Prevalence and predicting factors of endocrine dysfunction in children with NF1 and optic gliomas.

Santoro C[1], Perrotta S[1], Scilipoti M[1], Cirillo M[2], Quaglietta L[3], Cinalli G[4], Cioffi D[5], Di Iorgi N [6] Maghnie M [6], Galizia A [6], Parpagnoli M[7], Messa F[7], De Sanctis S [8], Vannelli S[8], Marzuillo P [1], Miraglia del Giudice E[1], Grandone A[1]

1: Dipartimento della Donna, del Bambino e di Chirurgia Generale e Specialistica, Università degli studi della Campania "Luigi Vanvitelli", Naples, Italy
2: Dipartimento di Scienze Mediche, Chirurgiche, Neurologiche, Metaboliche e dell'Invecchiamento, Università della Campania "Luigi Vanvitelli", Naples, Italy.
3: Department of Pediatric Oncology, Santobono-Pausilipon Children's Hospital, Posillipo Street, 226, 80122, Naples, Italy
4: Department of Pediatric Neurosurgery Santobono-Pausilipon Children's Hospital, Naples - Italy.
5: Department of Pediatrics Santobono-Pausilipon Children's Hospital, Naples - Italy.
6 : Department of Paediatrics, IRCCS Istituto Giannina Gaslini, University of Genova, Genova, Italy
7: 'Meyer' Children Hospital, Florence, Italy;
8: Pediatric Endocrinology, Regina Margherita Children Hospital, University of Turin, Turin, Italy.

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 endocrinological complications of OPGs involving the chiasm in children with NF1.

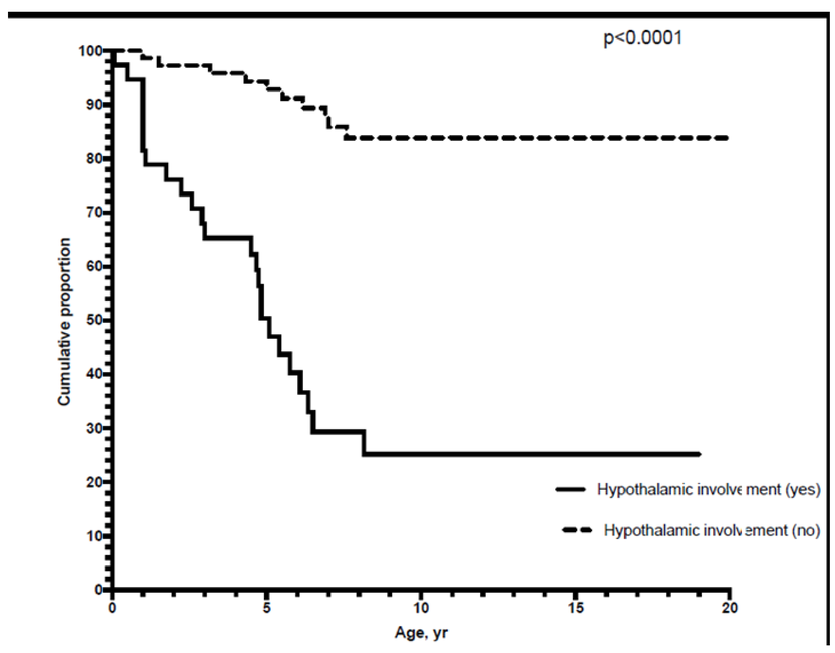
METHODS

We retrospectively evaluated children with NF1 and OPG seen between 1997 and 2017 at four Italian institutions (University vanvitelli, naples, santobono Hospital, Naples, Mayer Hospital , Florence, Gaslini Hospital , Genova, Regna Margherita Hospital, Turin. We studied those endocrinopathies occurring before radio- or chemo-therapy or surgery. OPGs were classified according to the modified Dodge classification (MDC).

RESULTS

The median age at diagnosis of NF1 was 1.8 years (range 0.1-12.8) and at diagnosis of OPGs was 4.2 years (range 0.4-13.7). Median follow up was 9 years (range 0.2-35).
109/117(93.1%) OPGs were MDC1, 73/117(62.3%) MDC2, and 53/117(45.2%) MDC3/4. The chiasm was involved in 73(62%) tumors, hypothalamus in 37(32%).
Endocrine disorders were identified in 35(29.9%) children. Median age at diagnosis of endocrinopathies was 7.8 years (range 1.4-12.9 years). Among patients with endocrine disorders, the proportion of patients who later underwent any treatment for OPGs (both chemotherapy and/or surgery) was higher than in those without endocrine disorders (65.8%vs24.4%; p=0.0001).
Considering the entire population the cumulative proportion of patients free from endocrine disease at 10 years of follow-up was 65.9%.
Endocrine free survival declined up to 8 years post OPGs diagnosis. Hypothalamic involvement was the stronger single independent predictor of endocrine disorders (HR: 7.48(95%CI:3.5-15.85),p<0.0001). Another independent predictor was age at OPGs diagnosis < 5 years (HR:2.51(1.09-5.8),p:0.03). Central precocious puberty (CPP) was diagnosed in 25 (14 males) children (71.4%) (median age 8 years;range:3.5-10.5), followed by GHD in 4(11.4%) children (median age 9.4 years;range 8.4-11.5), diencephalic syndrome in 4(11.4%) children (median age 4.6 years;range 1.4-5.8), growth hormone hypersecretion in 2(5.7%) children (median age 4 years; range 3.9-4.1).

	Patients with OPG	Patients with endocrinological problems	Patients without endocrinological problems due to OPG	p value (chi square)
Total number (n, %)	117 (100)	35 (29.9)	82 (70.1)	-
Gender (n, %)	52 M (44.4)	17 M (48.6)	35 M (42.6)	0.38
Median age at NF1 diagnosis (yrs, range)	1.83 (0-12.25)	1.3 (0-6.7)	1.91 (0.1-12.25)	0.03
Inheritance (S/Mo)				
Sporadic	77 S (67.5)	19 S (54)	58 S (71)	0.485
Maternal	20 M (17)	9 M (25)	11 M (13)	0.163
Paternal	20 P (17)	7 P (20)	13 P (16)	0.634
Median duration of NF1 follow up (yrs; range)	7.91 (0.2-24.5)	9.66 (1.9-15.5)	6.25 (0.5-24.5)	0.03
Median age at OPG tumor diagnosis (yrs; range)	7.58 (0.4-12.9)	3.2 (1.33-11.9)	5.66 (1.25-12.9)	0.001



CONCLUSIONS

Endocrine disorders are common in patients with NF1 and OPGs independently from any treatment. Hypothalamic involvement and young (<5 years) age at OPGs diagnosis were predictors of endocrine disorders. CPP was the most prevalent diagnosis while GHD was not common as previously described. A high index of suspicion for very rare endocrine disorders such as diencephalic syndrome and growth hormone hypersecretion is important in these patients, especially in younger ones.
Patients with OPGs and endocrine disorders, because of the frequent hypothalamic involvement, need a particularly careful follow-up as they are more at risk to need treatment, both CT and surgery.

References

1: Gan HW, Phipps K, Aquilina K, Gaze MN, Hayward R, Spoudeas HA. Neuroendocrine Morbidity After Pediatric Optic Gliomas: A Longitudinal Analysis of 166 Children Over 30 Years. J Clin Endocrinol Metab. 2015 Oct;100(10):3787-99. doi: 10.1210/jc.2015-2028. Epub 2015 Jul 28. PubMed PMID: 26218754.

2: Bizzarri C, Bottaro G. Endocrine implications of neurofibromatosis 1 in childhood. Horm Res Paediatr. 2015;83(4):232-41. doi: 10.1159/000369802. Epub 2015 Feb 5. Review. PubMed PMID: 25659607.

3: Cnossen MH, Stam EN, Cooiman LC, Simonsz HJ, Stroink H, Oranje AP, Halley DJ, de Goede-Bolder A, Niermeijer MF, de Muinck Keizer-Schrama SM. Endocrinologic disorders and optic pathway gliomas in children with neurofibromatosis type 1. Pediatrics. 1997 Oct;100(4):667-70. Review. PubMed PMID: 9310522.

4: Jaing TH, Lin KL, Tsay PK, Hsueh C, Hung PC, Wu CT, Tseng CK. Treatment of optic pathway hypothalamic gliomas in childhood: experience with 18 consecutive cases. J Pediatr Hematol Oncol. 2008 Mar;30(3):222-4. doi: 10.1097/MPH.0b013e318162bd6a. PubMed PMID: 18376285.

We have no conflicts of interesse to declare.

58ESPE RFC11-002
Pituitary, neuroendocrinology and puberty
Anna Grandone
Poster presented at: ESPE 2019 VIENNA
PosterSessionOnline.com