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Abdominal signs of von recklinghausen's disease a rare case report and revue of literature

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Abstract
Von recklinghausen's disease is a dominant genetic disease whose incidence is 1 in 4000 of all cases are spontaneous mutations, it belongs to phacomatoses and is part of neurocristopathy. The disease manifestations are extremely variable. The abdominal manifestations during this disease is well described in the literature, but of relatively rare occurrence.
We report in this article the case of a patient aged 2 years, recently admitted to the pediatric surgery department for a retro-vesical pelvic mass discovered on the abdomino-pelvic ultrasound performed in the etiological assessment of chronic diarrhea in von recklinghausen disease. The patient underwent a surgery with favorable post-operative follow up, histopathological evaluation of the piece returned to a bladder wall ganglioneuroma associated with diffuse neurofibroma. Association of neurofibromatosis 1 and ganglioneuroma is rarely reported in the literature.
The follow-up of patients with nf1 is clinical and radiological in the quest for complications that could involve the patient's prognosis, hence the urgency of the surgical management of complications of benign or malignant tumor.

Keywords: neurofibromatosis 1, ganglioneuromatosis, surgery

1. Introduction
Neurofibromatosis type1 or Von Recklinghausen disease is a progressive multi-systemic disease transmitted according to the autosomal dominant inheritance pattern. Among the most common genetic diseases, it accounts for 95% of all neurofibromatosis [1].
Affect multiple organs, with a particular predilection for the skin and the nervous system [2].

2. Case report
Boy aged to 2 years old, consults for pelvic mass. With father and 2 sisters followed for neurofibromatosis type 1.
he presented chronic diarrhea (4 - 6 stools a day) associated with a prolonged fever -Abdominal examination: finds a flexible abdomen; not hepatomegaly or splenomegaly.
Dermatological examination: multiple coffee-milk tasks (>6) in all the body, of different sizes, the largest of which was 12 mm; without neurofibromas or lentigines.
In addition there is in the back a hyperpigmented lesions extended from the base of the thorax to the upper third of the two thighs and the Ano-perineal region.
The neurological examination shows a good axial and peripheral tone, normal acquired walking. Moreover, no motor deficit, the sign of babinski is negative, and a good cognitive development according to the age of the child. There is also no evidence of intracranial hypertension, and examination of the cranial pairs has been normal.
A cystoscopy of 03/09/2018 revealed a normal bladder with walls dented on its posterior face, not mass intra vesical. The ureters had normal appearance.
The initial management consisted of a transrectal biopsy of the mass done on 26/09/2018.
The anatomo-pathological examination is as follows: The cuts showned a rectal mucosa and a nerve fibers on schwannian contain mature ganglionic nerve cells: appearance suggestive of a well-differentiated neuroblastic tumor.
- Abdominal CT occuredt a pre-rectal retro-vesical process, with heterogeneous density. It measures 43 x 34 x 64 mm vs 48 x 35 x 67 mm. it infiltrates forward the bladder with irregular parietal thickening of the upper and posterior walls measuring 13 mm maximum; it had contact with the rectum without signs of invasion; appearance suggestive of a ganglioneuroblastoma. Figure 1

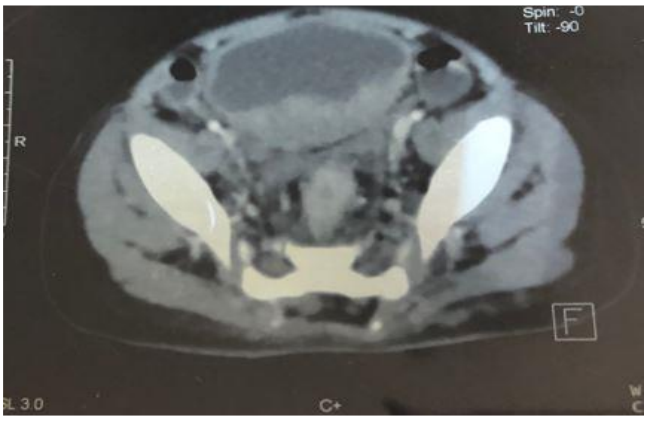

Fig 1: CT scan showing the appearance of the tumor

In addition, the adrenals are of normal size and morphology. Deformations of the last two sacred pieces.
A surgical procedure was then decided: the bladder was open vertically revealing an obvious tumor, it included a part of the posterior wall of the bladder, but showed no extra-vesical extension, a total resection of the mass passing normal zone macroscopically is performed, the bladder was closed afterwards. figure 2, figure 3).
Anatomo-pathological examination of the part concluded to a Ganglioneuroma of the bladder wall, associated with diffuse neurofibroma.
The postoperative consequences were simples.
The patient was then referred to the pediatric medical oncology consultation; or no adjuvant treatment has been indicated.

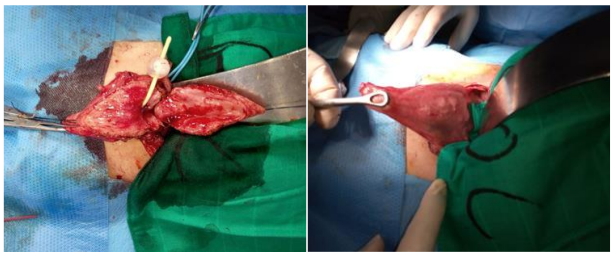

Fig 2 and 3: Intraoperative images of the bladder tumor

3. Discussion

NF1 is the most common phacomatosis and neurofibromatosis.
It represents 95% of all NF. Its prevalence is approximately one in 4000 [3].
There is no predominance of sex or race [4]. There are mainly neurological, dermatological, ophthalmological and orthopedic disorders [4, 5].
Clinically, the signs can be classified into 2 categories: cardinal signs and complications.
This disease have several complications that can be part of its manifestations.
Most of the complications of NF1 are secondary to the compressive nature of visceral neurofibromas in the urinary, digestive or pulmonary systems.

a. Digestive complications

The involvement of the digestive tract is estimated at 12 to 40% of NF1 cases, especially after 11 years [6].
It is either a secondary lesion to extradigestive neurofibromas compressing or even invading the digestive structures, or a primitive lesion by specific neurogenic or glandular lesions located in the digestive tract. Indeed, NF1 can be accompanied by digestive manifestations such as hyperplastic lesions of the plexuses, ganglioneuromatoses [7], gastrointestinal stromal tumors (TSD) [8, 9, 10], duodenal and ampullary endocrine tumors (somatostatinoma [11].
The frequency of digestive neurofibromas has been estimated at about 2% of NF1 patients [4], most often at the level of jejunum [6].
Indirect involvement is secondary to the extension of retroperitoneal tumors, they are most often asymptomatic, sometimes revealed by an abdominal mass syndrome. The infiltration is sometimes impressive, extending into the peritoneal cavity, the hepatic parenchyma and the mediastinum.
Diagnosis is assisted by ultrasound and abdominal CT. The degeneration is still to be feared and only a biopsy can possibly remove the doubt.

The digestive tumors encountered during NF1 can be classified into 5 categories [12, 13]:

- neurogenic tumors (neurofibromas, plexiform neurofibromas, malignant peripheral nerve tumors, Triton tumor, ganglioneuroma [8].
- Neuroendocrine neoplasia (carcinoid tumors, pheocromocytomas, paragangliomas, gangliocytic paragangliomas)
- Non neurogenic gastrointestinal mesenchymal tumors (Gastrointestinal stromal tumors, leimyomas, leiomyosarcoma)
- Embryonic tumors (rhabdomyosarcomas, neuroblastomas, Wilms tumor) - Other tumors (gastrointestinal adenocarcinoma, pancreatic adenocarcinoma, biliary adenocarcinoma).
- These attacks can be localized or diffuse, sometimes associated with each other.

The locations in order of decreasing frequency are jejunum, stomach, ileum, duodenum, colon and mesentery, exceptionally the liver (hilum or extrahepatic tract) or pancreas.
They are often asymptomatic, revealed by palpation or by ultrasound [14].
For the intestine, the manifestations may be a pseudo Hirschprung, abdominal pain, transit disorders, digestive haemorrhage, occlusion or intestinal perforation.
For gastric locations, patients may have dyspepsia, ulcerative pain or digestive haemorrhage, and cholestasis for the liver if neurofibroma is located on the biliary or periportal tract.
Indeed, in hepatic localizations, plexiform neurofibromas often infiltrate the portal spaces and the perihepatic region. Their surgical exeresis is often delicate or impossible, and only their extension can mark the malignant transformation

b. Uro-genital complications

Urogenital involvement during NF1 is rare, it affects preferentially the bladder [15, 16] (as the case of our patient). The first case of bladder involvement in children was described in 1932 by Kass [17].
The clinical signs of NF1-related urinary involvement are often obstructive (dysuria - acute urinary retention) [18] sometimes hematuria [19], recurrent urinary tract infections [20], unilateral or bilateral ureterohydronephrosis [19, 21, 22]
Acute retention of urine and constipation secondary to compression of the digestive structures are signs rarely found in NF1 patients [23].
Neurofibromas are benign tumors that develop along nerve sheaths. They can also develop in autonomic nerve plexuses and perivascular plexuses of the viscera such as the digestive tract, bladder, kidney or ureter.
In case of vesical neurofibroma, the cystoscopy shows the presence of submucosal nodules with a mucosa of normal appearance but the biopsy confirms the diagnosis. Bladder localization can be isolated [24].
The malignant degeneration of neurofibromas or the appearance

of neurofibrosarcoma "novo" is a possibility to be feared but relatively rare and unpredictable [25, 26]. This risk is seen in 19 to 29% of cases and increases with age.

The differential diagnosis of vesical neurofibromas infiltrating the adjacent structures arises with rhabdomyosarcoma, ganglioneuroma, and retroperitoneal fibrosis, but the presence of a notion of NF1 must first evoke the diagnosis of plexiform neurofibroma [27].

Other histological forms may affect the bladder: paraganglioma [28], leiomyosarcoma, transitional carcinoma [29], rhabdomyosarcoma [19, 30, 31], ganglioneuroma [32, 33].

Prostatic involvement is often of mesenchymal type (sarcomas) [34, 35] sometimes of glandular type [36].

The classic renal impairment is renovascular arterial hypertension due to dysplasia of the medial-arterial with bulky peri-adventitious nerve hypertrophy, or sometimes secondary to aneurysmal involvement [15].

NF1 may be accompanied by membranous glomerulonephritis [37] or renal failure with infarction [38].

Urogenital malformations may complicate NF1 (horseshoe [39] kidney, polycystic, megaureter).

External genital involvement is marked by macroorchidism, penoscrotal hypertrophy or clitoral hypertrophy [19].

Fertility can also be achieved [40]. As for the endocrine lesions, the totality of the glands can be reached with however a preponderance for the adrenal glands. The

Pheochromocytoma remains the most anomaly. Much more rarely, a Conn [41] adenoma or a primary hyperparathyroidism [42] can be seen in the framework of an NF1. Rhabdomyosarcomas, Wilms tumors and neuroblastomas are more common in NF1. Malignant tumors of the nerve sheaths are the main complication of NF1 in adulthood. They develop from isolated or plexiform nodular neurofibromas or schwannoma [26].

In the case of our patient, bladder involvement consisted of ganglioneuromatosis of the bladder wall, associated with a diffusé neurofibroma of incidental discovery on the abdominopelvic ultrasound performed in the context of the exploration of chronic diarrhea.

The ganglioneuroma and neurofibroma association is rare at any age, but especially in children. Our case is only the third reported case of this rare lesion complex,

The literature found two cases of this association, it was for the first case, a girl aged 6 years followed for NF1, which had diffuse ganglioneuromatosis of the bladder wall associated with a plexiform neurofibroma revealed by painless hematuria [33]. The second reported case is expensive in a 3-month-old infant who initially consulted for stunting [32].

Diarrhea can be explained by secretion of vasoactive intestinal polypeptide (VIP) by the tumor. Generally ganglioneuroma is a nonsecreting tumor, but some authors report rare cases of ganglioneuroma with secretion of catecholamine or vasoactive intestinal polypeptide (VIP); responsible for diarrhea and hgh blood pressure.

c. Treatment of tumors in neurofibromatosis 1

Surgical excision is the treatment of choice for all symptomatic tumors occurring in patients with NF1. As benign tumors occurring in these patients always carry a risk of malignant degeneration, surgical excision of these tumors is advocated. But like the risk of malignant degeneration and malignant tumor development even after surgery, surgical excision of the benign asymptomatic form of tumors is still controversial [13, 43].

4. Conclusion

Unfortunately, the therapeutic strategy is limited to the treatment of different manifestations. However, with gene therapy, it will be possible in the near future to intervene at the origin of the disturbances and overcome all the pathological consequences. The development of multidisciplinary centers for the care of patients

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