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SHORT REPORT

A family report of Crohn's disease in three children immigrating from Albania to Greece and review of the literature

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Abstract

Cases of immigrant families affected by IBD have rarely been reported and seem to be of exceptional interest towards a better understanding of disease aetiopathogenesis.
The first case of Crohn's disease in a family of immigrants from Albania to Greece with three offspring is described herein. A family with three children, one 22 year-old male and two 18-year-old twin females immigrated from southern Albania to northwest Greece ten years ago. The whole family lived in the same house and had no previous history of bowel or other chronic diseases. Two years ago the boy complained of diarrhoea, perianal pain and loss of weight. Subsequent investigation revealed ileal and perianal Crohn's disease. One year after Crohn's disease was diagnosed in the boy, one of the twins was diagnosed with ileal Crohn's disease. Six months afterwards, the second twin underwent emergency appendectomy due to acute appendicitis; four months later she was diagnosed with ileal Crohn's disease.
Genetically predisposed individuals seem to be vulnerable to a continuous pressure of a still unknown environmental factor(s). In addition, lifestyle modification seems to represent a predisposing factor toward inflammatory bowel disease in immigrants.

1. Introduction

Nowadays, immigrant ethnicities or immigrants have accumulated in sufficient an adequate number in many host countries to allow epidemiological observation in IBD. Migration studies showed that in Israel the incidence of IBD among European and American immigrants differs from those who immigrated from Asia and Africa.[1,2] In Hungary, there are also some observations regarding the influence of racial factors with Roma (Gypsy) population having less than half of the IBD incidence of the rest of the population.[3]

An epidemiological study of Crohn's disease in Leiden, the Netherlands, showed that the lack of Crohn's disease cases in

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the migrant population has almost reached significant levels when compared to native population.[4] In UK, over a 15-year period only six patients of Afro-Caribbean origin presented with ulcerative colitis from a community of this ethnic extraction numbering almost fifty thousand persons.[5] In Bangladeshis in East London, the incidence of IBD has increased and that of abdominal tuberculosis has fallen over the last decade.[6]

In USA there is a varying incidence of IBD in the minority populations.[7] A study in Texas has shown that African Americans and whites predominantly had CD whereas Mexican Americans predominantly had UC.[8] In the same study, a family history of IBD was more common in whites than in black Americans. In Canada, aboriginal Canadians show significantly lower rates of both Crohn's disease and ulcerative colitis compared to native Caucasians.[9] Family cases of immigrants affected by IBD have rarely been reported and seem to be of exceptional interest towards a better understanding of disease aetiopathogenesis and potential risk factors related to immigration. We describe herein the first family case of Crohn's disease with three children immigrating from Albania to Greece.

2. Family report

A family with three children, one 22 year-old male and two 18-year-old twin females immigrated from southern Albania to northwest Greece ten years ago. The entire family lived in the same house and history of bowel problems of other chronic diseases of any kind of atypical symptoms all these years was unremarkable.

The ancestry of the family was of common Albanian origin and parents were unrelated to each other. None of the family members was current or ex-smoker.

Two years ago the boy complained of diarrhoea (10 watery bowel movements per day), perianal pain and a 10 kg loss of weight and was referred to our Department. Subsequent investigation revealed ileal and perianal Crohn's disease and the boy was began treatment with azathioprine at a dose of 2 mg/kg. Despite initial response to azathioprine, Crohn's disease recurred frequently and necessitated consistent steroid treatment. Specifically, in order for the patient to achieve remission a dose of 16 mg/d methylprednisolone was required. After careful consideration the boy was switched to Infliximab monotherapy (5 mg/kg) and he has since then achieved long-term ileal and perianal disease remission.

One year after the Crohn's disease diagnosis in the boy, one of the twins was admitted for investigation of one-month diarrhoea (6 watery bowel movements per day) and persisting amenorrhoea for the previous year. Patient was anemic with hemoglobin at 9.5 g/dl and iron deficient. Subsequent investigation revealed ileal Crohn's disease with large serpigenous ulcers and severe inflammation. The girl was started on therapy with corticosteroids (induction scheme with methylprednisolone at 24 mg/d and subsequent tapering) and azathioprine maintenance treatment (2 mg/kg). In addition, patient received intravenous iron for the correction of iron deficiency.

Currently the patient is in long-term remission with Hb at 12 g/dl while amenorrhoea ceased.

Six months after Crohn's disease was diagnosed in the first of the twins, the second twin was diagnosed with acute appendicitis and as a result, underwent emergency appendectomy at another hospital. Post-surgery recovery was laborious with abdominal sepsis and fistula formation at the site of incision and the patient required long-term antiobiotic treatment with ciprofloxacin and metronidazole. The pathology of the removed appendix was not supportive of Crohn's disease at that time and the twin was discharged after one month of hospitalisation in very good condition and without any treatment. However four months later the same twin complained of diarrhoea (4 watery bowel movements per day), lower right quadrant abdominal pain and a 5 kg loss of weight. Subsequent investigation with conventional endoscopy and capsule endoscopy confirmed ileal Crohn's disease. The girl was started on induction therapy with corticosteroids (16 mg/methylprednizolone with tapering scheme) and azathioprine at 2 mg/kg and is currently in remission. No extraintestinal manifestations have been recorded so far in any of the three siblings.

We attempted genetic testing but unfortunately both parents and children refused to sign the consent form required in our biobanking facilities in order to proceed further with genetic analysis.

In addition, the change in habits and lifestyle of this migrant family was thoroughly investigated using the ECCO EpiCom scheme for environmental factors related to IBD (http://www.epicom-ecco.eu). However it has not been possible to identify any environmental factor that could clearly be related to the high incidence of IBD in this family.

3. Discussion

We presented herein the first family report of Crohn's disease in immigrants from Albania to Greece. This family case demonstrates some interesting characteristics that are worthy of discussion.

First, all three offspring were diagnosed with the same type of inflammatory bowel disease, namely Crohn's disease. Crohn's disease had the same phenotype in all three with ileal involvement plus the perianal location in the male patient. However, the presenting symptoms were not identical.

Second, it is anecdotally reported that Crohn's disease is extremely rare in Albania while ulcerative colitis is not infrequent [J.B personal communication]. By contrast, Crohn's disease seems to be somewhat frequent in northwest Greece (mean annual incidence now is 1.6 per 10^5 inhabitants), although comparatively lower to the rates of northern Europe that is increasing.[10] Of note, the distance between family origin and immigration place was less than 100 km. However, it has to be emphasized that before 1993 borders were closed and there was no possibility of trade or freedom of travel between Albania and Greece.

Although there is a lack of sufficient statistical evidence from Albania, we have the impression that currently the inflammatory bowel disease in Albania very much resembles that of Greece as it was three decades previously[11] and that is probably evolving. Along these lines, the incidence of Crohn's disease in immigrant South Asians is significantly lower compared to that of Europeans.[12] Of note, IBD occurs sporadically among the immigrant Asian population in

Britain.[13] The epidemiological changes that are taking place in Asia mirror that of the Western experience witnessed over the previous 50 years and seem to occur in parallel with the rapid socioeconomic development taking place in Asia. It appears that certain racial groups are more prone to developing IBD than others, when exposed to hypothetical environmental factors. For instance, Indians in South-East Asia exhibit higher rates compared to the Chinese and Malays.[14] According to a study from Québec immigrance has been an independent predictor of Crohn's disease occurrence among population.[15] In another study from Manitoba, higher incidence of IBD was directly related to higher average family income, reversibly related to immigrant and aboriginal Canadian populations, and smaller average family size.[9] Tuberculous colitis must be always excluded in cases occurring in the immigrant population.[16,17]

Third, during this decade of immigration to Greece this family, like many others, abandoned the Albanian and adopted the modern Greek lifestyle, including diet. Modern Greek lifestyle and diet still has many Mediterranean characteristics but in urban areas and big cities it is gradually changing to a more 'westernised' nutritional model. 'Westernised' seems to be more of an operant term than 'industrialized' because in highly-industrialized Asian countries such as Japan and Korea, IBD incidence is still low, but increasing.[18]

Fourth, the time frame of sequential diagnoses — truly a domino effect — points towards an environmental factor to which all three siblings, and probably also their parents were exposed during the same period of time of their stay in Greece. At this time there is no explanation why the parents were not affected by Crohn's disease. It would be of exceptional interest if any other family members could be investigated for any evidence of silent Crohn's disease at the time of diagnosis of the disease in the three siblings.[19] In the first reported instance of familial Crohn's disease, the father developed Crohn's disease almost three decades after his arrival in Canada. Another interesting report is that of a family of five children, all five of whom had Crohn's disease.[20] Familial Crohn's disease screening could explain some of the mystery of familial aggregation but for the time being it is considered medically and ethically inappropriate.

Fifth, it is noteworthy that all three children from Albania developed Crohn's disease after many years of immigration to Greece. This phenomenon has been observed worldwide in immigrant and familial immigrant cases and it is pointing towards an aetiological factor that is continuously or intermittently attacking the immune system. In Birmingham, in a study with Asian immigrants and age- and sex-matched white Caucasians, it has been shown that the age of onset of UC was related to age at immigration with a mean interval of 11 years.[21]

In a three-year prospective study[22] among Europeans and first- and second-generation South Asians in Leicester it was shown that extensive colitis was more common in second-generation South Asian migrants than in the first generation and was comparable to that of the European community.

For immigrants, the mean duration of residence in Canada before developing IBD was 8.9 years for Crohn's disease patients and 13.5 years for ulcerative colitis patients.[23]

Finally, familial occurrence for Crohn's disease and for inflammatory bowel disease is probably less frequent in Greece compared to northern Europe and America. According to retrospective studies, familial clustering of IBD in Greece does not exceed 3% in adult cases[24–26] and 8.5% in pediatric cases.[27]

In a large study from the Netherlands, the most frequently observed positive relationship was among siblings and in two families, three offspring had Crohn's disease.[28] Further studies are required to confirm those findings with ethnically divergent populations.[29] Interpretation of epidemiological data on racial, ethnic and familial variations in immigrant populations must be done with caution, as IBD diagnostic facilities in some countries are not yet largely available. Furthermore, the effect of emigration towards a more accessible health care system has not been adequately addressed. Understanding the chain of events leading to Crohn's disease in familial cases is difficult. Based on the particulars of the present family case it is logical to hypothesize that genetically predisposed individuals seem to be vulnerable under the continuous pressure of a still unknown environmental factor(s). In addition, lifestyle and diet modification seem to represent an important predisposing factor to inflammatory bowel disease in immigrants.

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