

Optic Pathway Glioma

Moderators

Dr PSC Dr HKG

- 1 % of CNS tumors
- 3-5 % of pediatric tumors
- 65% of patients are younger than 5 years of age
- Occur with equal frequency in males and females
- Majority are pilocytic astrocytomas
- Indolent nature, CSF dissemination is rare

- 25 % occur in optic nerve ; 60% involve the chiasm
- 1/3 of patients with OPG have neurofibromatosis 1 (NF1)

- Pilomyxoid astrocytoma (PMA)
 - Subtype of PA
 - at a younger age
 - monotonous ,bipolar spindle cells with an angiocentric arrangement within a myxoid background
 - local recurrence 55-76%
 - CSF dissemination -11-14 %

Clinical Features

- Spectrum of findings ranging from lesions confined to just the optic nerve, lesions affecting the optic chiasm and hypothalamus and lesions with diffuse involvement of a large part of optic pathway.

- Decrease in visual acuity, visual field deficits (85% of pts)
- Acute visual loss (hemorrhage)
- Proptosis with deviation of affected eye
- Suprasellar gliomas extending into third ventricle cause obstructive hydrocephalus
- Macrocephaly ,failure to thrive in infancy
- Headache , vomiting ,decrease in school performance

- 50 % of children have endocrine abnormalities
- Mostly GH deficiency and precocious puberty
- Precocious puberty is more common in patients with NF1
- Diabetes insipidus is rare (more common with germinoma , craniopharyngioma)
- Diagnosis is often delayed , tumors can be large at discovery

- Diencephalon syndrome :
- Described by Russel
- Attributed to leptin –ghrelin system
- Manifest as lack of weight gain and emaciation
- Normal oral intake and height
- Nystagmus , torticollis, head bobbing (rare)
- Rare cause of failure to thrive

Imaging

- Plain X ray –
 - enlarged optic canal
 - J shaped sella turcica
- CT scan
 - Enlargement of optic nerve
 - Calcification or cysts (d/d – meningioma ,craniopharyngioma)
 - Hypodense on NCCT , variable enhancement on contrast

- MRI
 - Imaging of choice
 - Can be used to monitor progression or response to treatment
 - Hypo-iso on T1, hyper on T2
 - Variable enhancement on contrast
 - Cyst formation around a solid tumor

- Fusiform enlargement, elongated length of optic nerve
- redundancy of the nerve in the mid orbit is characteristic
- (compare with the opposite side)

- Small chiasmal tumors show expansion of chiasm
- Large globular suprasellar gliomas show extension into third ventricle
- Gliomas of chiasm and hypothalamus are often indistinguishable because of lack of anatomic border between these structures.
- Enhance heterogeneously on contrast (d/d germinoma which enhances uniformly)

- Diffuse optic pathway glioma
 - Affects the entire optic pathway
 - more common with NF1
 - B/l involvement- “mustache” sign
 - Variable pattern of growth
 - High incidence of precocious puberty(25%)
 - Manifests in younger age(2-3 years); females
 - Assoc other congenital abnormalities

- CTA/MRA
 - Visualize the Circle of Willis in assoc with suprasellar gliomas
- MRS
 - Increased creatine –choline ratio
 - Decreased NAA peak

- Diffusion-weighted MRI may be particularly useful in NF patients, as it has been shown to more effectively differentiate optic gliomas from hamartomas and myelin vacuolization than other means

- Sener RN. Diffusion MRI in neurofibromatosis type 1: ADC evaluations of the optic pathways, and a comparison with normal individuals. *Comput Med Imaging Graph* 2002;26:59–64.

Radiological classification of optic pathway gliomas: experience of a modified functional classification system

¹T TAYLOR, MBChB, MRCP, FRCR, ¹T JASPAN, BSc, FRCR, FRCP, ²G MILANO, MD, PhD, ¹R GREGSON, FRCS, FRCOphth, ³T PARKER, BSc, PhD, ³T RITZMANN, BMedSci, ³C BENSON, BMedSci and ³D WALKER, BMedSci, BMBS, FRCP, FRCPCH ON BEHALF OF THE PLAN STUDY GROUP

The British Journal of Radiology, 81 (2008), 761–766

Differential diagnosis

- Pituitary adenoma
- Craniopharyngioma
- Germ cell tumour
- Hypothalamic hamartoma

Screening in NF1

- No conclusive evidence that early detection of tumors would reduce the rate of vision loss
- Loss of visual acuity is the most reliable and clinically most important indicator of visually symptomatic OPGs, and serial visual acuity measurements are the best way to follow patients with OPGs

- Computerized visual field testing, usually requiring approximately 6.5 minutes per eye, can be performed reliably in young children
- Color vision loss usually accompanies visual acuity deficits.

Role of VEP

- Sensitive method of detecting OPGs
- It is an electrophysiological measure of the integrity of the visual pathway
- Serial VEPs would be hard to interpret because small changes in amplitude and delay without changes in vision are of uncertain clinical significance

- The current guidelines suggest that screening should continue until 7 years of age in asymptomatic children with NF1, because the first 6 years of life constitute the time of maximal risk for OPG development
- MRI of the brain and orbits should be used to confirm the diagnosis of OPG once an abnormal eye examination has been documented.

- Radiological progression has been variably defined in the literature as an increase in tumor size, optic pathway extension or hypothalamic involvement, or a change in the pattern of enhancement.

- Clinical progression has been defined as the onset of new neurological symptoms or endocrinological abnormality, or a change in visual acuity alone or visual field loss combined with impaired visual acuity.

Treatment

- Incidentally detected without significant symptoms can be followed with serial imaging
- If diagnosis is uncertain , biopsy may be performed

- Regarding affected NF-1 patients, Packer *et al* have suggested that gliomas found during their routine work up should not be treated so long as there is no evidence of progressive disease.

- Packer RJ, Sutton LN, Bilaniuk LT, *et al*. Treatment of chiasmatic/hypothalamic gliomas of childhood with chemotherapy: an update. *Ann Neurol*

1988;23:79-85●

- When the pt has symptoms or tumor progresses on follow up- treatment is indicated

Chemotherapy

- Considered to be the first line treatment
- Fewer side effects than with RT
- < 3 Yrs it is the only adjuvant treatment because intellectual and other functions are well preserved
- 5 year recurrence free survival remains about 60%

- Effectively postpones RT
- Children with diencephalon syndrome improve

- In the young population with neurofibromatosis type 1 (NF-1)–associated OPHPA, decisions to initiate chemotherapy are generally made without biopsy and are guided by ophthalmological and imaging examinations.

- Leonard JR, Perry A, Rubin JB, King AA, Chicoine MR, Gutmann DH. The role of surgical biopsy in the diagnosis of glioma in individuals with neurofibromatosis-1. *Neurology*. 2006;67:1509–1512.●

- In cases of sporadic OPHPA in non-NF-1 patients, a biopsy or a partial resection by craniotomy to confirm histology remains the first mode of treatment

- Fouladi M, Wallace D, Langston JW, et al. Survival and functional outcome of children with hypothalamic/chiasmatic tumors. *Cancer*. 2003;97:1084–1092.

- Use of concurrent carboplatin and vincristine in a 10-week induction phase, followed by 48 weeks of maintenance
- This regimen resulted in a progression-free survival (PFS) of 75% at 2 years and 68% at 3 years. Children aged 5 years or younger had a notably more favorable overall rate of response.

- Packer RJ, Ater J, Allen J, et al. Carboplatin and vincristine for children with newly diagnosed progressive low-grade gliomas. *J Neurosurg* 1997;86:747–754.

- 10 year survival is 74- 96% after chemotherapy with or without surgery
- Chemotherapy improves quality of life by eliminating or delaying RT

- Optic nerve glioma

- Surgical resection is useful in children with no useful vision , severe eye threatening vision proptosis or a painful eye that has not responded to chemotherapy
- If both eyes are affected , no indication for surgery is present

- Surgery

- Subfrontal approach with orbital unroofing
- Affected optic nerve is excised from the globe to the chiasm(leave 2-3 mm from the chiasm to preserve decussating fibers from the opposite eye)
- Avoid damage to LPS and oculomotor nerves to avoid undesirable proptosis
- Orbital roof must reconstructed to avoid undesirable proptosis

- Chiasmal hypothamic tumours
 - 50% of pts have obstructive hydrocephalus
 - Fenestration of septum pellucidum or biventricular shunt may be required
 - ETV is not feasible
 - Surgical treatment is usually delayed until symptoms appear
 - Tumor debulking can be performed for progressive tumors

- Incomplete surgical resection does not affect survival
- Provides histological verification, cytoreduction , increases CSF flow
- Risks – visual , endocrine disturbances, hypothalamic or neurovascular injury

- Surgical approach
 - subfrontal
 - pterional
 - Anterior transcallosal

- Diffuse optic pathway glioma
 - Surgical resection is not feasible

Radiation therapy

- Older children and those with progressive disease on Chemotherapy , or relapse after completion of chemotherapy
- Types
 - External beam (conformal or intensity modulated)
 - Stereotactic
 - Proton beam

- Provides better long term tumor control
- Progression free 5 year rates are around 90%

- Second tumors
- Malignant transformation of benign gliomas
- Cerebrovascular complications (post radiation vascular occlusive disorder)
 - more common in children with NF1
 - More common in suprasellar gliomas
- Endocrine dysfunction
- Neurocognitive dysfunction
- Hypothalamic dysfunction

- NF patients are at a higher than average risk of developing subsequent endocrinopathy, developmental abnormalities, neurocognitive dysfunction, and vasculopathy.

Kortmann RD, Timmermann B, Taylor RE, et al. Current and future strategies in radiotherapy of childhood low-grade glioma of the brain.

Part II: Treatment-related late toxicity. *Strahlenther Onkol* 2003;179:585–597 •

- When radiation therapy is required, typical doses range from 45 to 60 Gy in 1.8- to 2.0-Gy fractions

- Grabenbauer GG, Schuchardt U, Buchfelder M, et al. Radiation therapy of optico-hypothalamic gliomas (OHG)—radiographic response, vision and late toxicity. *Radiother Oncol* 2000;54: 239–45.

Outcome

- Negative prognostic indicators
 - Young age
 - tumor location posterior to chiasm
 - PMA subtypes
 - Diffuse optic pathway glioma
 - High microvessel density