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Retrocaval mass in patient with von Recklinghausen disease. Case report

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SUMMARY: **Retrocaval mass in patient with von Recklinghausen disease. Case report.**

G. CAVALLARO, D. CROCETTI, G. PEDULLÀ, S. GIUSTINI, C. LETIZIA, G. DE TOMA

Type I Neurofibromatosis (NF1) is an autosomal-dominant inheritable disorder, with an incidence of 1:3,000, and a prevalence of 1:4,000 to 5,000. Pathogenesis is based on mutations of the NF1 gene, a tumor suppressor gene encoding a cytoplasmic protein named neurofibromin that controls cellular proliferation. Patients affected by NF1 typically present with cutaneous neurofibromas, café au lait spots and eye involvement, but they can also be affected by various visceral tumors, such as neurofibromas (nodular or plexiform type), gastrointestinal stromal tumors or endocrine tumors, such as pheochromocytomas. Visceral neurofibromas are often asymptomatic but when growing in size they may present with pain, palpable abdominal mass, symptoms secondary to bowel obstruction or main vessels compression, and even gastrointestinal bleeding when mucosa or submucosa are involved. In these cases surgery becomes mandatory in order to remove all neoplastic tissue.

The Authors describe a case of a young man affected by NF1 with associated retrocaval abdominal mass with compression and displacement of the inferior vena cava, thus requiring a complex surgical procedure

RIASSUNTO: **Massa retrocavale in paziente affetto da malattia di von Recklinghausen. Caso clinico.**

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La neurofibromatosi di tipo I (NF1) è una malattia a trasmissione genetica autosomico dominante, con una incidenza di 1:3000 e una prevalenza di 1:4000-5000. La patogenesi si basa su mutazioni del gene NF1, gene onco-soppressore che codifica una proteina chiamata neurofibromina, che controlla la proliferazione cellulare. I pazienti affetti da NF1 presentano tipicamente neurofibromi cutanei, macchie caffelatte e interessamento oculare e possono essere affetti da neoplasie viscerali di varia natura, come neurofibromi, tumori stromali gastrointestinali, tumori endocrini (feocromocitoma). I neurofibromi viscerali sono spesso asintomatici, ma aumentando di dimensioni possono manifestarsi come massa addominale e/o provocare dolore, sintomi di occlusione intestinale o compressione sui grossi vasi, e talora emorragie endoaddominali o gastrointestinali. In questi casi l'approccio chirurgico diventa obbligatorio pe rimuovere il tessuto neoformato.

Gli Autori descrivono un caso clinico di un giovane adulto affetto da NF1 con associata neoformazione retrocavale che comprimeva e dislocava la vena cava stessa e che ha richiesto una complessa procedura chirurgica.

KEY WORDS: Neurofibromatosis - Abdominal mass - Surgery.
Neurofibromatosi - Massa addominale - Chirurgia.

Introduction

Type I Neurofibromatosis (NF1), known as von Recklinghausen disease, is an autosomal-dominant inheritable disorder, with an incidence of 1:3,000, and a prevalence of 1:4,000 to 5,000 (1). The pathogenesis is based on mutations of the *NF1* gene, a tumor suppressor gene encoding a cytoplasmic protein named neurofibromin that controls cellular proliferation (2-7).

Neurofibromas are the most common visceral tumors in NF1 patients. They are composed of Schwann cells, fibroblasts, and myxoid matrix and take origin from a peripheral nerve or a plexus (plexiform neurofibromas).

Visceral neurofibromas are often asymptomatic (65%) but when growing in size they may present with abdominal pain, palpable abdominal mass, symptoms secondary to bowel obstruction or main vessels compression, and even gastrointestinal bleeding when mucosa or submucosa are involved. In these cases surgery becomes

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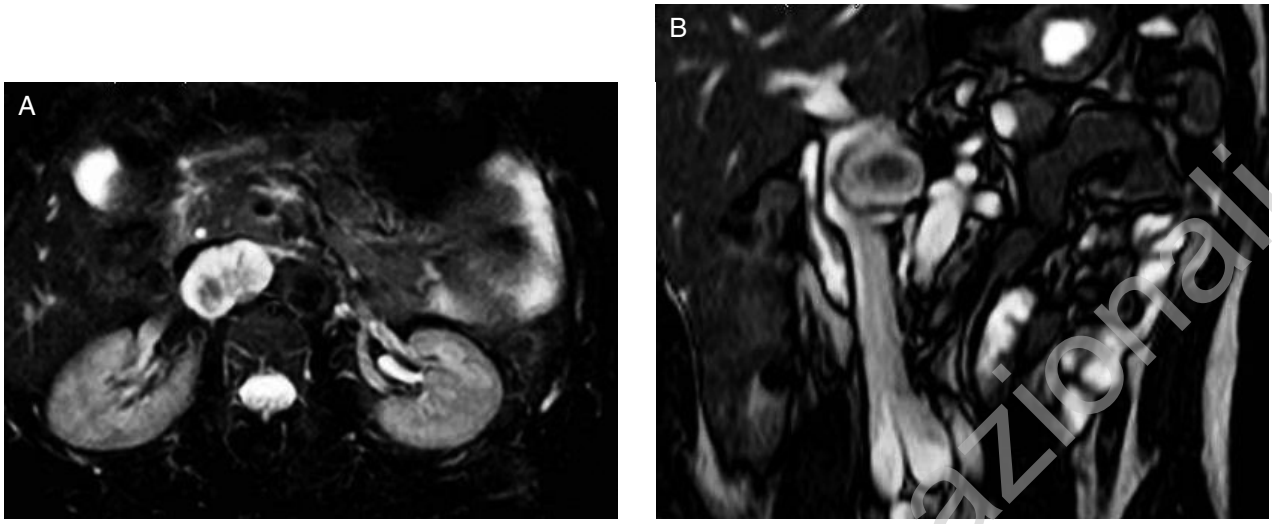

Fig. 1 A and B - MRI shows the retrocaval neurofibroma, compressing and displacing anteriorly the inferior vena cava.

mandatory in order to remove all neoplastic tissue. Plexiform neurofibromas involve paravertebral nervous plexus or many nerve fascicles inside a large-sized nerve, are often bilateral and simmetric,and grow up and invading and displacing surrounding structures, such as paravertebral muscles.

The Authors describe a case of a young man affected by NF1 with associated retrocaval abdominal mass in retroperitoneum, with compression and displacement of the inferior vena cava, thus requiring a complex surgical procedure.

Case report

M.M.,46-year old man, affected by NF1, hypertension and a pelvis bone cyst. Due to chronic low back pain and lower limbs edema, the patient underwent abdominal MRI that revealed a neurogenic tumor about 4.8 cm in diameter, located in right lumbar paravertebral position. The tumor compressed and displaced anteriorly both the inferior vena cava and right renal vein. MRI showed another neurogenic mass (4.6 cm in diameter), located in the pelvis, between internal and external left iliac vessels (Figs 1 and 2). Laboratory test showed no abnormalities. The patient was admitted to our Department, in order to remove both visceral tumors. Through total midline incision, extensive mobilization of the inferior vena cava (Fig. 3), right renal vessels and right kidney-adrenal were performed with careful division of three posterior lumbar veins and of right adrenal vein, in order to achieve a complete resection of the retrocaval mass. Excision of the left iliac tumor required careful dissection of left ureter and both internal and external iliac vessels.The retrocaval and iliac masses measured respectively about 5.0 and 4.5 cm in diameter (Fig. 4), and showed, irregular shape, greyish colour and elastic consistency.

Postoperative course was uneventful.

At histology, both tumors showed nerve-like fascicular architecture, cells with sinusoidal nucleus leaking chromatin and eosinophilic cytoplasm with indistinct margins. These fascicules were in myxoid or fibrous matrix. Immunohistochemistry revealed positive reaction to anti-neurofilament antibodies.

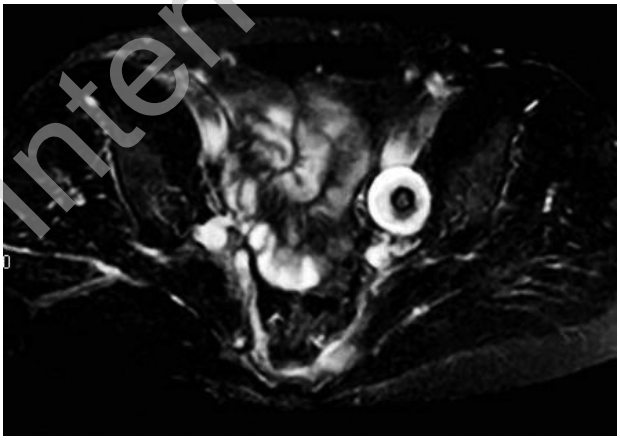

Fig. 2 - MRI. Left iliac neurofibroma.

Discussion

Abdominal manifestations of NF1 include five kinds of tumors: neurogenic tumors (neurofibromas, malignant peripheral nerve sheath tumors [MPNSTs], and ganglioneuromas); neuroendocrine tumors (pheochromocytomas and carcinoids); non-neurogenic gastrointestinal stromal tumors (GISTs); embryonal tumors; and miscellaneous (1, 8). Non-neoplastic associations may also include cardiovascular disorders such as hypertension and a high frequency of congenital heart and vascular diseases (valvular pulmonary stenosis, arterial aneurysms) (9).

Tumors of neuroendocrine origin are gastrointestinal neuroendocrine tumors (carcinoids) and mainly pheochromocytomas. The association between pheochromocytoma and NF1 is well defined and accepted (10). Furthermore, patients with NF1 present an increased risk

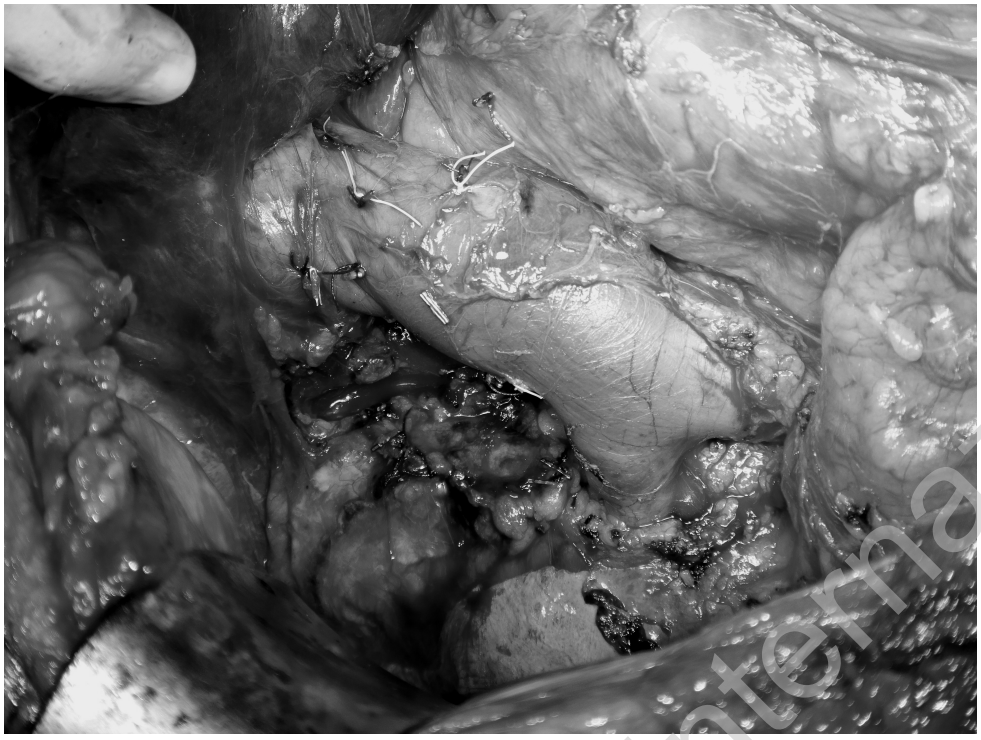

Fig. 3 - Inferior vena cava after tumor excision.

to develop GISTs, mesenchymal neoplasms of the gastrointestinal tract arising from the interstitial cells of Cajal of the myenteric plexus (11, 12). In patients with NF1, the incidence of GISTs is increased up to 25 per cent (13); moreover, NF1-associated GISTs present peculiar characteristics compared with sporadic GIST. They usually arise from the small bowel rather than the stomach, are often multiple, present early (median age 50 years), and have a less aggressive behaviour (14 -16). The miscellaneous group of tumors related to NF1 are adenocarcinomas, involving the whole gastrointestinal tract (17).

Neurogenic tumors include neurofibromas, ganglioneuromas and MPNSTs. MPNSTs are the most common malignancy in patients with NF1. These tumors can arise from pre-existent plexiform neurofibromas (10%). Ganglioneuromas are benign tumors that originate from sympathetic ganglia and are frequently localized in the paravertebral plexus, in the adrenal glands and rarely, as polyps, in the gastrointestinal tract. Neurofibromas are the most common abdominal and gastrointestinal tumors in NF1 patients. They are composed of Schwann cells, fibroblasts and myxoid matrix and take origin from a peripheral nerve or a plexus (plexiform neurofibromas) (18). The former are well-defined lesions confined to the nerve, the latter are complex and disordered masses involving the entire plexus or multiple fascicles of a large-sized nerve with totally modified architecture (18). Moreover plexiform neurofibromas are exclusive of NF1 and may develop into MPNST.

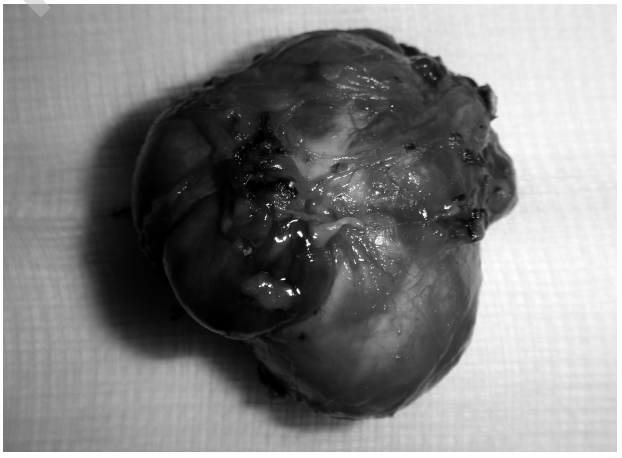

Fig. 4 - Specimen of the retrocaval tumor.

Neurofibromas are often asymptomatic (65%) but when growing up they may cause symptoms and signs due to compression, displacement or obstruction of surrounding structures, such as small or large bowel. They may present with chronic or acute pain, or gastrointestinal bleeding when the mucosa or submucosa are involved (19, 20). Compression of large abdominal vessels (vena cava, aorta, etc.) seems to be very rare.

Imaging findings depend on tumor localization. On CT scan, neurofibromas appear as smooth, round, or tubular masses homogenously hypoattenuating (21), whe-

reas on MRI they typically present low signal intensity on T1-weighted images and high signal of cystic or myxoid areas and low signal of the collagenous and fibrotic tissue on T2-weighted images with enhancement after gadolinium administration. Plexiform neurofibromas appear with the characteristic "ring-like" pattern resulting from their fascicular architecture (22). Neurofibromas of the gastrointestinal tract often appear as thickening of the bowel wall or multiple nodules recognized at conventional barium examination as mural rigidity, external mass effect, or scalloping of the mucosa. Neurofibromas localized in the gastrointestinal tract are often incidentally detected during surgery for associated tumors. Extraperitoneal neurofibromas are often single and can be localized everywhere in the retroperitoneal space, mainly in the paraspinal position.

Surgical removal, when technically feasible, prevents local infiltration and malignant transformation (23). However, complete removal is not always possible and often, when neurofibromas involves large vessels or other "vital" structures, surgery becomes very demanding and requires technical skill and dedicate experience. In our case removal of the retrocaval mass required extensive and careful isolation of the inferior vena cava and right renal vessels and division of posterior lumbar veins.

Early diagnosis of these abdominal manifestations is very important because of the risk of malignancy, organic complications, or hemorrhagic–obstructive complications, such as in case of tumors of the gastrointestinal tract. Mutation testing attains the diagnosis of neurofibromatosis in over 95 per cent of patients; however, it is still unable to predict disease severity (24).

Because of the variety of clinical manifestations of NF1, the severity of this disorder ranges from benign (75%) to very aggressive conditions (25%). Patients with a complete deletion in the *NF1* gene seem to present a characteristic phenotype with cognitive impairment, a high number of neurofibromas, and dimorphism (25). Recent studies reported an association between microdeletions and a higher risk of developing MPNST (26). The importance of severity prediction is evident to program a closer follow-up and, moreover, to obtain prenatal and preimplantation diagnosis (27).

Conclusion

NF1 unpredictable course and the lack of a definitive treatment impose an annual clinical evaluation by a multidisciplinary pool of clinicians in highly specialized centers.

Clinical manifestations of NF1 present a wide range of severity depending on timing, extension, and number of mutations of the *NF1* gene.

Based on our experience, abdominal masses associated with NF1 should be approached in case of compression, obstruction, bleeding and when the size of neoplasm is more then 4 cm in diameter for increased risk of malignant transformation and possible compressive/obstructive complications, mainly in young patients.

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