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## Case report

## Features of CT and EUS in mesenteric plexiform neurofibroma with Neurofibromatosis type I: A case report ☆☆☆★☆☆

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## ABSTRACT

Plexiform neurofibroma (PNF) is a rare benign tumor of the peripheral nerve, belonging to a subtype of neurofibroma. PNF is common in the head, neck and trunk. It is uncommonly observed in the mesentery. We report a case of mesenteric PNF in a 64-year-old man history of neurofibromatosis type I (NF1), which caused abdomen pain. In addition, the computer tomography (CT) and endoscopic ultrasonography (EUS) manifestations of mesenteric PNF were analyzed. The imaging appearance of a mesenteric plexiform neurofibroma is that many low-density (CT) /mixed echo (EUS) soft tissue masses surrounding the superior mesenteric artery, but not surrounding the superior mesenteric vein. Our case adds to the limited literature regarding NF1 presenting with mesenteric PNF. The computer tomography and endoscopic ultrasonography may facilitate confirm diagnosis of mesenteric PNF.

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## Introduction

Plexiform neurofibroma (PNF) is a benign peripheral neurofibroma. It belongs to a subtype of neurofibroma, characterized by twisting masses on the nerve stem and its branches. Most of them occur in patients with neurofibromatosis type 1 (NF1) [1]. PNF is one of the most common tumor types in NF1 in the abdominal cavity, but PNF occurring in the mesentery was rarely seen clinically. A case was collected by us, and its computer tomography(CT) and endoscopic ultrasonography(EUS) performances was analyzed.

## Case report

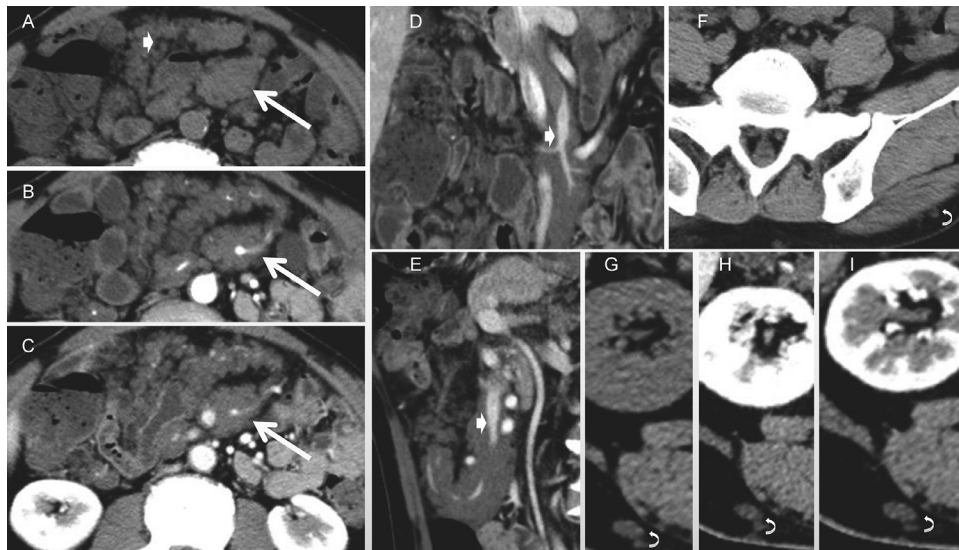
A 64-year-old man was admitted to our hospital because of the pain in left upper abdomen, but he had no history of abdominal distention or vomiting. Physical examination showed multiple cutaneous café-au-lait macules in the limbs, thorax and abdomen, and multiple freckling in the axillary or inguinal regions. Multiple subcutaneous nodules were found in the forearm, chest and abdomen. Laboratory data were unremarkable. The patient's sister and daughter had multiple subcutaneous nodules, similar in nature to the patient. The daughter's skin had multiple café-au-lait macules of different sizes.

Non-contrast CT of the abdomen demonstrated multiple soft tissue masses in the intestinal mesentery with clear

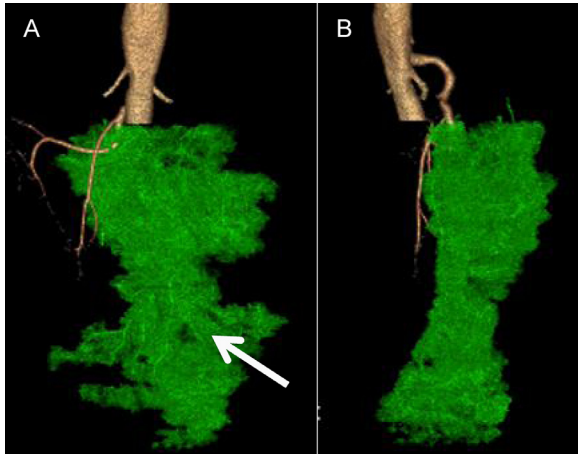
boundary and homogeneous density which was slightly lower than the density of muscle tissue at the same level. Scattered fat density can be seen between these hypodense masses with no obvious signs of invasion and metastasis to surrounding tissues and organs. These masses were not significantly enhanced after intravenous injection of iodine contrast agent. Meanwhile, we observed the mesenteric blood vessels were wrapped by these masses, without obvious invasion of the blood vessel wall. Multiple small hypodense subcutaneous nodular with clear boundaries were found in the abdomen. The largest one in the scan range was about 13mm in diameter. They did not significantly enhanced after intravenous injection of iodine contrast agent (Fig. 1). Volume rendering technique(VRT) three-dimensionally shows the superior mesenteric artery being surrounded by intra-abdominal lesions. (Fig. 2).

Linear 7.5 MHz EUS revealed that multiple mixed echogenic masses were distributed on the mesentery, resembling grape clusters. When we explored the mesenteric vessels, we found that the lesion had only grown along the superior mesenteric artery (SMA) and did not involve the adjacent superior mesenteric vein (SMV) (Fig. 3, Video.1).

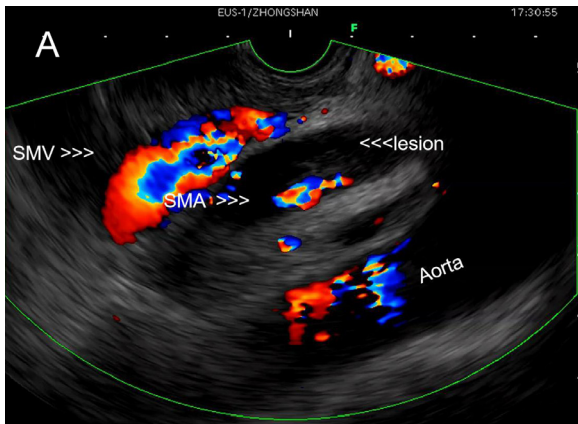
Malignant tumors in the abdominal cavity could not be ruled out. Laparoscopic biopsy was performed, and the mesentery was obviously thickened. A large number of small, smooth, grayish-white and hard nodular structures are found in the mesentery of the small intestine, starting at the mesenteric boundary of the small intestine and extending almost to the base of the mesentery. The tumor surrounds the su-



**Fig. 1** – A 64-year-old man with mesenteric plexiform neurofibromas. Abdominal CT (A-C), (F-I):Axial planes; (D):coronal planes; (E):Sagittal planes showed multiple soft tissue masses (long white arrow, A-C) in the intestinal mesentery, with clear boundaries and no obvious signs of infiltration and metastasis. Their density was homogeneous and lower than muscle tissue at the same level. Scattered fat density was found between these hypodense masses (short white arrow, A). There was no obvious enhancement with these masses in the arterial phase (B) and venous phase (C) after intravenous injection of iodine contrast agent. These masses wrapped the mesenteric vessels, but the blood vessel wall was not significantly infiltrated (short white arrow, D-E). In addition, there were multiple subcutaneous nodular in the abdomen (curved white arrows, F-G), with soft tissue density, clear boundaries and no obvious enhancement in the arterial phases (curved white arrows, H) and venous phases (curved white arrows, I) after enhancement.



**Fig. 2 – Volume rendering technique (VRT). Mesenteric vessels (white arrow, 2A) surrounded by intra-abdominal masses (green lumps, 2A & B).**



**Fig. 3 – Endoscopic ultrasonography (EUS) findings. Linear 7.5 MHz EUS for stomach and duodenum revealed that multiple mixed echogenic nodules were distributed on the mesenteric membrane, resembling grape clusters. The lesion only grows along the superior mesenteric artery and does not involve the adjacent superior mesenteric vein (A).**

superior mesenteric artery and a small amount of fatty tissue. (Fig. 4, Video.2). Histopathological examination shows spindle cell hyperplasia in the mesenteric nodules. Hematoxylin and eosin staining at high magnification (200 ×) (Fig. 5A) show a low degree of cellular atypia, and absence of nuclear division. S-100 (Fig. 5B) and fibroblasts CD34 (Fig. 5C) immunostaining reveals positivity. The pathological diagnosis was PNF. There was no evidence of malignant transformation. Combined with the clinical manifestations and family history of the patient, the clinical diagnosis was NF1. After laparoscopy, the surgeon learned that the tumor surrounds the superior mesenteric artery and its branches. The tumor cannot be completely removed. According to reports in the literature [2], surgical resection should be avoided for tumor that cannot be completely removed. Otherwise, the recurrence rate and malignant transformation rate of the tumor will increase. In addition, pathol-

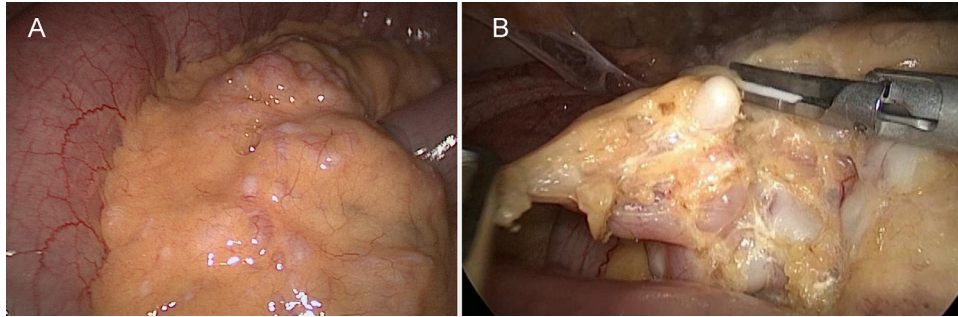
ogy showed that the tumor had no evidence of malignancy for the time being. So the patient was treated non-surgically with serial imaging for surveillance. As of April 27, 2020, the patient's abdominal CT images showed no significant changes in the tumor.

## Discussion

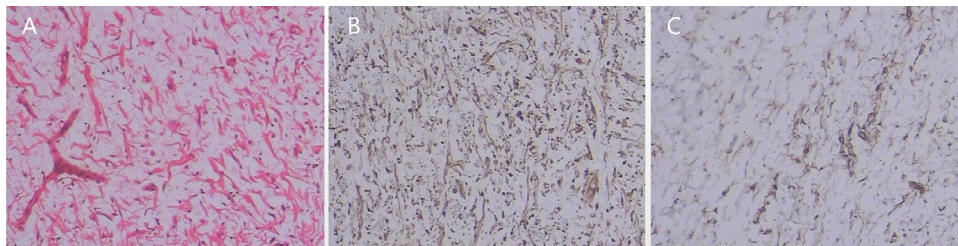
Neurofibromatosis is a autosomal dominant genetic disease that belongs to cutaneous nerve syndrome and often involves the skin, bones, trunk, nerves, etc [3]. According to the different genetic loci, it is mainly divided into neurofibromatosis type I and type II. NF1 pathogenic gene is located on chromosome 17q11.2 [4]. NF1 is a multiple organ damaging disease, which is caused by abnormal development of neural crest cells due to NF1 gene defect. It is characterized by multiple café-au-lait macules, freckling in the axillary or inguinal regions, Lisch nodules (iris hamartomas), peripheral neurofibromatosis, skeletal deformity, and tumors of the central nervous system, mental neurodevelopmental disorders (eg learning disabilities, anxiety, attention deflection, etc.) are closely related, as well as various malignant tumors throughout the body. The above-mentioned patient meets the NF1 clinical diagnostic criteria revised by the National Institutes of Health (NIH) in 1997 [5].

Due to the different size, location and infiltration of different types of PNF, the treatment options are also different [6]. Superficial PNF only grows in skin and subcutaneous tissue. It does not change the growth pattern. It can be completely removed when the tumor is small, which can effectively improve the patient's quality of life. Displacing PNF, because the boundary between the tumor and the surrounding tissue is clear and not invasive, the tumor should be actively surgically treated if conditions are permitted. Invasive PNF is characterized by diffuse growth, blood vessels and nerves were wrapped, and surrounding tissues were violated. The operation is difficult. The tumor cannot be completely removed and the recurrence rate is high. Clinically, the principle of treatment is to reduce the pain of the patient and improve the quality of life. Accurately identifying the PNF classification before operation is very important. But it is hardly to judge the shape and growth location of PNF only by clinical examination, meanwhile CT and EUS can better distinguish the shape, size and location of tumor, which can further evaluate its biological behaviour. Then we can provide imaging evidence for treatment and surgical plan.

Approximately 30% of patients of NF1 associated with PNF. The proposal of plexiform neurofibroma originated from the 19th century pathology used to describe tissue invasive growth involving surrounding tissues. It is composed of Schwann cells, fibroblasts and peripheral nerve cells. Schwann cells are mainly proliferated and form typical clusters. The shape structure can expand and grow outside the cell, grow along the long axis of the nerve bundle and its branches, and even spread around the nerve. Immunohistochemical staining was positive for vimentin, S-100 protein, axonal neuron enolase or neurofilament protein in the plex-



**Fig. 4 – Macroscopic appearance of the laparoscopic biopsy specimen. Laparoscopic biopsy showed a significant thickening of the mesentery, A large number of small, smooth, grayish-white and hard nodular structures are found in the mesentery of the small intestine(A). The tumor surrounds the mesenteric blood vessels and a small amount of fatty tissue (B).**



**Fig. 5 – Histopathological findings of the tumor. Histopathological examination shows spindle cell hyperplasia in the mesenteric nodules. Hematoxylin and eosin staining at high magnification (200 x) (A) show a low degree of cellular atypia, and absence of nuclear division. S-100(B) and fibroblasts CD34(C) immunostaining reveals positivity.**

iform structure, and scattered positive for epithelial membrane antigen. PNF is belongs to a subtype of neurofibromas, which is more frequent in children. It is common in the head and neck, trunk, limbs, and may also appear in the abdominal cavity, retroperitoneum, bladder, breast, stomach and other parts. According to the occurrence location of PNF, morphological characteristics and different manifestations of surrounding tissues, it was mainly divided into 3 subtypes [6]. (1) Superficial PNF, which means the tumor is located in the skin and subcutaneous tissue. The state is clear, not involving the muscular layer. (2) Displacing PNF, according to the tumor involving the muscular layer or its fascia, which grows along the plexus or spinal cord and cauda equina. The boundary can be identified, and it is not manifested as diffuse growth. (3) Invasive PNF, the tumor grows diffusely, involving more than 3 layers of structure, invading the surrounding tissues and wrapping in adjacent blood vessels, nerves, and lymphatics. PNF has the potential of malignant transformation and is recognized as the precursor of malignant peripheral nerve sheath tumors (MPNST) in NF1 patients [7]. About 10% of patients with NF1 develop MPNST, which usually arise within a pre-existing PNF [8]. In the abdomen, PNF often occurs in the retroperitoneal cavity and the paravertebral region, however, it is rare in the gastrointestinal tract. Gastrointestinal plexiform neurofibroma may arise from mucosa, muscular layer, serosa or mesenteric nerve, most of which are located in jejunum (43%), followed by stomach (41%), ileum, duodenum, colon and small intestine mesentery [9]. Mesenteric

PNF originates from the autonomic nerve fibers accompanying the mesenteric blood vessels, mainly composed of nerve sheath cells and fibroblasts. The lesions are mainly located in the mesentery, wrapped the mesenteric vessels with clear boundaries. Abdominal CT showed mesenteric PNF eccentrically distributed on the intestine, with a clear boundary to the intestinal wall, homogeneous density, and lower density than muscle [10]. It's reported that PNF manifests as a low-density mass due to the presence of a large number of extracellular matrix in tumor tissues and the normal fats between the masses [11]. The mesenteric nerve plexus grows along the SMA distribution. Therefore, the characteristic finding of EUS is that the mass only grows along the SMA and does not involve the adjacent SMV. Laparoscopy revealed a large number of small, smooth, grayish-white and hard nodular structures are found in the mesentery of the small intestine, starting at the mesenteric boundary of the small intestine. Fats wrapped by nodules, further confirm the low-density on CT images. The clinical manifestations of mesenteric PNF are not typical, and vary according to the organs involved. Among them, gastrointestinal bleeding caused by lesions involving the bowel or blood vessels is the most common. Other common symptoms include abdominal pain, bloating, diarrhea, and abdominal mass. Larger tumors can also cause intestinal obstruction, intussusception, and intestinal torsion.

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## Conclusion

Mesenteric PNF on CT showed multiple soft tissue masses distributed eccentrically in the mesentery on the one side of intestine. CT scan after intravenous injection of iodine contrast agent showed that these masses were not significantly enhanced. The characteristic finding of EUS is that the mass only grows along the SMA and does not involve the adjacent SMV. In addition, under the guidance of ultrasound images and Doppler images, accurate EUS-FAN can be performed on the lesions to avoid major bleeding. Therefore, CT and EUS are of great significance for mesenteric PNF patients to formulate treatment measures and operation plans.

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## Author contributions

Guang-qiang Chen, Yong-you Wu, Duan-min Hu, Ye-ting Li had the idea for the article; Feng-yun Zhong, Hao Chen, Xue Ding, Qian Wu, Qiu-chen Guo performed the literature search and analysis; Ye-ting Li drafted original draft; Guang-qiang Chen, Duan-min Hu, Feng-yun Zhong, Yong-you Wu critically revised the work; All authors read and approved the final manuscript.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2021.04.071](https://doi.org/10.1016/j.radcr.2021.04.071).

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