, hepatobiliary abnormalities are considered extra-intestinal characteristics (STANGE *et al.*, 20006; SOUZA *et al.*, 2002), whose manifestation is common when CD affects the colon region (STANGE *et al.*, 2006).

The ileum and colon, normally, are the most compromised gastrointestinal tract regions by intestinal obstruction, inflammatory mass and abscess (FARMER *et al.*, 1985; MEKHJIAN *et al.*, 1979).

The inflammatory cause of CD is unknown yet, however, not only environmental factors, such as diet and microorganism, but also inherited factors might contribute in part for the individual susceptibility variation, for this disorder (TAYLOR; YANG; ROTTER, 2001). Nevertheless, it is believed that in susceptible individuals the present pathology results in a sequence of cascade events and processes, initiated by one or more hypothetic antigens (JAFRI; PASRICHA, 2003). The innate immune response to intestinal flora expresses bacterial metabolites through intestinal receptors and macrophages, inducing a large liberation of pro-inflammatory mediators (CARIO; PODOLSKY, 2000; ALLISON; POULTER, 1991). Therefore, interleukin 1b (IL-1b), tumor necrosis factor-alpha (TNF-a) and interleukin 6 (IL-6) are able to lead a selective innate immune response (BAUMANN; GAULDIE, 1994). Therefore, leucocytes recruitment and addition of integrins and selectins proteins result in transmural inflammation with granulomas (GUSTOT *et al.*, 2005).

Recently, NOD2/CARD15 was the first gene associated to CD (HUGOT *et al.*, 2001; OGURA *et al.*, 2001), present in chromosome 16q12. The three possible mutations are not necessary or yet not sufficient to express the phenotype of this disorder; thus, they are not able to explain more than 20% of genetic predisposition in Caucasians (GASCHE; GRUNDTNER, 2005). Additional, the mutations in NOD2 are rarely detected in Japanese (INOUE *et al.*, 2002; YAMAZAKI *et al.*, 2002), suggesting that this gene is might not be determinant.

Machida and others (2005) suggested for the first time that the gene correlated to N-acetyltransferase (NAT2), might be one of the possible genetic factors for predisposition of CD development. The NAT2 is responsible to constitute the protection biochemistry barrier against xenobiotics provided by food, intestinal bacteria and toxins. Thus, its diminution implies in increasing of gastrointestinal tract permeability, and consequently, accumulation of these agents in the body results in inflammatory diseases, especially CD. The Crohn's disease activity is classified in three categories: mild, moderate and severe (STANGE *et al.*, 2006; STEPHEN *et al.*, 2001). The first one involves symptoms as fever, dehydration, abdominal mass and weight loss inferior to 10% of original weight. However, the moderate category is applied to patients that do not present improvement with treatment, severe weight loss, significant anemia, constant vomiting and nausea, and abdominal pain. Finally, severe category, despite of the intensive treatment, the symptoms persist even more, presenting high fever, cachexia, besides intestinal obstruction and evidences of abscess presence.

The treatment of a patient with active disease in the ileal region preferentially is done with the use of glucocorticoids, especially budesonide 9mg/day due to its low side effects. The mesalazine, however, is not recommended because it does not demonstrate efficient effects. Conversely, the utilization of antibiotics, associated or not with mesalazine is recommended. Nonetheless, the treatment for moderate CD preferentially recommends the using of budesonide 9mg/day, as well as antibiotics, in case there are suspicious of septic complications (TRAVIS *et al.*, 2006; JAFRI; PASRICHA, 2003). The severe category of CD

initially should be treated with systemic corticoids, being necessary the addition of azathioprine for patients that would present relapse.

The mesalazine is an aminosalicylate used for inflammatory bowel diseases due to its local actions (JAFRI; PASRICHA, 2003), and it is considered an effective treatment for ileal, ilealcolonic, and colonic compromised regions (MALCHOW et al., 1984; SUMMERS et al., 1979). Even so, recently, this concept has changed (COSNES et al., 2005), after studies had revealed that mesalazine was not so effective as placebo for treatment of ileal and colonic activity in CD (TRAVIS et al., 2006; FEAGAN, 2004).

The immunomodulators are important because of their capacity to induce and maintain immune tolerance, or active stage of absence of specific response to antigen through depression of lymphocytes proliferation, or still due to cytotoxicity of natural killer cells (JAFRI; PASRICHA, 2003). Therefore, azathioprine, consists in a second line of treatment for patients with CD in severe category or still those ones that are resistant or dependent on steroids (PEARSON et al., 1995). Furthermore, studies conducted by the same authors revealed that the using immunomodulator was probably not significant because the administration was belated and inadequate during the disease course. On the other hand, according to D'Haens, Geboes e Rutgeerts (1999), even if administrated in the beginning of the pathology, the immunomodulators could not supply prevention effect against the development of stenoses and fistulas. Pearson and others (2000) observed that azathioprine not only present positive effects to maintain CD remission, but also points out the capacity to save and reduce the necessity of steroids to take care of patients. However, the main reason is still the occurrence of surgeries due to complications during the disease

course, such as intestinal obstruction and stenosis (COSNES et al., 2005).

The adopted proceeding to carry out a surgery must be individualized, objective and to promote economic resections, since patients are normally in inadequate nutritional condition. Further, large resections are not a guarantee of better results, since normally it is not possible to predict recurrence and their localizations (STANGE et al., 1995; RUTGEERTS et al., 1995).

In the case reported there was a necessity of surgery resection in the ileal-colonic region, which allowed an improvement of patient's general condition. In addition, the utilization of immunomodulators with a controlled diet, demonstrated to be important factors to maintain the life quality of the patient. On the other hand, the analysis of the values obtained through the survey (PONTES et al., 2004) showed better results for intestinal symptoms, systemic symptoms and social aspects; whereas for emotional aspects it was a lower:

Furthermore, recent analyses demonstrated that determined lived events could be associated with high risk of relapse (MAWDSLEY; RAMPTON, 2005). The depression, and in lower intensity the stressful lived events, might be the relapse precursors (MARDINI; KIP; WILSON, 2004).

CONCLUSION

In conclusion, it is evident that genetic variation and environmental factors, must be meticulous studied to define the type of immunological susceptibility and prevent adverse events from the drug treatments. Hence, since expanded knowledge about its etiology to health care professionals, it will provide attitudes and specific preventive treatments according to the necessity of each patient looking for a better life quality.

Doença de Crohn em adulto na região de Maringá: relato de caso e revisão

Resumo

A doença de Crohn e a colite ulcerativa são as principais patologias crônicas relacionadas com a desordem de inflamação intestinal. As causas ainda são desconhecidas, mas estudos epidemiológicos

sugerem que a imunologia, a genética e o ambiente sejam os possíveis fatores. Além disso, a doença de Crohn pode acometer qualquer parte do trato gastrointestinal, principalmente as regiões do íleo terminal e do cólon, e é caracterizada por ser uma desordem granulomatosa, fibrosa, e segmentar. Portanto, devido à dificuldade de se entender a sua etiologia e à falta de dados adequados correspondentes à sua incidência, em alguns casos o tratamento nem sempre é adequado. Dessa forma, o presente trabalho teve como objetivo relatar um caso de doença de Crohn em adulto, e também expandir o conhecimento com relação a essa patologia.

Palavras-chave: Crohn, doença de – epidemiologia; inflamação intestinal.

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