Advanced Research in Gastroenterology & Hepatology
ISSN: 2472-6400

Juniper Publishers
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Case Report
Volume 14 Issue 3 - January 2020
DOI: 10.19080/ARGH.2020.14.555889

Adv Res Gastroentero Hepatol

Multiple Gastrointestinal Stromal Tumors of the Duodenum Associated with Neurofibromatosis Type

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Submission: December 31, 2019; **Published:** January 07, 2020

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Abstract

A 69-year-old woman patient, with known neurofibromatosis type 1(NF1), was admitted to our hospital for melena. Gastrointestinal endoscopy revealed several submucosal tumors with ulcer in the second of the duodenum. The patient underwent subtotal stomach-preserving pancreaticoduodenectomy (SSPPD). Those tumors were diagnosed gastrointestinal stromal tumors (GISTs) in the duodenum with NF1-related.

Keywords: Neurofibromatosis type 1; Von Recklinghausen's disease; Gastrointestinal stromal tumors; Duodenum

Abbreviations: NF1: Neurofibromatosis Type 1; VRD: Von Recklinghausen's Disease; GISTs: Gastrointestinal Stromal Tumors; CT: Computed Tomography; EUS: Endoscopic Ultrasound; SSPPD: Subtotal Stomach-Preserving Pancreaticoduodenectomy; PDGFRA: Platelet-Derive Growth Factor Receptor A polypeptide

Introduction

Neurofibromatosis Type 1(NF1), also known as Von Recklinghausen's Disease (VRD), is a hereditary autosomal dominant disease with an incidence rate of from 1/2,000 to 1/5,000 in most population base studies [1]. NF1 is a dominantly inheritable disease with abnormality at chromosome 17q11.2, which leads to a loss of neurofibromin, a tumor suppressor protein [1,2]. Therefore, patients with NF1 have a higher risk of developing various malignant neoplasms, with Gastrointestinal Stromal Tumors (GISTs) developing in approximately 5-25% of patients with NF1 [3]. We report a case of the multiple GISTs of the duodenum associated with NF1.

Case Report

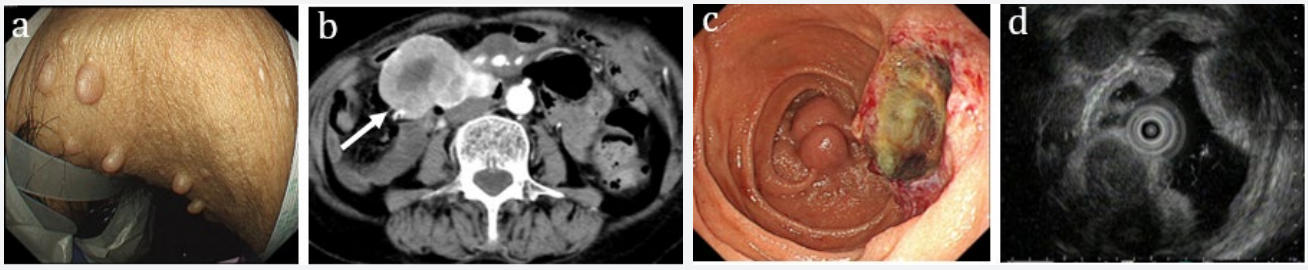

Figure 1: Diffuse cutaneous multiple neurofibromas on the skin (a). Abdominal computed tomography (CT) revealed tumors (arrow) with contrast effect in the second of the duodenum (b). Gastrointestinal endoscopy revealed several submucosal tumors with ulcer in the second of the duodenum (c). Endoscopic ultrasound revealed multiple low echoic masses from the muscle layer (d).

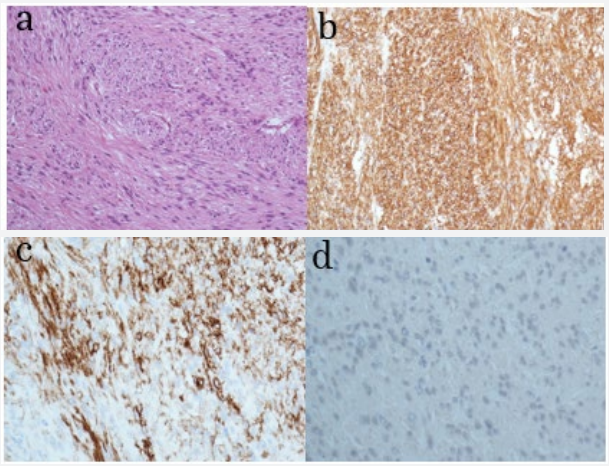

Figure 2: Pathological examination (HE staining ×200) of the tumors revealed the fascicular proliferation of spindle-shaped cells (a). Immunohistochemical staining revealed that the tumor cells were positive for c-kit (b), CD34 (c), and for negative desmin (d).

A 69-year-old woman patient, with known NF1, was admitted to our hospital for melena the physical examination revealed diffuse cutaneous multiple neurofibromas on the skin (Figure 1a). Abdominal Computed Tomography (CT) revealed tumors with contrast effect in the second of the duodenum (Figure 1b). Gastrointestinal endoscopy revealed several submucosal tumors with ulcer in the second of the duodenum (Figure 1c). Endoscopic Ultrasound (EUS) revealed multiple low echoic masses with clear boundary derived from the muscle layer (Figure 1d), suggesting the diagnosis of GISTs. The patient subsequently underwent Subtotal Stomach-Preserving Pancreaticoduodenectomy (SSPPD). Pathological examination (Hematoxylin and Eosin staining) of the tumors revealed the fascicular proliferation of spindle-shaped cells, predominantly in the muscle layer (Figure. 2a). Immunohistochemical staining revealed that the tumor cells were positive for c-kit and CD34(Figure. 2b & 2c), but the cells were negative for S-100 and desmin (Figure. 2d). Thus, those tumors were confirmed GISTs in the duodenum with NF1.

Discussion

NF1 should be suspected in the presence of multiple cutaneous neurofibromas, café au lait spots, axillary or inguinal freckling [4]. It is a dominantly inheritable disease with abnormality at chromosome 17q11.2 [1,2]. This gene encodes a GTPase activating protein which can regulate the activity of the p21 product of the ras oncogene, and which seems to play an important role in controlling cellular proliferation and differentiation in a wide range of tissues. Different gene mutations are involved in the development of the various clinical manifestations of NF1, including malignant tumors, with GISTs [5]. Therefore, GISTs is reported developing in approximately 5-25% of patients with NF1 [3].

GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract, originating from the progenitors of intestinal cells of Cajal, which regulate digestive tract motility [6]. Sporadic GIST has been considered to involve specific KIT (CD117) or Platelet-Derive Growth Factor Receptor α Polypeptide (PDGFRA) signaling - driven tumors, KIT and PDGFRA activating mutations are the oncogenic mechanisms in most sporadic GISTs. In NF1-related GIST, mutation in KIT and PDGFRA are rarely found [7-9]. Sporadic GIST can occur within the entire gastrointestinal tract, in which it accounts for the largest proportion of 60-70% in the stomach, 25-30% in the ileum to jejunum, 5-15% in the colorectum, and 5% in the duodenum [10]. By contrast, NF1-related GISTs are located in the small intestine usually in the jejunum and characterized by their tendency for multiplicity [11]. In the present case, the clinical manifestations corresponded to typical NF1-related GISTs.

Conclusion

Duodenal GISTs are rare neoplasms which may be associated with NF1. The clinician should be aware of this entity in patients with known NF1 disease presenting with gastrointestinal symptoms or intra-abdominal mass.

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How to cite this article: Shigenaga Matsui, Hiroshi Kashida, Kenji Nomura, Yoriaki Komeda and Masatoshi Kudo. Multiple Gastrointestinal Stromal Tumors of the Duodenum Associated with Neurofibromatosis Type. Adv Res Gastroentero Hepatol, 2020;14(3): 555889.
DOI: 10.19080/ARGH.2020.14.555889

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