**Case Reports**

# Neurofibroma of the vaginal wall

**S. Baulies,** *M.D.*; **M.T. Cusidó,** *M.D.*; **P.J. Grases[1],** *M.D.*; **B. Úbeda,** *M.D.*; **M.A. Pascual,** *M.D.*; **R. Fábregas,** *M.D.*

*Department of Obstetrics, Gynecology and Human Reproduction, and [1]Pathological Anatomy Department, Institut Universitari Dexeus, Barcelona (Spain)*

**Summary**

*Background:* Von Recklinghausen's disease is characterized by cutaneous manifestations but it is a systemic disease which may affect the genitourinary tract. *Case:* A 20-year-old woman with a history of type-1 neurofibromatosis attended our center due to a vaginal nodule. Surgical treatment consisted of an incisional biopsy of the nodule. The anatomopathological diagnosis was plexiform neurofibroma. *Conclusion:* Periodical check-ups are recommended in asymptomatic vaginal neurofibroma whereas its radical excision should be avoided as such surgery is highly aggressive.

*Key words:* Vaginal neurofibroma; Genital neurofibroma; Neurofibromatosis; Vaginal nodule.

## Introduction

Von Recklinghausen's disease or type-1 neurofibromatosis (NF1) is a hereditary disorder of autosomal dominant transmission that affects 1 in 3,000 people. It is characterized by a mutation of the NF1 gene and its main phenotypic feature is the presence of multiple skin neurofibromas and café-au-lait spots. Neurofibromas may affect any organ of the body, including the cardiovascular system, gastrointestinal tract and larynx [1]. Genitourinary involvement is less common, the bladder and vulva being the organs most often affected [2]; however, a few cases of vaginal involvement have been described [3-5].

This paper presents the findings from a single case and describes the typical features of neurofibromatosis (NF), an uncommon systemic disease, which nevertheless may be seen among women attending a gynecology clinic.

## Case Report

A 20-year-old woman with no remarkable family history came under our care. She had menarche at 12 years of age with normal menstrual cycles. The patient had never had a gynecological check-up but had been diagnosed at ten years of age with type-1 NF; the genetic test was positive. The rest of her family tested negative. The patient presented skin manifestations (café-au-lait spots and a cutaneous neurofibroma on her chest), but without ocular involvement. She brought along the results of a cranioencephalic magnetic resonance imaging (MRI) scan performed seven years previously, which showed multiple supra- and infra-tentorial hamartomatous lesions that had remained stable at her last check-up earlier this year.

Following a clinical course of several years involving intermenstrual spotting and dysmenorrea which had worsened during the last year, she attended our center for a check-up. Physical examination revealed a tumor occupying the whole of the anterior left lateral wall of the vagina with extrinsic compression and displacement of the urethral meatus (Figure 1). The patient did not report any discomfort or pelvic pain during sexual relations, although she described having noticed an alteration in the direction of her urine stream over the last few years.

After obtaining a normal cervical cytology abdominal pelvic ultrasound (US) and pelvic MRI were performed. The US (Figure 2) showed an anteverted uterus with regular morphology and a homogeneous myometrial pattern; the adnexa were normal. However, in the upper third of the vagina, toward the left of the central area, there was a well-circumscribed and encapsulated nodule (probably intramural) measuring 47 x 41 x 27 mm which appeared not to be affecting the bladder or cervix. A color Doppler study showed the nodule had minimal vascularization. MRI also revealed an intramural vaginal tumor with irregular contours localized on the anterior wall of the vagina. This mass, which measured approximately 7 x 4 x 2 cm and extended from the vaginal dome to the vulvar region, was predominantly hypointense in T2 with small foci of greater intensity on the inside. No vesical involvement was observed (Figures 3 and 4).

The clinical diagnosis was an adenomyotic nodule versus neurofibroma with compromised micturition, and it was thus decided to intervene surgically. An incisional biopsy was performed, the outer portion of the tumor being excised by means of a wedge resection using the cold scalpel technique; the edges were then brought together and the urethra checked for permeability (Figure 5). The patient presented no post-operative complications.

Anatomopathological findings confirmed the diagnosis of plexiform neurofibroma.

The patient is currently being followed-up annually and has shown a satisfactory clinical evolution, and the micturition problems have disappeared.

*Pathological anatomy*

The macroscopic findings showed an irregular specimen consisting of shiny, moist tissue, light yellowish-gray in color, with a weight of 3 g and measuring 3 x 1.5 x 1 cm.

Histopathological study using hematoxylin-eosin stains revealed a tumor consisting of tortuous nerve bundles and a plexiform pattern. The fibers presented mixoid changes of mul-

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Fig. 1a

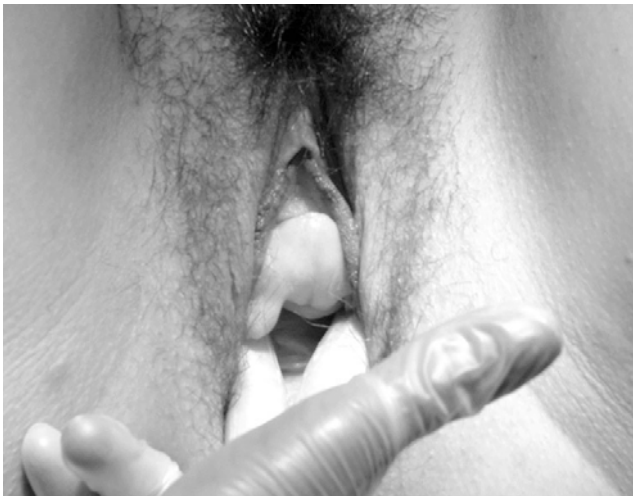

Fig. 1b

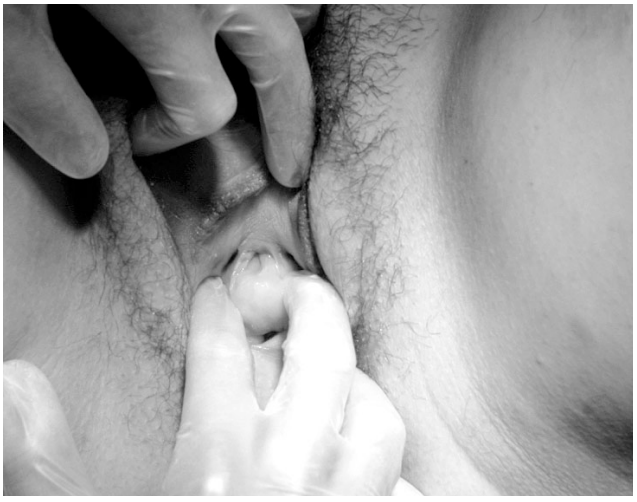

Fig. 2

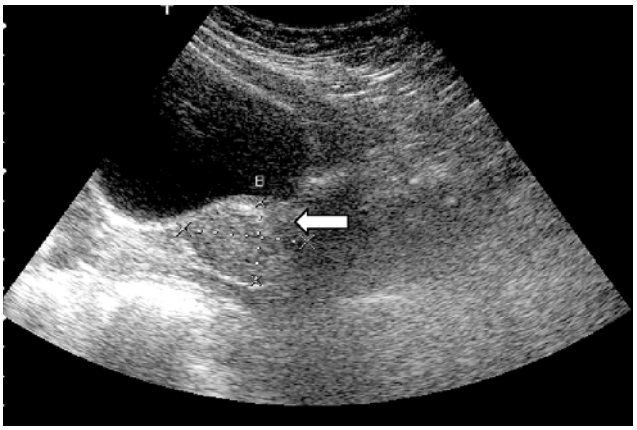

Fig. 3

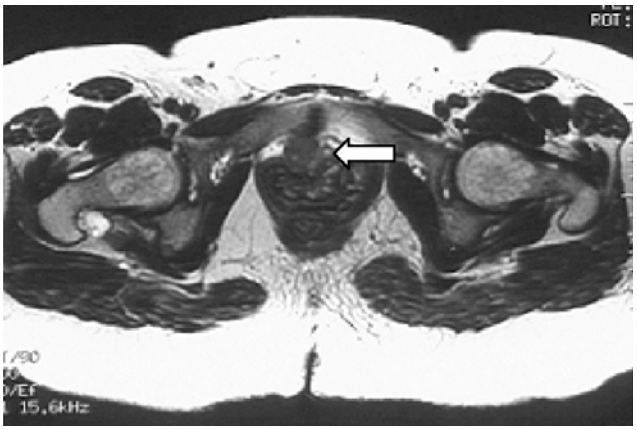

Fig. 4

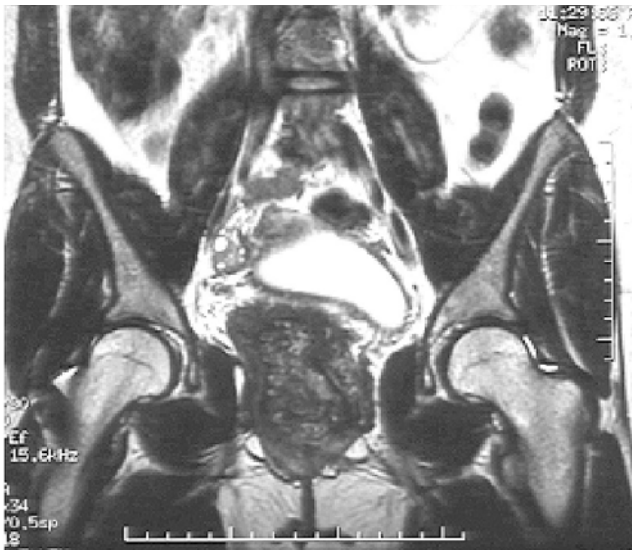

Figure 1. — Tumor on the anterior left lateral wall of the vagina (a) compressing the urethral meatus (b).

Figure 2. — Transvesical ultrasound. Longitudinal slice showing an encapsulated nodule which does not appear to affect the bladder or cervix.

Figure 3. — MRI. Axial slice in T2 showing an intramural tumor on the anterior vaginal wall; the signal is hypointense and there is no urethral involvement (arrow).

Figure 4. — MRI. Coronal slice - mass causing bulging in the anterior wall of the vagina but without vesical involvement.

tifocal origin. These plexa were surrounded by NF tissue showing fusiform cells. No atypias or other signs of malignancy were found (Figure 6). The lesion was observed to be partially covered by normal vaginal mucosa and was in extensive contact with the resection margin. In terms of immunohistochemistry, the cells from the nerve plexa as well as some from the surrounding tissue expressed the S-100 protein.

The diagnosis was a plexiform neurofibroma of the vaginal wall.

## Discussion

NF is a hereditary disorder of the tissues derived from the neural crest, although tissues and organs of mesodermic origin may also be affected (2). It is characterized by the presence of progressive anomalies of the skin, central and peripheral nervous systems, skeleton, and internal secretion glands, and may occasionally affect other organs and systems such as the digestive, cardiovascular

Fig. 5

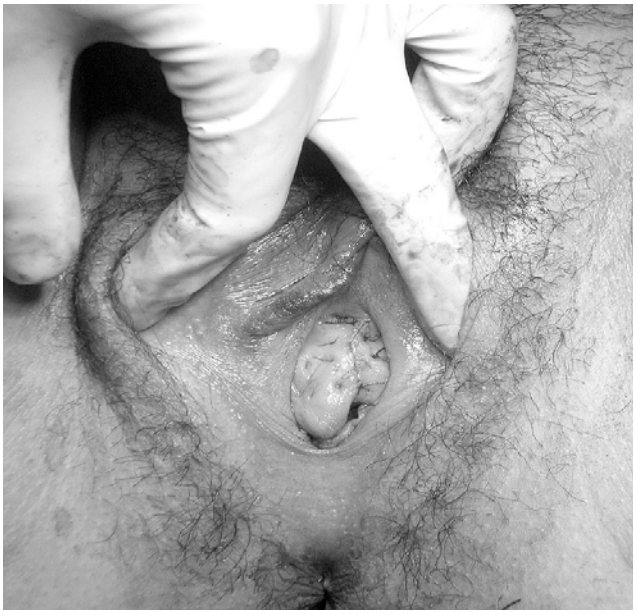

Figure 5. — Appearance of the vulva after surgery.

Fig. 6

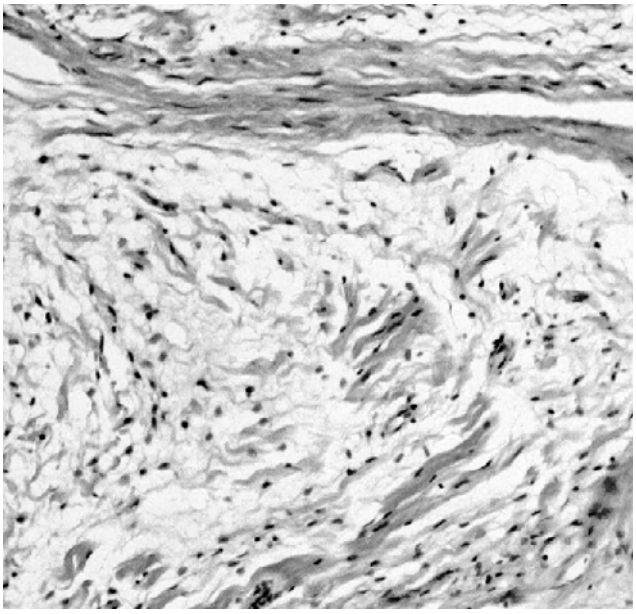

Figure 6. — Microscopic appearance of the lesion.

and genitourinary apparatus. Two types of NF have been described: type-1 neurofibromatosis (NF1) or von Recklinghausen's disease, which affects 85% of patients, and type-2 or central neurofibromatosis (NF2), which affects 10-15%. Both types are the result of autosomal dominant inheritance with complete penetrance and variable expressivity, although 50% of cases are due to *de novo* mutations.

The NF2 gene is located on chromosome 22 and the disease is characterized by bilateral acoustic schwannomas in patients with little or no cutaneous signs of NF. However, patients with NF1 rarely develop neurinomas of the eighth cranial nerve [1].

NF1 affects one in every 3,000 people. Its gene is located on chromosome 17 and normally acts as a tumor suppressor gene encoding the protein neurofibromin, which is expressed in several tissues and functions as a negative regulator of intracellular ras-GTP signaling. The characteristic clinical features of the disease are café-au-lait spots and skin neurofibromas, which increase in size and number during childhood and especially following puberty. Extracutaneous manifestations occur in one percent of cases and are more likely to affect the bladder or the gastrointestinal tract [6]. Genital involvement is rare, the vulva and clitoris being the areas most commonly affected. The cardinal symptoms are highly variable, including metrorrhagia, dyspareunia and chronic pain, and depend, above all, on the area affected; thus, clitoral neurofibromatosis may be the cause of intersexual states [7]. The first case of vaginal NF was described by De Jorio and Belfiore in 1970 [3]. In recent years numerous cases of NF with vulvar or clitoral involvement have been reported, although the literature contains few reports of vaginal neurofibromatosis and those which have been published are not always related to NF1 [4, 5]. In our case the neurofibroma was NF1 and was confined solely to the vagina, with the only effect being alterations to micturition.

It is not usually difficult to diagnose a neurofibroma in a patient with skin neurofibromas and café-au-lait spots. Although US is usually the first imaging technique used to study the pelvic region, both computed tomography (CT) and MRI scans are necessary to accurately define the characteristics of the nodule and its limits. MRI is preferable to a CT scan as it offers a multi-plane view and is able to differentiate tissue; it is also useful for characterizing lesions and determining the extent of a tumor.

The current diagnostic criteria for NF1 are those approved in 1988 by the NIH Consensus Development Conference [8]. The differential diagnosis of a vaginal nodule includes adenosis (due to the mother being exposed to diethylstilbestrol or post-treatment of a condylomatosis with 5-fluorouracil), polyps, leiomyomas, rhabdomyomas, hemangiomas, neurofibromas and malign tumors (rhabdomyosarcoma, adenocarcinoma) [9].

The treatment for cases of genitourinary neurofibromatosis has yet to be established and may be conservative or surgical depending on the extent of the disease and the clinical features. Neither radiotherapy nor chemotherapy has proved beneficial [2].

As there is malign degeneration in approximately five percent of people with NF1 [2], it is necessary to perform a biopsy in those patients where this is suspected. In our case, an incisional biopsy was performed to confirm the diagnosis of neurofibroma and treat the altered micturition. After surgery the patient evolved favorably and the micturition problems disappeared. Complete excision of a vaginal neurofibroma requires highly aggressive

surgery and recurrence is common. Therefore, in asymptomatic women the advice is to monitor the situation through periodic check-ups involving a pelvic US and MRI to detect possible changes in the characteristics and size of the tumor.

In sum, the diagnostic procedures to be used when faced with a vaginal nodule are, firstly, a pelvic US (either vaginal or abdominal), followed by MRI to characterize and determine the extent of the tumor. When a vaginal neurofibroma is diagnosed, strict monitoring through imaging tests every six months is recommended in asymptomatic women to detect any changes in tumor consistency and size. If there is suspicion of malignancy or symptomatology it is advisable to perform an incisional biopsy to determine the diagnosis and resolve the clinical signs. However, radical excision of a vaginal neurofibroma should be avoided as such surgery is highly aggressive and does not offer significant benefits (neurofibromas frequently reoccur). Moreover, it may cause serious postoperative problems including painful hypersensitivity in the area of the incision, possible damage to nerve endings leading to hypostesia, and even constrictions which may hinder future sexual relations.

## References

[1] Weiss S.W., Goldblum J.R.: "Enzinger and weiss's soft tissue tumors". 4th ed. St, Louis, MO, Mosby Inc, 2001.

[2] Wilkinson L.M., Manson D., Smith C.R.: "Best cases from the AFIP: Plexiform neurofibroma of the bladder". *RadioGraphics.,* 2004, *24* (suppl. 1), S237.

[3] De Jorio A., Belfiore M.: "Rare case of vaginal localization in the course of Recklinghausen's disease". *Rass. Int. Clin. Ter.,* 1970, *50*, 105.

[4] Dekel A., Avidan D., Bar-Ziv J., Ben David M., Goldman J.A.: "Neurofibroma of the vagina presenting with urinary retention: review of the literature and report of a case". *Obstet. Gynecol. Surv.,* 1988, *43,* 325.

[5] Sharma J.B., Wadhwa L., Malhotra M.: "Huge localized vaginal neurofibromatosis: an unusual cause of postmenopausal bleeding". *J. Obstet. Gynaecol. Res.*, 2004, *30,* 96.

[6] Gordon M.D., Weilert M., Ireland K.: "Plexiform neurofibromatosis involving the uterine cervix, myometrium and ovary". *Obstet. Gynecol.,* 1996, *88*, 699.

[7] Wei E.X., Albores-Saavedra J., Fowler M.R.: "Plexiform Neurofibroma of the Uterine Cervix". A*rch. Pathol. Lab. Med.*, 2005, *129,* 783.

[8] National Institutes of Health consensus development: "Neurofibromatosis". *Arch. Neurol.,* 1988, *45*, 575.

[9] Grasses P.J.: "Vulva: lesiones benignas. Patología ginecológica: bases para el diagnóstico morfológico". Barcelona, Masson, 2003, 3.

Address reprint requests to:
S. BAULIES CABALLERO, M.D.
Department of Obstetrics Gynaecology
and Human Reproduction
Institut Universitari Dexeus
C/Gran Via Carles III, 71-75
08028 Barcelona (Spain)
e-mail: sonbau@dexeus.com