Multiple gastrointestinal stromal tumors and pheochromocytoma in a patient with von Recklinghausen's disease

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A B S T R A C T

INTRODUCTION: Neurofibromatosis type 1 is a genetic disease characterized by neoplastic and non-neoplastic disorders involving tissues of neuroectodermal and mesenchymal origin. Herein, we present a case with von Recklinghausen’s disease, right adrenal heochromocytoma and multiple gastrointestinal stromal tumors.

PRESENTATION OF CASE: A forty-eight year old male patient was admitted to our Emergency Department with melena. His physical examination revealed multiple neurofibromas all over the skin, kyphosis, multiple cafe au lait spots and Lisch nodules on the eye and, melena on digital rectal examination. Abdominal computerized tomography scan showed a mass on right adrenal gland and multiple soft tissue mass lesions between distal part of pancreas and small bowel. Adrenal mass was determined as a pheochromocytoma and small bowel lesions were verified as stromal tumors.

DISCUSSION: In patients with NF1, pheochromocytomas and GISTs are well known neoplasms seen with increased incidence than the general population.

CONCLUSION: In patients with NF1, any symptoms with other systems should be managed carefully for underlying malignancy.

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1. Introduction

Neurofibromatosis type 1 (von Recklinghausen’s disease-NF1) is a genetic disease characterized by neoplastic and non-neoplastic disorders involving tissues of neuroectodermal and mesenchymal origin. NF1 is an autosomal dominant inherited disease with an incidence of about 1 per 3000 births and equally detected in both males and females. It is characterized by abnormal skin pigmentation (cafe au lait spots and axillary freckling), cutaneous and plexiform neurofibromas, skeletal dysplasias, and Lisch nodules. The classical triad of symptoms are cafe au lait spots, cutaneous neurofibromas and neoplasms of pheripheral and central nervous systems. Malignancies are found in 3–15% of the patients.1 Gastrointestinal abnormalities in patients with NF1 are reported to occur in up to 10–25% of patients including, mesenchymal neoplasms, neuroendocrine tumors of the duodenum, hyperplasias of intestinal neural tissues and other gastrointestinal neoplasms.2 Secondary neoplasms usually arise during midlife, later than cutaneous lesions in NF1 patients.2–4 In patients with NF1, pheochromocytomas have been identified in about 1% of patients and gastrointestinal stromal tumors (GIST) in 4–25%.2,5–9

There are a few case reports found in the English literature, including pheochromocytoma, multiple GISTs and NF1 in the same patient. Herein, we present a case with von Recklinghausen’s disease, right adrenal heochromocytoma and multiple GISTs.

2. Case

Forty-eight year old male patient was admitted to our Emergency Department with the complaint of blackish stool discharge. His physical examination revealed that, arterial blood pressure was 175/95 mmHg, heart rate was 102 1/min, multiple neurofibromas all over the skin, kyphosis, multiple cafe au lait spots and Lisch nodules on the eye. His neurological examination was normal and digital rectal examination showed melena. His hemoglobin level was 12.8 mg/dL and hematocrite level was 36%. He was hemodynamically stable on follow up period and no blood level decrease detected. Upper gastrointestinal tract endoscopy revealed a compression on stomach due to a mass, and multiple ulcers at third part of duodenum. The biopsy results from the duodenum was CD34(+) and C-Kit(+) confirming the diagnosis of GIST. Abdominal computed tomography scan showed a 22 mm mass on right adrenal gland and 4 cm soft tissue mass between the distal part of pancreas and small bowel, and there were two more lesions below this lesion with 2 and 3 cm in sizes. Biochemical analysis results were in normal range except urine catecholamine levels (Vanyl mandelic acid:...
3. Discussion

Neurofibromatosis type 1 is a complex disease, with patients having an increased prevalence of benign and malignant neoplasms throughout the body due to mutations of the NF gene leading to abnormal tumor suppression. The association between von Recklinghausen's disease and tumors of neurogenic and neuroendocrine origin, such as meningiomas and pheochromocytomas is well known. Pheochromocytoma occurs in about 1% of NF1 patients, the incidence of pheochromocytomas is much higher in patients with duodenal somatostatin producing endocrine tumors associated with NF1. The composite tumors in this syndrome are much rare, with isolated case reports. The coincidence of multiple GISTs and pheochromocytoma and NF1 is described as a few case reports within the literature. Our patient had both pheochromocytoma and multiple GISTs with NF1.

In one study performed in Swedish population, malignant tumors were reported significantly more often in the NF1 patients than what was expected in the general population. Pheochromocytomas are well recognized with NF1 and it is said to be 10 times more common than the general population. In a Korean study, among 125 NF1 patients, 9 carcinomas and 8 sarcomas were detected. All three GISTs were multiple in small bowel and they concluded that NF1 patients had a high risk of developing malignant tumors.

Gastrointestinal stromal tumors in NF1 patients have been reported to be the most common lesions of gastrointestinal tract, but symptomatic cases account for less than 5% of patients. The incidence of GIST in NF1 patients is varying from 4% to 25%. Although most GISTs arise in the stomach, GISTs in NF1 patients tend to be multiple and mostly located within the small bowel. Clinical symptoms related to the size and location of tumor, initial clinical manifestations varies; nonspecific abdominal pain, bleeding from gastrointestinal tract, palpable abdominal mass, perforation etc. In this case, melena was the initial clinical manifestation of the patient and duodenal GIST was detected in upper gastrointestinal tract endoscopy.

In NF1 patients, predisposition of tumorgenesis might be explained by overexpression of a tumor suppressor gene called neurofibromin. In patients with NF1, pheochromocytomas and GISTs are well known neoplasms seen with increased incidence.
than the general population. Most of the lesions cause no symptoms until they grow large in size and therefore it is difficult to detect them preoperatively. In patients with NF1, any gastrointestinal symptoms should be managed carefully. Early diagnosis of abdominal symptoms is very important because of the risk of malignancy and complications of tumors such as hypertension, bleeding and perforation.

Conflict of interest statement

None.

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None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Beyza Ozcinar: study design and writing; Nihat Aksakal: data collection; Orhan Agcaoglu: writing; Mustafa Tukenmez: data collection; Ibrahim A. Ozemir: data collection; Umut Barbaros: data collection; Nese Colak: study design; Yesim Erbil: study design.

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