Endocrinological Disorders in children with Neurofibromatosis type 1 and Optic Pathway Gliomas

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BACKGROUND

Children with neurofibromatosis type 1 (NF1) have an increased risk of developing optic pathway gliomas (OPGs) during childhood. Although these tumors usually have a benign course, some cases result in significant clinical symptoms, including endocrinological disorders.

OBJECTIVES

The aim of this study is to evaluate the prevalence and type of endocrinological complications of OPGs involving the chiasm in children with NF1.

METHODS

We retrospectively evaluated children with NF1 and OPG involving the chiasm, with (Dodge 3) or without (Dodge 2) hypothalamic involvement seen between 1997 and 2015 at our institute.Details on patient demographics, tumor location and endocrinological work-up were recorded.

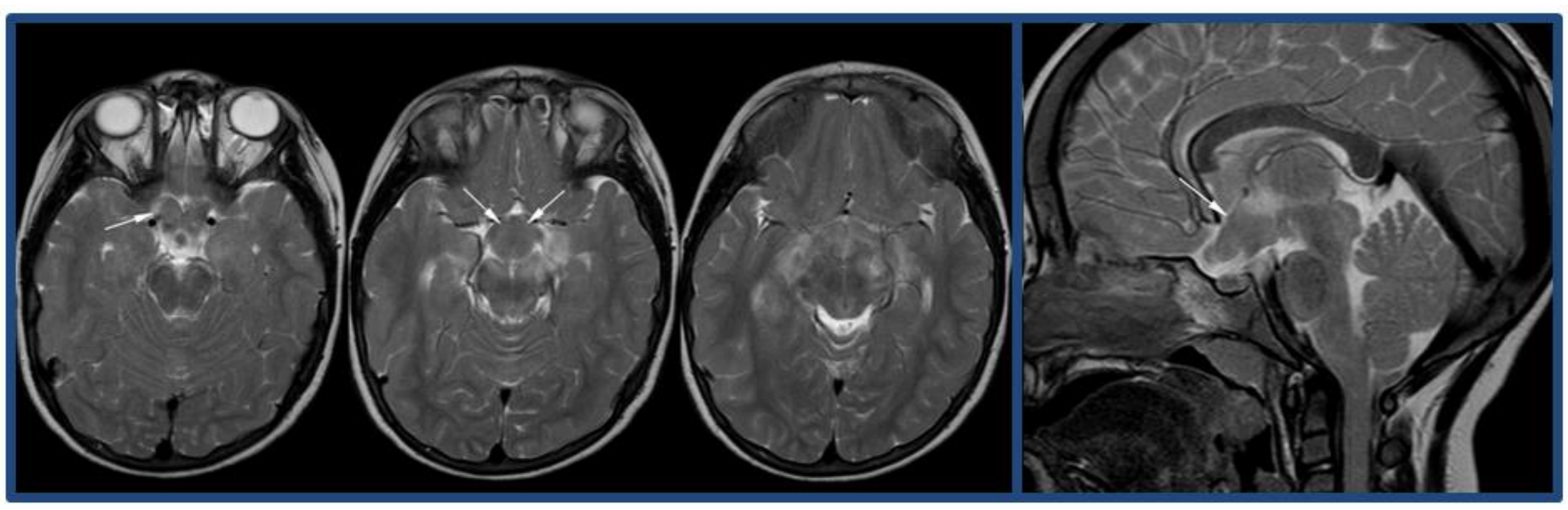
RESULTS

28 children (13 F) were identified (mean age at diagnosis of OPG 5.1 years). Patients underwent brain MRI mainly because of ophthalmic problems, 3 because of endocrinological signs. 16 patients showed OPG with chiasm involvement, 12 had a Dodge 3 tumor.
Eight patients presented with endocrinological disorders at the time of OPG diagnosis or during follow-up: diencephalic syndrome (2 girls of 5.5 and 0.9 years), GH hypersecretion (2 girls of 3.9 and 3.8 years) and central precocious puberty (in 3 boys of 3.2, 7.6 and 8.6 years and one 7.6 years old girl)(Table1). Among these patients seven had a Dodge 3 OPG (87.5%).
In two patients endocrinological disorders induced brain MRI execution (patients 6 and 8 of Table1)
Debulking surgery has been performed in 8/28 patients, while none has been irradiated. Three of these experienced endocrinological complications after surgery including: GH deficiency in a 9.8 years old boy, a central diabetes insipidus and anterior pituitary deficiency in a 5.6 years old girl with a previous diencephalic syndrome (patient n 4, Table1) and precocious puberty in a 7,7 years old girl with a previous GH hypersecretion (patient n 2, Table1, Fig. 1).

Table1: **details of patients with endocrinologiacl disorders**.
CPP: central precocoious puberty, GnRHa: gonadotrophin releasing-hormone analogues ; Oct: ocreotide; CDI: Central diabetes insipidus; APD: anterior pituitary deficiency ; DP: desmopressin; HyC: Hydrocortisone

Patients ID/sex	Endocrinological Disorders	Age at onset (years)	Age at first MRI (years)	DODGE	Therapy	Others treatments	Others endocrinological disorders	Age	Therapy
1) M	CPP	3,2	1,4	3	GnRHa	Chemotherapy	None		
2) F	GH hypersecretion	3,9	3,4	3	Oct	Surgery, Chemotherapy	CPP	7,7	GnRHa
3) F	CPP	7,6	1,6	2	GnRHa	none	None		
4) F	Diencephalic Syndrome	5,5	1,11	3	None	Surgery, Chemotherapy	CDI, APD	5,6	DP, HyC LT4
5) M	CPP	7,6	6,5	3	GnRHa	none			
6) F	Diencephalic Syndrome	0,9	1,2	3	None	Surgery, Chemotherapy	None		
7) M	CPP	8,6	3,9	3	GnRHa	None			
8) F	GH hypersecretion	3,8	3,9	3	None	none			

Figure 1 Magnetic resonance of patient 2.
Axial T2-weighted images of patient 2 shows: the OPG involving both the nerves (A) (arrow), the chiasm (B) (Arrow) and the posterior tracts (C). Typical unidentified bright objects are visible in figures B and C too. Sagittal T2-weighted images show the hypothalamic involvement (D) (arrow).



CONCLUSIONS

Our data suggest that endocrinological disorders frequently occur (28,5%) in children with NF1 and OPG, in particular in those with a specific hypothalamic involvement. Herein we report several rare endocrinological disorders such as diencephalic syndrome, GH hypersecretion and male CPP. A careful auxological follow-up is desirable in children with NF1 given endocrine sign may represent the first element of suspicion of OPG. Those patients with OPG involving the hypothalamic region should be strictly endocrinologically monitored.

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We have no conflicts of interest to declare.

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