Acromegaly is not associated with irritable bowel syndrome: a pilot study

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Abstract

BACKGROUND: In acromegaly, the gastrointestinal system is under the influence of excessive growth hormone (GH) and insulin like growth factor-1 (IGF-I). Increased bowel length and delayed transit time may cause functional disturbance of the bowel. The objective of the current study is to evaluate the frequency of irritable bowel syndrome (IBS) in cases with acromegaly.

PATIENTS AND METHODS: Twenty-three active cases with acromegaly newly diagnosed between 2010–2011 were included in the study. The control group consisted of ninety gender and age-matched healthy controls (HC). All cases were questioned for presence of IBS using Rome III criteria. Abdominal ultrasonography and colonoscopy results of acromegalic patients were obtained. In addition, cases with acromegaly were evaluated for their quality of life and status of depression by using the Acromegaly Quality of Life Questionnaire (AcroQoL) and Beck Depression Inventory (BDI), respectively.

RESULTS: The median GH and IGF-1 levels of cases with acromegaly were 5.72 [IQR: 2.2–34] ng/ml and 753 [IQR: 503–1050] ng/ml, respectively. The median AcroQoL score of patients with acromegaly was 56 [IQR: 43–71.5] and the median BDI score was 16 [IQR: 11–21]. Rome III diagnostic criteria were positive in 2 of 23 acromegaly patients and in 3 of 90 HC (p=0.26). IBS was present in 1 of 23 of the acromegaly patients compared to 3 of 90 HC (p=0.81).

CONCLUSION: Although acromegaly and IBS may cause similar gastrointestinal symptoms, acromegaly is not associated with a greater incidence of true IBS.

Abbreviations

GH	- Growth hormone
IGF-1	- Insulin-like growth factor-1
IBS	- Irritable bowel syndrome
AcroQoL	- Acromegaly Quality of Life Questionnaire
HRQoL	- Health-related quality of life
BDI	- Beck Depression Inventory

ORIGINAL ARTICLE

INTRODUCTION

Acromegaly is an endocrine disorder characterized by chronic excess of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Excessive GH and IGF-1 are responsible for various complications involving different organ systems. The gastrointestinal system is one of these systems and is under the influence of the GH-IGF-1 axis in acromegaly. Major changes in the gastrointestinal system include dolichomegacolon, slow colonic transit, and increased prevalence of colonic polyps (Resmini *et al.* 2007; Colao *et al.* 2004; Orme *et al.* 1998). GH has a mitogenic and anti-apoptotic effect on many tissues, including colonic tissues (Renehan *et al.* 2003; Thomas 1998; Ross 1999), so it may also cause increased prevalence of colonic adenoma in acromegalic patients (Klein *et al.* 1982; Ituarte *et al.* 1984; Brunner *et al.* 1990; Ezzat *et al.* 1991; Ortego *et al.* 1994; Ladas *et al.* 1994; Vasen *et al.* 1994; Terzolo *et al.* 1994; Delhougne *et al.* 1995; Colao *et al.* 1997; Jenkins *et al.* 1997 ; Renehan *et al.* 2000). Hypothetically, in addition to all these organic changes, functional disturbance of gastrointestinal system may also occur in acromegaly.

Irritable bowel syndrome (IBS) is a functional disorder of gastrointestinal system characterized by abdominal pain and/or discomfort, together with disturbed bowel habits (Ohman & Simrén 2007; Longstreth *et al.* 2006; Pyleris *et al.* 2012). It is one of the most common gastrointestinal disorders (Quigley *et al.* 2006). The pathogenesis and pathophysiology of IBS is complex and has not been resolved completely, yet. Psychosocial factors, abnormal gastrointestinal motility and secretion, and visceral hypersensitivity are contributing factors to IBS pathogenesis (Ohman & Simrén 2007). Abnormal gastrointestinal motility and secretion may lead to the main symptoms of IBS (Ohman & Simrén 2007). In patients with IBS, there is also a correlation between symptoms and stress (Dobie *et al.* 2004). Anxiety and depression have an impact on autonomic function and the hypothalamicpituitary-adrenal axis in response to various stressors (Jarrett *et al.* 2003; Bohmelt *et al.* 2005; Dinan *et al.* 2006).

In cases with acromegaly, increased bowel length, altered bowel motility and psychosocial changes due to the chronic disease may contribute to the presence of IBS in these patients. In the current study, our aim was to evaluate the frequency of IBS in acromegaly.

PATIENTS AND METHODS

We included 23 patients with active acromegaly that had been diagnosed in the preceding 12 months at the Endocrinology-Metabolism Out-patient Clinic, Cerrahpasa Medical Faculty, University of Istanbul between 2010 and 2011. The control group was composed of 90 healthy volunteers matched for age and gender. All of the patients with active acromegaly were newly diagnosed: 15 had not received any treatment, whereas 7 had been referred to our center with ongoing activity after they had surgery, and had been receiving octreotid-LAR treatment, which was discontinued 5 months earlier. The presence of clinical findings, failure to suppress nadir GH level to less than 1 ng/ml during oral glucose tolerance test and high levels of IGF-1 adjusted for age and gender in a case were taken as evidence of active acromegaly. None of the patients were receiving octreotide analogue treatment during the study period. None of the acromegaly patients were hypothyroid during the study period and blood glucose levels of all the cases with diabetes mellitus were under control. One patient with previously diagnosed hypocortisolism was on replacement steroid therapy.

The study protocol was approved by the Ethics Committee of Cerrahpasa Medical School, The University of Istanbul. All the patients read the informed consent forms before enrolling into the study and signed them.

All the acromegaly cases and healthy controls were given a questionnaire to identify symptoms of IBS according to Rome III diagnostic criteria. It is a short questionnaire which supports the diagnosis of IBS in the presence of recurrent abdominal pain or discomfort, associated with 2 or more of the following: Improvement with defecation; and/or onset associated with a change in frequency of stool; and/or onset associated with a change in form (appearance) of stool, having begun at least 6 months earlier, and lasted for at least 3 months (Drossman *et al.* 2006).

A colonoscopy was performed on all acromegaly cases by the same gastroenterologist (E.C.). An abdominal ultrasonography was also done. Only the cases with positive Rome III criteria with a normal abdominal ultrasonography and/or colonoscopy were diagnosed with IBS.

Patients with acromegaly were given the Beck Depression Inventory (BDI) and Acromegaly Quality of Life Questionnaire (AcroQoL) to evaluate for symptoms of depression and quality of life, respectively. The BDI is a 21-question multiple-choice self-report inventory which is helpful for measuring the severity of depression (Beck *et al.* 2008). Each question has 4 statements and each answer is scored on a scale of 0 to 3.The level of depression is assessed on the basis of these scores. The total score indicates the severity/seriousness of depression. An analysis of the validity and reliability of its use with the Turkish population has been conducted and a cut-off score of 17 was reported (Hisli 1988). AcroQoL is a disease-specific questionnaire used to assess health related quality of life (HRQoL) in patients with acromegaly (Webb *et al.* 2002; Deyneli *et al.* 2003). It is comprised of 22 questions with five possible responses and each response is scored between 1–5. The maximum score is 110 points (best HRQoL), while the worst score is 22 (worst HRQoL) (Webb *et al.* 2006; Webb 2006). The resulting scores were standardized on a scale running from 0 (worst HRQoL) to 100 (best HRQoL), by using a formula which is stated in literature (Webb 2006).

Data were statistically analyzed using the SPSS 15.0 package program. When the distribution was not normal, a nonparametric test (Mann-Whitney U test) was used. The results are presented as median and interquartile range [IQR]. χ^2 test was also used when it was necessary. P <0.05 was considered statistically significant.

RESULTS

The mean age of the acromegaly patients and healthy controls (HC) was 43.26±11.2 and 42.03±9.44 years, respectively (*p=0.59*). Female/Male distribution were 10/13 in acromegaly group and 33/57 in HC (*p*=0.55). The median time between the onset of symptoms and diagnosis of acromegaly was 30 months [IQR: 12–76] and from diagnosis of acromegaly until the study period was 1 month [IQR: 1–6].

The median GH and IGF-1 levels of cases with acromegaly were 5.72 [IQR: 2.2–34] ng/ml and 753 [IQR: 503–1050] ng/ml, respectively. The median AcroQoL and BDI scores of patients with acromegaly were 56 [IQR: 43–71.5] and 16 [IQR: 11–21], respectively.

Rome III diagnostic criteria were positive in 2 of 23 acromegaly patients and in 3 of 90 HC (*p*=0.26). However, a polyp was detected on the sigmoid colon by colonoscopic examination in 1 of the 2 acromegaly cases with positive Rome III criteria. When this was taken into consideration, IBS was present in 1 of 23 acromegaly patients, still making the statistical difference between acromegaly cases and HC insignificant (p=0.81) (Figure1).

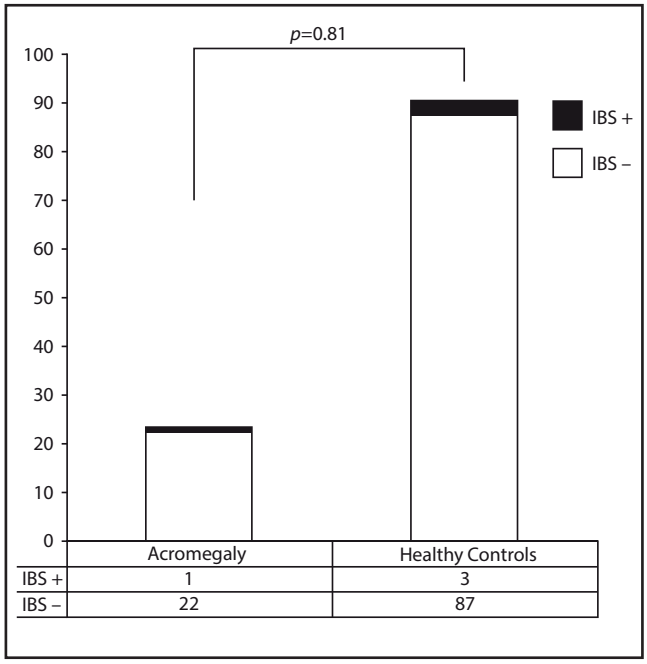

Fig. 1. Number of cases with and without IBS in each group

DISCUSSION

Results of the current study demonstrated that, although acromegaly is known to be associated with many gastrointestinal symptoms, increased incidence of IBS was not found in active and newly diagnosed cases with acromegaly.

Acromegaly is notorious for its gastrointestinal involvement, which includes, for example, an increased incidence of colonic polyps and cancer (Orme *et al.* 1998). Moreover, delayed gastric emptying, altered intestinal motility, increased formation of cholecystic stones secondary to somatostatin analogues and prolonged colonic transit time in both treated and untreated patients contribute to gastrointestinal involvement in cases with acromegaly (Thomas *et al.* 2005; Dowling 2000; Dharmsathaphorn 1985).

IBS is one of the most commonly diagnosed gastrointestinal syndromes characterized by chronic abdominal pain and altered bowel habits. ROME III criteria are commonly used for the diagnosis and classification of IBS. Although the exact underlying mechanism of IBS is not certain, both IBS and acromegaly are associated with psychopathology, including anxiety and depression, and altered intestinal motility (Resmini *et al.* 2007; Ohman& Simrén 2007; Tiemensma *et al.* 2010). These common characteristics raise questions about a possible relationship between IBS and acromegaly.

Although psychopathology has been previously reported in patients with acromegaly (Tiemensma *et al.* 2010), in our study median BDI scores did not reveal depression and the median AcroQoL scores were above the average. With these scores, it was unlikely that depression or limited quality of life would contribute to a possible association between IBS and acromegaly.

When only ROME III criteria were taken into consideration, two patients seemed to be positive for IBS. Since acromegaly is associated with biliary and colon pathologies, these possibilities should be carefully addressed. After exclusion of the cases with a pathologic finding in ultrasonography and/or colonoscopy, the frequency of IBS significantly decreased in acromegalic patients (1/24).

In conclusion, while the gastrointestinal symptoms of acromegaly and IBS are similar, acromegaly is not associated with a greater incidence of true IBS.

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Conflict of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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