Neurofibroma Cholecystitis, a Rare Manifestation in Neurofibromatosis Type 1: A Case Report

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Abstract

BACKGROUND: Neurofibromatosis Type 1 (NFT-1) is one of the most common inherited disorders and is due to spontaneous genetic mutations of the NF-1 gene. This gene codes for the tumor suppressor gene Neurofibromin. Tumors commonly associated with this disease include neurofibromas, gliomas, and peripheral nerve sheath tumors; all of which have significant malignant potential.

CASE: Our patient presented with gastrointestinal manifestations relating to NFT-1, which is an exceedingly rare occurrence. A cholecystectomy was performed for symptoms of cholecystitis due to the tumor, which was not seen on preoperative imaging studies.

CONCLUSION: A high index of clinical suspicion, and appropriate protocols for the diagnosis and treatment of intra-abdominal neoplasms in patients with NFT-1 needs to be established. This would allow for the early diagnosis and treatment of occult gastrointestinal tumors and their complications in this group of people with NFT-1. These steps could then help reduce the associated morbidity and mortality in individuals with NFT-1 and gastrointestinal manifestations of this complex disease.

Introduction

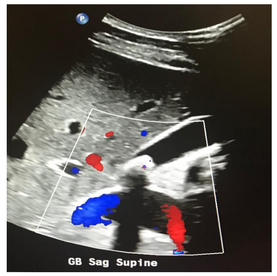
While Neurofibromatosis is a common inherited disorder, gastrointestinal manifestations of these tumors are exceedingly rare. Only 13% of patients with these neoplasms develop any gastrointestinal complaints, and even fewer present with these symptoms, which is very different from our case.

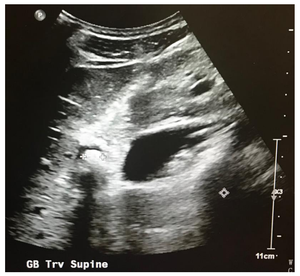
Interestingly, it has been shown that whole body MRI can be reliably used in patients diagnosed with NFT-1 to determine extent of their disease. This imaging modality has been found to demonstrate a distinctive cluster type pattern within NFT-1 patients, which aides in their identification [3].

NFT-1 associated gastrointestinal tumors are usually only identified when they become symptomatic. Most commonly these masses are diagnosed once they become quite large, begin to hemorrhage or cause obstructive symptoms which prompts evaluation. At this point they are often very difficult to treat due to their aggressive nature and nerve plexus origin which predisposes them to adhere to adjacent structures [4].

Similarly, tumors showing biliary manifestations are only seen in approximately 4% of NFT-1 patients who present with symptomatic abdominal tumors [6]. Even less common is gallbladder involvement with these neoplasms.

Furthermore, the most common presentation pattern of Neurofibromas that are found in the gallbladder are polypoid intraluminal masses, or intramural nodules. These types of neurofibromas can be identified as heterogeneous hypoechoic lesions on ultrasound, or as hypodense lesions with a hyperdense center and rim on CT with contrast [7].





Figures 1 and 2. Abdominal ultrasound: 1.5 x 0.9 x 0.9 cm mobile stone in the gallbladder

Case Presentation

A 23 year old male with Neurofibromatosis Type 1 presented to the Emergency Department complaining of progressively worsening intermittent right upper abdominal pain for 3 months with radiation to the right flank.

PHYSICAL EXAM: The patient was noted to have multiple cutaneous neurofibromas with many café-au-lait spots and several well-healed surgical scars from previous cutaneous mass excisions. His abdomen was notably tender with a positive Murphy's sign, indicative of hepatobiliary pathology. He had no scleral icterus or other signs of obstructive biliary disease. Preoperative imaging demonstrated cholecystitis but no signs of a mass on ultrasound and CT.

INTRAOPERATIVE: The patient was taken to the operating room where, intraoperatively, an inflamed, acute gallbladder was encountered. The cholecystectomy was relatively uncomplicated and completed without significant difficulty. Intraoperatively, a mass which resembled a large Calot's node was encountered and removed with the specimen.

POSTOPERATIVE: The patient progressed well and was discharged home on hospital day two. On follow up, he reported that his pain was completely resolved and he was healing well from the surgery. Since the surgery he has had no additional gastrointestinal complaints.

Pathology

The operative specimen was analyzed, and found to include a Neurofibroma with spindle cells

Some general diagnostic criteria for the surgical pathology of Neurofibromas include the following [28]:

- **Randomly oriented thin spindled cells with wavy, hyperchromatic nuclei (pictured)**
- Typically **hypocellular** in nature, with thin and thick collagen strands described as, "shredded carrot collagen"
- Variable myxoid material surrounding cells and collagen
- **Occasional mast cells and lymphocytes are common (pictured)**
- Tend to be diffusely S100 immunoreactive

The mass removed with the gallbladder was in fact a Neurofibroma and not related to Calot's node.

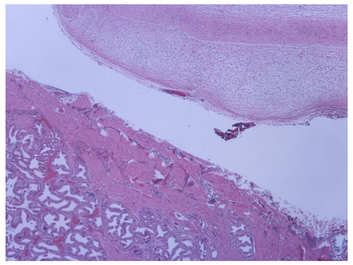


Figure 3. Neurofibroma adjacent to gallbladder

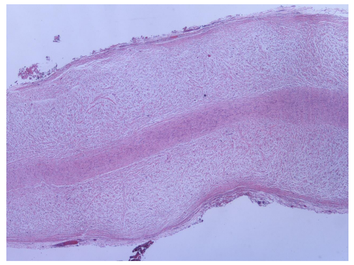


Figure 4. Neurofibroma

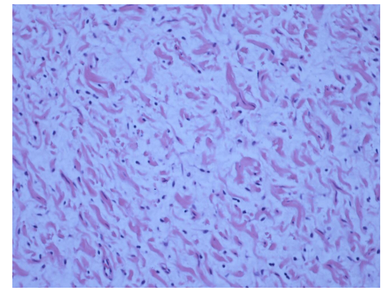


Figure 5. Neurofibroma with spindle cells with wavy nuclei without pleomorphism. Few mast cells seen.

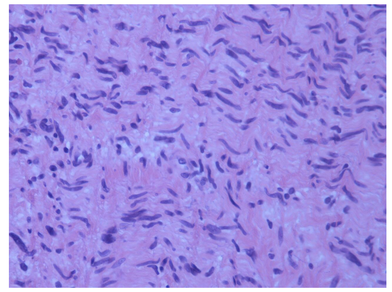


Figure 6. Cellular neurofibroma with spindle cells without pleomorphism arranged in fascicles.

Discussion

Patients with NFT-1 develop multiple tumors, most of which have malignant potential. NFT-1 patients have a decreased life expectancy which appears to be directly related to tumors progression and subsequent complications.

With NFT-1, the most common associated neoplasms include neurofibromas, gliomas, and malignant peripheral nerve sheath tumors. All of these carry a significant potential for malignant degeneration.

For intra-abdominal tumors associated with NFT-1, there have been many different imaging modalities used to identify the tumors associated with this complicated disease. Due to the nature of these tumors presenting with vague complaints, guidelines remain unclear for appropriate specific workup to direct next steps in therapy.

Ultimately the appropriate surgical treatments for intra-abdominal tumors associated with NFT-1 are based primarily on therapies relying on the patient's symptoms and findings on work up. While there are recommendations for surgical options targeted for the removal of such tumors (including local excision, pancreaticoduodenectomy, or complete or partial resection of the affected organs [7, 10, 20, 25]), these are directed by the current lack of standardized information available regarding these rare tumors and their natural histories and course.

Currently, there is a lack of standardized screening and treatment algorithms, which might otherwise allow for a more proactive identification and surgical treatment of the intra-abdominal tumors associated with patients with NFT-1.

Conclusions

Surgical intervention for Neurofibromas is variable and dependent on tumor identification, location, progression, and extent of metastasis, when present.

When possible, advanced imaging of NFT-1 patients may increase detection and aid in appropriate early treatment, of patients with occult gastrointestinal neoplasms.

However, as with diagnostic workup and screening protocols, there are no standardized or specific guidelines readily available regarding recommended surgical treatment and removal of the intra-abdominal tumors associated with NFT-1. This leads to reactive rather than proactive treatment, which oftentimes is only of limited use as the patient has already experienced significant symptomatic effects of the tumor's progression.

The clear conclusion drawn from ours and similar cases is that in a patient with NF-1 and gastrointestinal complaints, a link must be assumed and treatment including medical and surgical options should be aggressively pursued to prevent negative outcomes.

Targeted research and recommendations are needed to help decrease the associated morbidity and mortality in this group of patients, especially in light of the fact that the median survival from this disease is only age 31.

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