



OLGU SUNUMU/CASE REPORT

Hereditary angioedema may not be the only cause of abdominal pain in patients with hereditary angioedema!

Hereditör anjiödemli hastalarda karın ağrısının tek nedeni hereditör anjiödem olmayabilir!

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Abstract

Abdominal pain is one of the basic clinical presentations of the hereditary angioedema and danazol is a common medicine which has been used for long years in patients with hereditary angioedema. We present two hereditary angioedema patients with abdominal pain albeit under danazol treatment, whose final diagnoses was colon carcinoma. There are two consequences in this article which shall be insisted on: First; in patients with hereditary angioedema, the differential diagnosis of “abdominal pain” is always important even though hereditary angioedema diagnosis exists. And the second; It can be hardly speculated that long term danazol treatment may cause different malignancies.

Key words: Hereditary angioedema, danazol, colon cancer, abdominal pain, differential diagnosis.

Öz

Hereditör anjiödemlin temel klinik presentasyonlarından birisi karın ağrısıdır. Danazol hereditör anjiödem hastalarında uzun yıllar yaygın olarak kullanılmış olan bir ilaçtır. Burada nihai tanıları kolon karsinomu olan danazol tedavisi altında karın ağrısı olan iki hereditör anjiödem hastası sunulmuştur. Bu makalede 2 konu vurgulanmıştır. Birincisi; hereditör anjiödem hastalarında “karın ağrısı” ayırıcı tanısının, hereditör anjiödem tanısı mevcut olsa bile yapılması gereken bir semptom olma özelliğini koruduğunu vurgulamak; ikincisi ise uzun süreli uygulanan danazol tedavisinin maligniteler gibi olası bir advers etkisini ortaya koymaktır.

Anahtar kelimeler: Hereditör anjiödem, danazol, kolon kanseri, karın ağrısı, ayırıcı tanı.

INTRODUCTION

Hereditary angioedema (HAE) is known as a rare disorder. However, as it may occur at every generation because of its autosomal dominant transition pattern and because of upper respiratory way attacks which result in death, it is evaluated at the important diseases group. Although angioedema are widely known findings of HAE, abdominal pain may be the only presenting symptom¹.

The abdominal symptoms of HAE can present with nausea, vomiting, and abdominal tenderness, and

can mimic surgical and non-surgical abdominal diseases¹. Its frequency is reported as between 1/10.000 and 1/50.000 without race and sex discrimination².

HAE results from deficiency and/or dysfunction of C1 esterase inhibitor (C1-INH). There is no curative treatment of the illness. In the context of treatments, the basic approaches consist of preventive prophylactic applications and acute attack treatments. In the matter of treatment alternatives and application ways, there are a lot of resources in the literature³.

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There are two subjects in this article which shall be insisted on. The first is to emphasize that abdominal pain which is among the basic clinical presentations of the HAE keeps the feature of being a symptom of which its differential diagnosis has to be made even though HAE diagnosis exists and the second is to put forward the adverse effect of Danazol prophylaxis not informed before which is applied to reduce the frequency of attacks. For this purpose, 2 patients of two different centers and who have common features that are worth to be shared at the literature are discussed.

CASES

Case A

Type 1 HAE [C4 = 0.0168 (0.160-0.380 g/L), C1-INH level = 0.05 (0.15-0.35 g/L), C1-INH activity = 17 % (70-130 %)] diagnosis has been put for the male patient of age 60 who has complaints of edema at face and extremities and abdominal pain 10 years ago and after the diagnosis is put, he has been receiving Danazol and prophylaxis treatment till today. The treatment has begun with 100 mg / day and after that, in accordance with the clinical condition, it has been continued with 50 – 200 mg / doze daily or alternate day.

The frequency and severity of attacks of this patient have been continuing in limits which shall not affect his life quality too much. Only for a few times, it needed to be made CI inhibitor concentrate infusion because of orofacial attack. Although he continued Danazol treatment at the same dose, because there has been an increase especially in his abdominal complaints for approximately 10 months, the patient has been referred to Division of Immunology and Allergic Diseases for being evaluated.

The patient was expressing that, his abdominal pain is different than before, it is not in the way of attacks but continuous and that complaints of distension in the abdomen and constipation have also begun. Abdominal pain being in a different nature than HAE abdominal attack and its being together with other gastrointestinal symptoms, it was necessary to search for a reason other than HAE.

As a result of studies done with this clinical foresight, at the sigmoid colon, a mass lesion has been detected which narrows the lumen. The histological-pathological examination was

harmonious with mucinous adenocarcinoma. It has been decided to apply the patient surgical recession and following this chemotherapy by the consultation of the medical oncology specialist. As the patient has attacks which proceeds with larynx edema in his past medical history, before the surgical intervention, prophylaxis has been done with 1000 Units of CI inhibitor concentrate. During the surgical operation which lasted for approximately 5 hours and after this, no life threatening complication with HAE side has developed.

Case B

Type 1 HAE diagnosis has been put to the male patient of 39 years of age 8 years ago with typical symptomatology and laboratory findings [C4 = 0.024 (0.160-0.380 g/L), C1-INH level = 0.07 (0.15-0.35 g/L), C1-INH activity < 5 % (70-130 %)] As for prophylactic treatment, first it has been begun with 100 mg / day Danazol and while the symptoms of the patient who has been taking Danazol for 8 years were continuing with abdominal pain attacks for a period of 3-4 days once or twice a month, for approximately 3 months, abdominal pains “with longer periods” but “less severe” have begun. These pains have been accepted as the known “symptom” of HAE and only in the daily dose of Danazol there have been increases.

The abdominal pain not being able to be taken under control although the doze of Danazol was increased was making us think at the first sight that Danazol treatment might have been insufficient. It could have been an alternative approach to make C1 inhibitor infusion to the patient and examine its effects who has never had C1 inhibitor treatment concentrate treatment till that day.

In the physical examination, it has been detected slight distention at the abdomen, hyperactive intestine sounds and sensitivity at all quadrants with deep palpation. There was no rebound tenderness in the abdomen. The findings detected could still be accepted harmonious with HAE attack findings. However, the patient not to have done defecation for two days and that he didn't release gas yet and besides this the patient being different from the character he is used to has made us think about a different primary pathological probability.

By surgical acute abdomen pre-diagnosis, it has been consulted with abdominal surgeon, it has been learned that the patient has developed ileus. As a

result of controls related towards ethology, a mass which has resulted in obstruction at the descending colon has been detected. Colonoscopy biopsy was in harmony with mucinous adenocarcinoma. It has been detected that the tumor both did local spread and liver metastasis.

DISCUSSION

Abdominal attack is one of the clinical findings of HAE. Gastrointestinal colic progresses with nausea and vomiting. These symptoms are related to the edema on the wall of the intestine. It is seen at 70-80% of the patients. The abdominal pain is severe, the average pain score sensed by the patients is notified as 8.4 (1 the lowest 10 the most severe). Nausea and vomiting is seen at approximately one-third of the patients^{2,4}.

In both of the concepts presented above, patients who have experienced abdominal attacks for a long time are told. Both of the patients have understood that the nature of their abdominal pain has changed and they have consulted to the doctor by putting forward this. In Case A, the patient has sensed this change very late and he has consulted to the doctor late. However, in case B, the doctor following the patient could unfortunately not interpret the changing pain character as a reason which is not HAE. Case B has been diagnosed at our center that he has consulted very late.

Danazol is a medicine which is the derivative of ethisterone, a synthetic steroid. In year 1976, the first publications related to its use in the treatment of HAE have entered in the literature⁵. Its effect in stopping HAE attacks has been shown in many studies and it is a medicine which has been mostly used in long-term prophylaxis. Today, in the treatment of HAE, more active agents such as C1 inhibitor concentrate, bradykinin B2 receptor antagonist and plasma kallikrein inhibitor are used⁵. However, long-term prophylaxis can still be accepted as an appropriate alternative for selected patients. One of the important adverse effects which is related to Danazol is liver neoplasia. In the literature, there exists hepatocellular focal nodular hyperplasia and hepatocellular carcinoma⁷ concepts which are related to long-term Danazol use. In both of the concepts presented in this article, there is the unity of long-term Danazol treatment and colon

cancer. According to Pubmed scanning, no other concept has been reported which uses Danazol and develops colon cancer. However, there is also no literature knowledge related to that Danazol is effective in the development of colon cancer. In this unity presented, there can be the relationship of Danazol-cancer or it may be completely a coincidental situation. It is not possible to give a verdict with the information at hand.

In summary, HAE is an important illness as it doesn't have curative treatment and uncontrolled attacks may have fatal results. In the last years, the increase in the awareness of the illness both in the world and in our country increases the number of concepts which are followed. Especially in abdominal attacks, the concepts we present support that clinical findings should always be differentially diagnosed. Besides, although we couldn't put forward a definite cause-result relationship, we leave it to the interpretation of our peers for doing scans in the view of colon malignancies at patients who have been treated with Danazol for a long-term.

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