

# Endocrine manifestations in familial neurofibromatosis type 1 (a family case report)

Y. Ayadi, N. Lassoued, H. Ben Salem, S. Arfa, N. Hmida, W. Alaya, MH. Sfar  
Endocrinology Department, Taher Sfar University Hospital, Mahdia, Tunisia

## 1 INTRODUCTION

Type 1 neurofibromatosis, also called Recklinghausen's disease, is one of the most common genetic diseases. It is autosomal dominant inherited. Its diagnosis is based on the presence of a familial history of type 1 neurofibromatosis in a first-degree relative and on the presence of a set of clinical arguments namely the characteristic café-au-lait spots, neurofibromas, cutaneous lentigines, Lisch nodules in the iris and characteristic bone deformities. Endocrine manifestations may exist. The most common are pheochromocytoma and precocious puberty, but other endocrine disorders can be observed more rarely, namely delayed puberty, which we will discuss in this observation.

## 2 OBSERVATION

These are 3 patients with type 1 neurofibromatosis. They are 1st degree relatives (first cousins) followed in the internal medicine and endocrinology department of the Taher sfar CHU in Mahdia (Tunisia).

**Case 1 :** 20-year-old male patient with type 1 neurofibromatosis, who consulted for delayed onset of secondary sexual characteristics. In the family history we noted a neurofibromatosis type 1 in his father and a simple puberty delay in his mother (menarche at 17 years). On examination, the patient is in good general condition, his height is 1.77 m, his weight is 48 kg, for a BMI of 15.32 kg / m<sup>2</sup>. On endocrine examination, the patient is in clinical eucorticism and clinical euthyroidism. For the pubertal state, the patient presents a deep voice, an A1 P3 stage of hair growth according to Tanner's classification, the beard is absent.

The examination of the external genitalia shows pubescent testes with a volume of 25 mL for the left testicle and 20 mL for the right testicle. The penis has a normal size at 8 cm at rest. On examination, we noted an absence of any spontaneous or provoked erection, nor of a morning erection. The scrotal skin is well wrinkled and normally pigmented. The hormonal dosage shows testosteroneemia at 3.67 ng / mL, blood level of FSH at 1.99 IU / L, LH at 3.25 mIU / L, prolactinemia at 13.78 ng / mL, cortisol at 129.94 µg / L, TSH level at 2.091 mIU / L and FT4 level at 13 pmol / L. The hormonal dosage shows a central hypogonadism, which may be in favor of organic damage to the hypothalamic-pituitary axis or simple puberty delay. A hypothalamic-pituitary MRI was requested to guide the diagnosis.

**Case 2 :** 21-year-old male patient with type 1 neurofibromatosis, followed in the internal medicine department from the age of 14. In the family history we noted a neurofibromatosis type 1 in his father and his paternal aunt. The patient has no clinical or biological evidence for a hormonal disorder. He entered puberty at the age of 14 and the course of puberty was normal.

**Case 3 :** 21-year-old female patient with type 1 neurofibromatosis, followed in the internal medicine department from the age of 15. In the family history we noted a neurofibromatosis type 1 in her father, her paternal aunt and uncle. Clinical examination and biology revealed no evidence for an endocrine disorder, and for puberty, her menarche was at the age of 14 and secondary sexual characteristics were developing in a normal way. D

## 3 DISCUSSION

Type 1 neurofibromatosis can manifest by endocrine disorders. Pheochromocytoma is the most common manifestation with an occurrence frequency of 0.5 to 5% of patients with this disease.

The clinical signs of pheochromocytoma are induced by the excessive secretion of catecholamines. We can see a high blood pressure that can be paroxysmal or permanent, weight loss, a pallor due to peripheral vasoconstriction, a typical symptomatic triad also called "Menard's triad" associating: throbbing headaches, heart palpitations and tachycardia, and profuse sweats. It is recommended that NF1 patients be screened for pheochromocytoma if one or many of these clinical signs develops.

We can also observe puberty disorders. The most common is precocious puberty. It is caused in the most of the cases by optic glioma, which is the most common intracranial tumor in patients with neurofibromatosis, when this tumor affects the hypothalamic-pituitary axis.

The occurrence of delayed puberty in a patient with type 1 neurofibromatosis as seen in our observation (case 1) is not common.

## 4 CONCLUSION

The patients with type 1 neurofibromatosis have special problems because of their disease. That's why the identification of endocrine disorders can surely improve the life quality of these patients. Moreover, Type 1 neurofibromatosis being an autosomal dominant inherited disease, genetic consulting is necessary before marriage and before becoming pregnant.