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A Case of Isolated Neurofibroma of the Bladder in A Young Adult Man with No History of Neurofibromatosis Type 1: A Case Report

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ABSTRACT

Background and Objective: Genitourinary neurofibroma is a benign nerve sheath tumor commonly found in patients with neurofibromatosis type 1. This disease is very rare and can appear in all urinary tracts. Considering the rarity of neurofibromatosis of the bladder, the present case report is introduced with the aim of showing the importance of this pathology.

Case Report: The patient is a 25-year-old man who visited the urology clinic last month due to hematuria. The patient did not mention any other clinical symptoms. An ultrasound was requested for the patient, and a mass was reported in the bladder. The patient underwent mass resection through the urethra. In the pathological and immunohistochemical studies, the patient was diagnosed with neurofibromatosis. The general condition of the patient after surgery is good and the patient's symptoms are resolved.

Conclusion: According to the results of this study, the patient was symptomatic and had a mass in the bladder on ultrasound. Due to the lack of a previous diagnosis of neurofibromatosis type 1 for the patient and the lack of a definite diagnosis about the type of mass, the best treatment approach is surgery and complete removal of the mass. After the final diagnosis based on histopathological and immunohistochemical evaluations, the best approach is to follow up the patient with imaging.

Keywords: *Neurofibroma, Hematuria, Bladder Tumor, Urogenital Tract.*

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Introduction

Neurofibromatosis type 1 is an autosomal dominant disease with various clinical manifestations. Skin pigment changes, iris lisch nodules and multiple benign neurofibromas usually form the clinical picture. However, patients also have learning disabilities and may have skeletal abnormalities, vascular diseases, tumors of the central nervous system, or malignant tumors of the peripheral nerve sheath (1). Neurofibromas are the most common benign tumors of the peripheral nerve sheath. They often appear as a soft, skin-colored papule or small subcutaneous nodule and originate from the endoneurium and connective tissues of peripheral nerve sheaths. Neurofibromas are composed of Schwann cells, fibroblasts, perineurial cells and mast cells in a variable myxoid area (2). There are three main types of neurofibromas: localized (most common), diffuse, and plexiform. Although most neurofibromas occur sporadically and the risk of their malignant transformation is very low, the plexiform type is pathogenic for neurofibromatosis type 1 (3).

Genitourinary involvement of neurofibroma is a rare disease and the reported cases are limited to case report studies (4). The prevalence of neurofibroma in the genitourinary system is reported to be one in 3000, which is higher in men, and the age of diagnosis is between 20-30 years (5). Less than 70 cases of bladder neurofibroma have been reported in different studies (6). Diagnosing neurofibroma of the bladder is difficult and can be confused with other pathologies of bladder tumors, which is why the gold standard for its diagnosis is to take a pathological sample from the lesion. The introduced patient is a young man with no previous diagnosis of neurofibromatosis who referred to the urology clinic with the main complaint of hematuria and underwent surgery for a bladder mass. This mass was diagnosed as neurofibroma in histopathological and immunohistochemical study.

Case Report

This study was approved by the ethics committee of Babol University of Medical Sciences with code IR.MUBABOL.REC.1400.241. The patient is a 25-year-old man without any underlying disease who was referred to a urologist with main complaint of hematuria. The patient mentions that the hematuria started about a month before the visit. The patient did not report pain during urination, burning sensation in urination and recent fever and chills, hypogastric and flank pain. He did not mention the history of drug use. In the follow-up of the patient, he underwent ultrasound of the kidneys, bladder and urinary tract.

According to the ultrasound report, the thickness of the bladder increased by 9.5 mm and contains suspended echogenic particles, which may indicate the presence of blood, pus or urinary crystals. In addition, a polypoid mass with approximate dimensions of 14×16 mm was observed on the right side of the bladder and at the lower position of its outer wall, and it was suggested that the patient undergo cystoscopy to rule out transitional cell carcinoma (TCC). No signs of anemia were observed in the patient's test results. Other requested tests were normal. The patient underwent transurethral resection (TUR) and the bladder mass was removed. The mass was then sent to the pathology unit, where a benign spindle cell neoplasm consistent with neurofibroma was reported (Figures 1 and 2).

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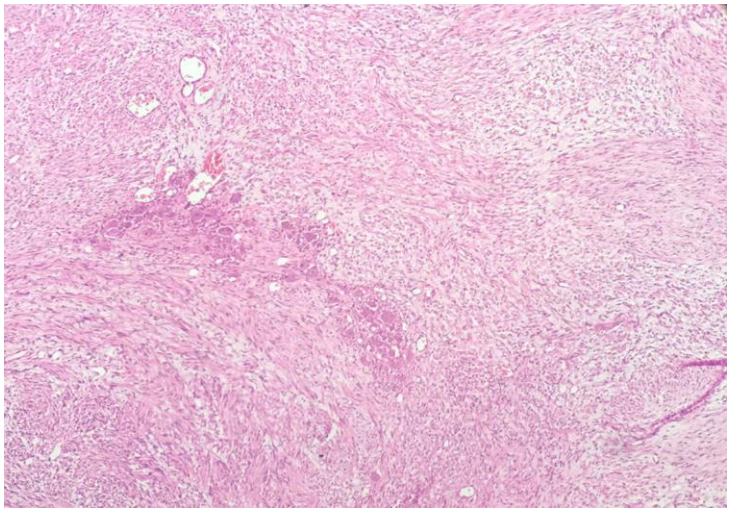


Figure 1. Pathology sample of the patient's bladder mass under the microscope with 10x zoom

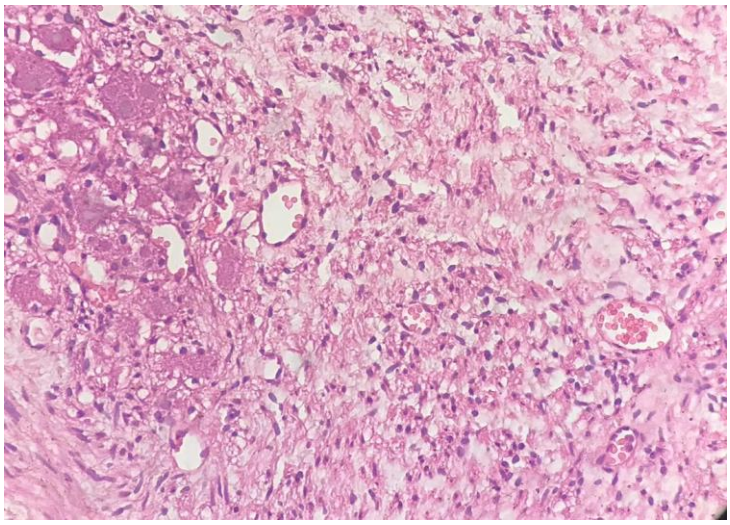


Figure 2. Pathology sample of the patient's bladder mass under the microscope with 40x zoom

In immunohistochemical evaluation, the mass was positive for CD34 and S100 receptors and a very low proliferation index was reported for Ki67. Chromogranin was also positive in ganglion cells. The mass was negative for synaptophysin. At follow-up, the patient noted that he tolerated the procedure well and that the hematuria resolved. Based on the pathological findings, the patient was advised to undergo genetic screening to diagnose neurofibromatosis type 1. Now, six months have passed since the follow-up of the patient and the patient has not had any problems.

Discussion

The importance of this patient is based on two points, the absence of a previous diagnosis of neurofibromatosis and the rarity of bladder neurofibroma. Isolated neurofibroma of the bladder is very rare

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and accounts for less than 0.1% of bladder tumors, usually seen with the genetic disease neurofibromatosis type 1. Due to the rarity of the disease, it can also be difficult to diagnose. Our patient referred only with macroscopic hematuria, while in the other mentioned cases, the symptoms of the patients are different. The symptoms reported at the time of visit may include heartburn, microscopic hematuria, recurrent infection of the genitourinary system, frequent urination, nocturnal enuresis, urinary retention due to the presence of a mass near the bladder neck, and even an asymptomatic bladder mass that is randomly diagnosed (7-11). Other typical manifestations of neurofibromatosis are rarely seen in patients presented with bladder neurofibroma (8). In the patient reported by Hosseini et al., the patient was a woman who was presented with dysuria and microscopic hematuria (6). In the case presented by Cabrera Castillo et al., the patient's symptoms included recurrent urinary tract infections and incomplete bladder emptying (12). Chakravarti et al. introduced two patients who were uncle and nephew, one with difficulty in starting urination, urgent and frequent urination and the other patient with frequent urination and nocturnal enuresis (13).

Imaging methods are useful for evaluating lesions in the abdominopelvic region, particularly in neurofibromatosis. Bladder involvement can be a focal lesion like our case, or may be in the form of diffuse thickening of the bladder wall (14). On magnetic resonance imaging (MRI), these lesions generally have low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. On T2-weighted MRI images, plexiform neurofibromas often show a target sign, with high signal intensity in the periphery and lower signal intensity in the center (15). However, the best diagnostic method is still cystoscopy and obtaining a pathological sample from the lesion.

The histology of neurofibroma cells consists of medium-sized spindle cells with elongated nuclei. In addition, S-100 immunohistochemical evaluation is positive in almost all cases of neurofibroma. The collagenized matrix is positive for Alcian blue in almost all cases (16). This histological appearance has a differential diagnosis with low-grade malignant peripheral nerve membrane tumor, leiomyoma, low-grade leiomyosarcoma, and rhabdomyosarcoma. Definitive diagnosis is made through immunohistochemical findings (17). These lesions can be managed in a variety of ways, but surgery appears to be the treatment of choice for symptomatic patients. Neurofibromas have an excellent prognosis and malignant transformation is very rare. There are no specific follow-up guidelines for this disease, but it is recommended that patient follow-up be considered which includes routine imaging to monitor local recurrence given the possibility of malignant transformation (9). Hosseini et al. also removed the patient's mass through the urethra and the patient's symptoms improved after surgery (6). Georgiadis et al. presented a patient with a bladder neck mass that was followed up with cystoscopy after resection of the mass. The patient underwent cystoscopy three times, and the tumor size increased again and the patient underwent mass resection. Bladder neck resection was suggested to the patient, and the patient preferred supportive care (5). Our patient became asymptomatic after surgery, but in the study of Wong-You-Cheong et al. (17), neurogenic bladder and atonic bladder and continuous macroscopic hematuria were reported, which indicates the need for long-term follow-up of patients.

In this study, we present a 25-year-old man with no previous diagnosis of neurofibromatosis with a bladder mass diagnosed as an isolated neurofibroma. Isolated neurofibromas of the bladder are extremely rare, so treatment recommendations are largely the same as other bladder masses. Resection of the tumor through the urethra is suitable for establishing the diagnosis in a symptomatic patient. Careful follow-up of the patient in the clinic is essential, and urinary symptoms should continue to be monitored, as urinary

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symptoms may be an early sign of recurrence. Follow-up cystoscopy evaluation should be accompanied by imaging evaluations to monitor potential local recurrence or progression.

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