THE OPTIC PATHWAYS GLIOMAS IN CHILDREN WITH NEUROFIBROMATOSIS 1

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ABSTRACT

Optic pathways gliomas have the maximal clinical expression in childhood around the age of 5, being the second tumor in neurofibromatosis type 1 in frequency.Considering their location,it describes three types of optic pathways gliomas: type I - retrobulbar gliomas, type II - optic tracts gliomas and type III - chiasmatic gliomas. Neuroimaging exams are essential in diagnosis and selection surgical patients. Management of these tumors is often difficult even they exhibit histological benign features. Patients harboring optic nerve gliomas with symptomatic and documented neuroimaging progression have indication of tumor resection. Optic nerve gliomas associated with neurofibromatosis type 1 have generally a good prognosis. Unfavorable prognostic factors are represented by the early clinical onset under 6 years of age and chiasmatic and retrochiasmatic location.

Keywords: optic pathways gliomas, neurofibromatosis type 1, children

Neurofibromatosis is an autosomal dominant transmition disease with complete penetrance and variable expressivity, included in the large group of phakomatoses and characterized by an increased susceptibility to develop benign and malignant tumors of neural structures. From the clinical point of view it was initially described two forms of neurofibromatosis (type 1 and 2) and later they were added five other forms of neurofibromatosis less frequently encountered in practice. The development of molecular biology in the 1980s, allowed the classification of the disease on genetic bases and demonstrate that genes implicated in neurofibromatosis 1(NF1) is located on chromosome 17 and that for neurofibromatosis 2 (NF2) on chromosome 22 (1).

Characteristic clinical features facilitates diagnosis in adults but in the pediatric population it must be considered that the clinical expession depends on the age of the child.. Disease penetrance reaches 100% around the age of 5 years. Preschool period is the maximum period of clinical expression in neurofibromatosis 1, so around the age of 5-6 years neoplastic lesions are diagnosed, like optic pathways gliomas and plexiform neurofibromas. Optic pathways gliomas are the second tumors in frequency in neurofibromatosis type 1 after neurofibromas and have the highest clinical expression in childhood around the age of 5 years (2). Gliomas of the optic pathways are extra axial tumors and they are usually histological low-grade astrocytomas situated anywhere from the retro bulbar region until optical radiation with possible extension to the hypothalamus. (3). Optic nerve gliomas occur in 14-36% of patients with NF1, and their presence is one of the diagnostic criteria of the disorder (4). Of the total optic pathways gliomas in the general population, 70% are associated with NF1. Bilateral optic nerve gliomas are considered pathognomonic for NF1. Optic nerves are affected unilateral or bilateral in 10% of cases, the optic chiasm is affected isolated in 1/3 cases, in 1/3 cases the tumor in-

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volved both optic nerves and optic chiasm, a quarter of cases have predominantly retrochiasmatic and hypothalamic involvement, and 5% cases there multicentric involvement (5,6).

Optic pathways gliomas in NF1 have the highest clinical expression in preschool period. Their frequency in children with NF 1 is 15 -20% but only a small percent (5-7%) of these will have an aggressive growth until the age of 6 years (7,8). During the school period these tumors are less likely to occur if the optic nerve gliomas were not previously appeared. The natural history of optic pathways gliomas is variable, varying from asymptomatic and non progressive tumors to rapidly increasing intracranial masses witch may exhibit characters of malignancy and leptomeningean dissemination. Over 50% of patients with documented optic pathways gliomas shows visual disturbances (9).

Optic pathways glioma classification

Topographicly, there are three types of optic pathways gliomas (3) this classification being useful to select the surgical indication and the surgical approach and to elaborate the prognosis.

The first type of glioma is the retro-bulbar optic glioma, situated in the front of the chiasma and it has two 2 subtypes:

- pure intraorbital glioma;
- intraorbital glioma with intracranial extension and chiasmatic involvement.

These type I tumors are expressed clinically by exophthalmus, amaurosis, unilateral or bilateral amblyopia.

In the second type are included optic tract gliomas (parapeduncular tumors) interposed between limbic areas, thalamus, hypothalamus and cerebral peduncle. Clinically, they manifests homonymous hemianopia, intracranian hypertension syndrome, temporal epilepsy, hemiparesis and endocrine dysfunction.

The third type of glioma of the optical pathways is chiasmatic glioma, subclassified into:

- chiasmatic glioma without hypothalamic invasion;
- chiasmatic glioma with hypothalamic invasion.

The symptoms of intracranial hypertension is generated by intrinsic mass effect of tumor but also by secondary hydrocephalus resulted from third ventricle compression. Hypothalamic impairment is clinically expressed by precocious puberty and diabetes insipidus (3).

Exploration neuroimaging

Neuroimaging is a crucial step in working-up the gliomas of the optical pathways.Visual function is assessed by the neuroofthalmologist but radiological images are essential in surgical management of these tumors.

In computed tomography (CT) the prechiasmatic intraorbital portion of optic nerv can be visualized, but there are great difficulties in the assessment of the retrochiasmatic tracts and optic chiasm. Optic nerve gliomas appear as fusiform dilatation of the intraorbital nerve with or without optical channel widening and thickening of the chiasm. The uptake of contrast agent ranges from imperceptible to moderate (Fig.1). In magnetic resonace imaging (MRI) gliomas appears as a fusiform enlargement of the optic nerve, accompanied or not by a large optical channel with hypo- or hyper- isosignal T1 and T2 (Fig. 2), with variable contrast enhancement after injection. The tumor can affect one or both nerves, optic chiasm or retrochiasmatic tracts, extending to the hypothalamus (10,11) (Fig. 3).

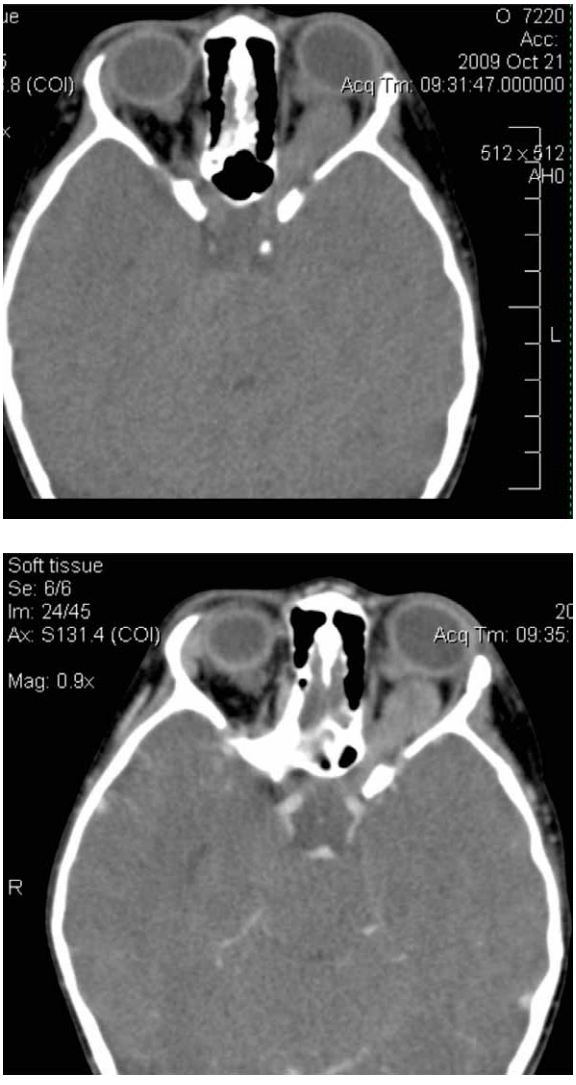

FIGURE 1. *Cranio-cerebral scan: left optic nerve glioma: (A) isodense enlargement of the left optic nerve with moderate contrast uptake (B) (personal case)*

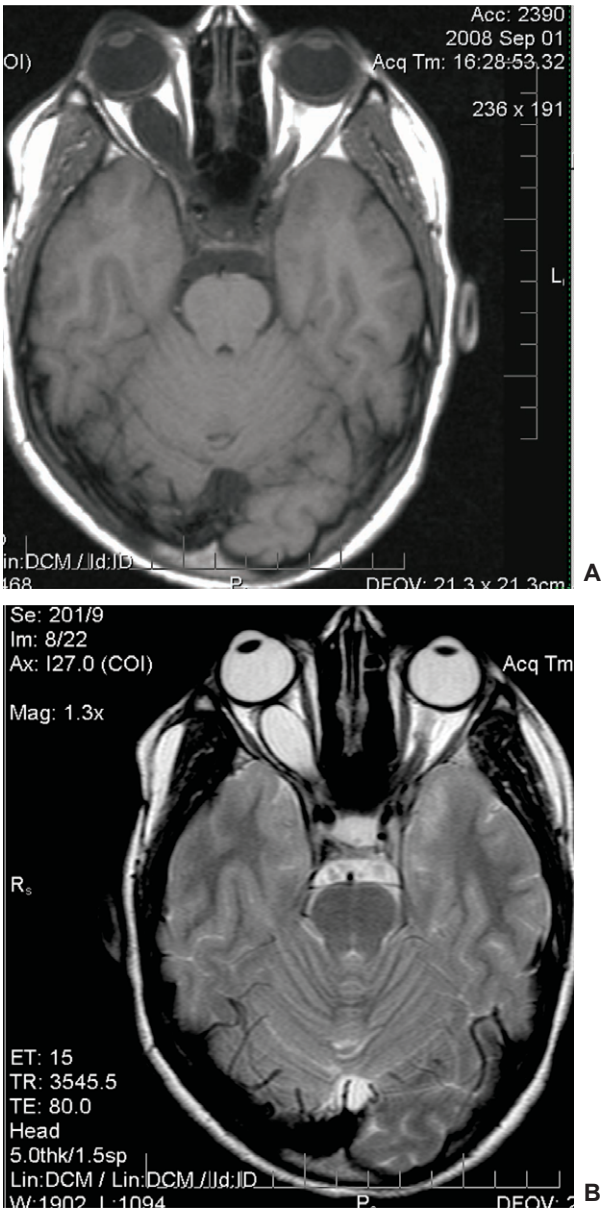

FIGURE 2. *MRI cranio-cerebral: right optic nerve fusiform enlargement with isosignal T1 (A) and hipersignal T2 (B) (personal case)*

The French Neurofibromatosis Network suggests the next algorithm of follow up in pediatric patients when there is clinical suspicion of neurofibromatosis type 1 (3,4):

For children under six years old with suspected NF1, a craniocerebral MRI exam will be done systematically because it is difficult to assess visual acuity of these patients considering the age and mental deficiencies associated. If no abnormality is detected, a new evaluation MRI is indicated over two years if meanwhile no visual disturbances occur. If the patient's age allows, a simple annual ophthalmologic surveillance that includes assessment of visual acuity and campimetry is sufficient. If a visually anomaly is detected, craniocerebral MRI is recommended To assess the degree of tu-

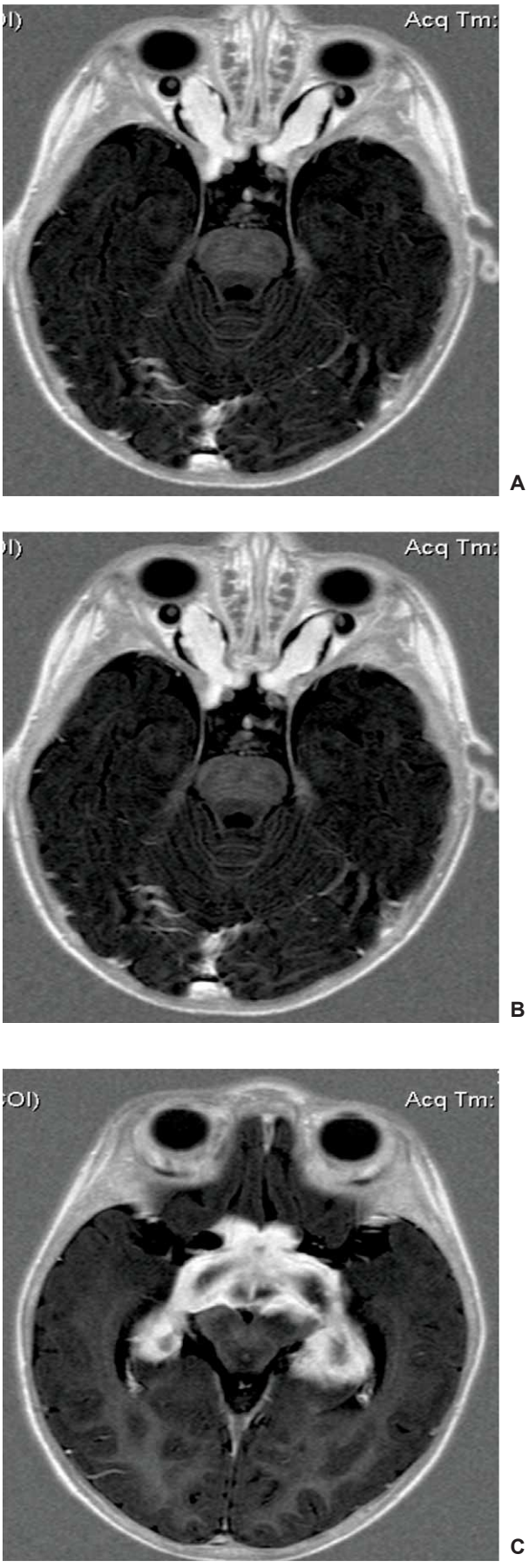

FIGURE 3. *MRI cranio-cerebral: bilateral glioma of optic pathways involving the optic nerve, chiasm, hypothalamus and optic radiation (personal case)*

mor progression and tumor aggressiveness it is recommended eyes examination and craniocerebral MRI once every three months in the first 6 months, then every 6 months up to a year and each year thereafter until puberty (4).

Differential diagnosis of optic nerve gliomas is done with other intraorbital expansive masses: meningiomas, plexiform neurofibromas, inflammatory processes, etc.

Management of optic pathways gliomas is difficult despite their benign histological characteristics. A patient with optic pathways glioma and visual function preserved and without signs of intracranial hypertension will be treated by the oncology service with or without prior biopsy. The role of chemotherapy is to stop tumor growth and to preserve as much as posible the visual function.

Patients with optic nerve gliomas unilateral or bilateral blindness or severe ambliopia, radio-documented progression and proptosis become candidates for tumor resection (12,13) (Fig. 4).

Patients harboring chiasmatic exofitic tumors with or without intraventricular component and secondary hydrocephalus may benefit from tumor decompression with improved clinical symptoms, namely the disappearance of intracranial hypertension syndrome and rarely improve visual function.

We present the following case to illustrate the surgical indication in optic patways gliomas:

The patient A.S, male, three years old age, came in the Department of Neurosurgery (Clinical Hospital for The Children *Sfanta Maria* Iasi) on November 2008 for sudden blindness and slight bilateral exophthalmos (Fig. 4A). The clinical examination reveals on skin more than six café au lait spots. The neurological examination was normal except his total blindness.The craniocerebral MRI reveals bilateral optic nerve tumors with extension into the chiasma (Fig. 4D). As the patient meets criteria for surgery (blindness and exoftalmus) it was proposed to his family the surgical ablation of intraorbital component of the tumor but the patient's family refused surgery motivating that this wil not restore the visual function. Six months later the patient returns with bilateral proptosis predominantly on the left (Fig. 4 D), epiphora and corneal ulceration. A bifrontal transcranian aproach was done with total ablation of the intraorbitar tumors and section of optic nerves in front of the chiasma (Fig. 4E). Postoperative course was favorable, the anterior pole of the eyeball becoming normal (Fig. 4 C).

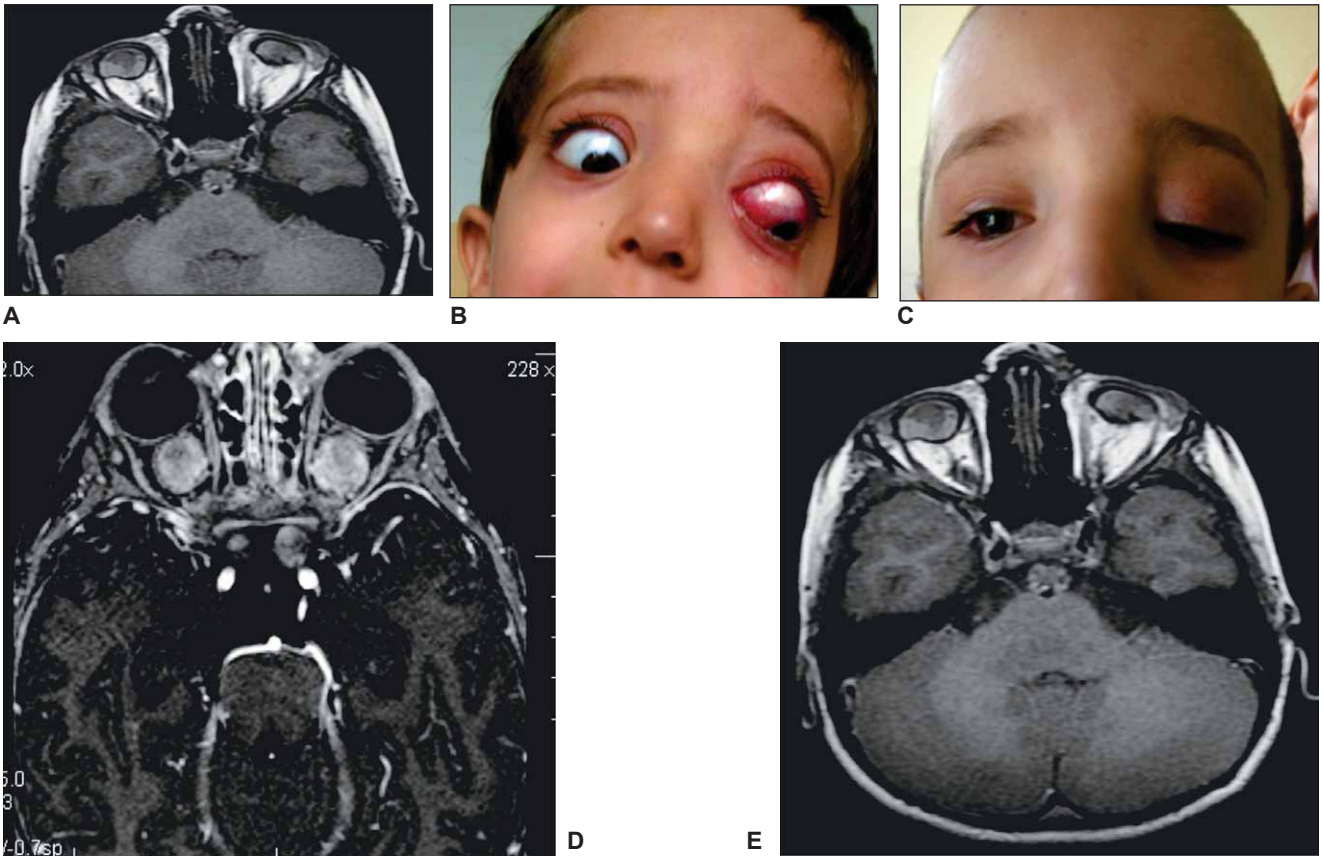

FIGURE 4. *MRI cranio-cerebral in bilateral optic nerve glioma with chiasmatic involvement: onset clinical aspects aspects (A) six monts later (B); postoperative clinical aspects (C). MRI cranicerebral – bilateral optic nerve gliomas with chiasmatic involvement (D).MRI – craniocerebral: gross total ablation of intraorbital tumors (E) (personal case).*

Patients with optic nerve glioma and useful vision and those with chiasmatic infiltrative tumors and pathognomonic appearance in MRI are not candidates for tumor resection. Exceptionally, in some patients with optic nerve glioma and preserved visual function, the tumor can be resected and preserve the optic nerve and vision (14).

Surgery is curative for tumors of the optic nerve without extension into the chiasma, but almost 25% of tumors involve chiasma prior to surgery. Incompletely removed tumors will be refered to oncologist. Temozolamide chemotherapy (Temodal) has the advantage of oral administration and is used to treat chiasmatic infiltrative gliomas or tumors resected incompletely. Radiotherapy is contraindicated in children both because of adverse effects on the myelination process as well by promoting malignant degeneration of pre-existing cerebral gliomas or radio-induced tumor appearance (15,16,17).

Optic nerve gliomas in the NF1 generally have a good prognosis, progression of these lesions is met to the 5-18% of cases. Prognostic factors are represented by the clinical onset and topography of the tumor younger age and the involvment of the chiasma beeing unfavorable prognosis factors. A study by Schroder et al. in 1999 on 29 patients with NF1 and optic patways gliomas, shows that the lesion remained stable at 11 children and visual deficit progressed to 14. The children were explored by MRI were and visual evoked potentials. Children with unfavorable outcome had lower age at onset (3.2 years versus 5.8) years and had a higher frequency of strabismus, optic atrophy, defects impaired visual field and optic chiasm involvement (18).

The tumors diagnosed after the age of 6 years remain stable for a longer time, which also allows an increase in the interval between ophthalmologycal examinations.

There are rare cases of spontaneous regression or decrease in size and contrast up-take without therapeutic intervention. Malignant transformation is possible but very rare.

CONCLUSIONS

Optic pathways gliomas in neurofibromatosis patients have clinical expression in early childhood. Annually follow-up radio imaging in pediatric patients with optic pathways gliomas seems to be sufficient to detect tumor growth and predict a neurosurgical intervention. Ophthalmologic follow –up is especially useful in older children but it is insufficient in young children or those with mental impairments commonly associated with neurofibromatosis.There are rare cases of optic pathways gliomas spontaneous regression or decrease in size and contrast enhancement without therapeutic intervention.Malignant transformation of optic pathways gliomas is possible but very rare.

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