*East African Medical Journal Vol. 92 No. 10 October 2015*
ETIOLOGIES OF UNILATERAL EXOPHTHALMIA IN CHILDREN AT UNIVERSITY HOSPITAL OF BRAZZAVILLE
P. W. Atipo-Tsiba, MD, FEBO, Ophthalmology Department, O. F. Atipo-Tsiba, Haematology Department, F. A. Itiere Odzili, ENT Department, B. Ossibi Ibara, Infectious Diseases Department and G. Ekouya Bowassa, Paediatric Department, University Hospital of Brazzaville, Congo.

Request for reprints to: Dr P. W. Atipo-Tsiba, Head of Clinic at University Hospital of Brazzaville, Republic of Congo and Assistant Professor at Marien Ngouabi University of Brazzaville, Republic of Congo. E-mail: atipo.kani@gmail.com

# ETIOLOGIES OF UNILATERAL EXOPHTHALMIA IN CHILDREN AT UNIVERSITY HOSPITAL OF BRAZZAVILLE

P. W. ATIPO-TSIBA, O. F. ATIPO-TSIBA, F. A. ITIERE ODZILI, B. OSSIBI IBARA and G. EKOUYA BOWASSA

## ABSTRACT

***Bacground*: Exophthalmia is an abnormal movement of the eye in an antero-posterior plane. It reflects the existence of an expansive intra-orbital process (new formation or abnormal increase of the size of a normal anatomical structure). Inspection and Hertel's exophthalmometer may suffice for the diagnosis, even in its minor forms especially when it is unilateral. In poor countries, infant mortality linked to the causes of unilateral exophthalmia (UE) is lly high into question the infections and cancers.**
***Objective*: To list the main causes of UE in children at the University Hospital of Brazzaville (UHB), and assess the prognosis with a decline of two months.**
***Design* : A descriptive and analytical historical cohort.**
***Setting*: The Ophthalmology department of the University Hospital of Brazzaville.**
***Subjects*: Forty eight children seen for UE between January 2009 and December 2013. Each child had been seen three times over a period of two months, with an interval of one month between each consultation.**
***Results*: The mean age was 5.50 ± 1.20 years. Boy/Girl sex ratio was 1.08. Traumatic orbital haematoma (50%), retinoblastoma (22.91%) and orbital cellulitis (20.83%) were the main etiologies. Metastases (6/18) and ophthalmoplegia (4/18) were the major complications. The overall mortality rate was 20.83%, with a share of retinoblastoma-related mortality at 80%.**
***Conclusion*: Early diagnosis of retinoblastoma, before the onset of proptosis, can reduce paediatric deaths relating to unilateral exophthalmia.**

## INTRODUCTION

Exophthalmia is an abnormal movement of the eyeball in antero-posterior plane (1, 2). It demonstrates the existence of an expansive process within the orbit displacing forward the eye. This process may be a neoplasm or normal anatomical structure of the orbit which, for pathological reasons, abnormally increased in size (1- 4).

Radiography calculates the eye-orbital index (IOO), the latter sign exophthalmia when above 70. This index also serves to classify exophthalmia in 3 grades: Grade I IOO above 70 and less than 100, Grade II IOO equal to 100 (bicanthale line is tangent to the eyeball), Grade III IOO higher than 100 (the eyeball is forward) (1-5).

However, a simple clinical inspection suffice to strongly suspect exophthalmia even minimal, especially when it is unilateral. The affected side, the palpebral fissure is more open and Hertel's exophthalmometer confirms the diagnosis.

Although we do not have exact statistics, several observations allow us to affirm that infant mortality linked to the causes of UE is high in poor countries. In case the infection and tumour pathology, which alone account for just over 65% of cases of child exophthalmos (1, 2, 5).

This investigation had as objective to list the main causes of UE in children at the UHB, and secondarily to evaluate the prognosis with a decline of two months.

## MATERIALS AND METHODS

It was a descriptive and analytical historical cohort, conducted between January 2009 and December 2013 in the Ophthalmology department of the UHB. Only children seen for UE, whatever the etiology, had been retained. The definition of exophthalmia was clinical using Hertel's exophthalmometer (all these children had been seen by one same doctor). It was positive when there was a difference of at least 2 mm between the two eyes.

Whenever it was necessary to confirm or refute the diagnosis, as well as under the impact of balance sheet, the following paraclinical examinations were performed: MRI CT-scan, abdominal ultrasound, blood culture, blood count, culture of nasal secretions on usual media (Blood, Chocolate, Agar), histological examination, myelogram, thyroid markers (T3, T4, TSH, anti TSH antibodies), C-Reactine Protein (CRP).

The children had all stayed at the hospital with different hospital stays according to the respective clinical situations. They all benefited from the best available treatment. In particular in cases of retinoblastoma, enucleation was the rule when the general condition permitted, with or without chemotherapy. In very advanced cases (metastases), palliative care referred analgesic were prescribed.

After informed consent of the parents (verbal consent), each child had been seen three times, with a gap of one month between each visit.

Based on a survey sheet, the criteria studied were:

– at the first consultation: etiology, visual acuity (VA), presence or absence of métasases in the case of cancer, general condition
– in the second consultation: VA, general condition, presence of complications absent at the first complication
– at the third consultation: VA, general condition, presence of complications absent at the second complication.

All the children were old enough to speak. The VA was evaluated using the Snellen chart located 5 m. VA was equal to zero in the absence of light perception to counting fingers.

The general condition was evaluated using the following parameters: fever, anaemia, asthenia, weight loss and jaundice. In the absence of these parameters, the general condition was considered satisfactory. In the presence of two of these parameters, the general condition was considered moderately satisfactory. In the presence of more than two of these parameters, the general condition was considered bad. The McNemar $\chi 2$ was used as the statistic test, confidence interval 95% and threshold of the probability (p) significant if $p < 0.001$.

## RESULTS

It was a series of 48 children.

The mean age was 5.50 ± 1.20 years (3.00 years - 10.50 years).

The Boy/Girl (25/23) sex ratio was 1.08.

At the first consultation:

The etilogies of UE are shown in Table 1.

**Table 1**

*Etiologies of unilateral exophthalmia in children, between January 2009 and December 2013, in the Ophthalmology department of University Hospital of Brazzaville*

| Etiologiy | Effective | Frequency% |
|---|---|---|
| Orbital Haematoma | 24 | 50.00 |
| Retinoblastoma | 11 | 22.91 |
| Orbital Cellulitis | 10 | 20.83 |
| Optic nerve glioma | 01 | 2.08 |
| Graves' disease | 01 | 2.08 |
| Sarcoidosis* | 01 | 2.08 |
| Total | 48 | 100 |

*Sarcoidosis: as part of the lachrymal salivary Mikulicz's syndrome

The orbital haematoma numbered 24 cases, different causes were: beaten six cases, accident of the public highway 18 cases.

A case of optic nerve glioma in context of Van Recklinghausen's neurofibromatosis (Figure 1).

Ten cases of orbital cellulitis: Nine secondary to ethmoiditis (germs Staphylococcus aureus, Streptococcus salivaris), 1 case in the context of HIV / AIDS: germ (Pseudomonas aeruginosa).

VA evolution is shown in Table 2.

**Table 2**
*Evolution of visual acuity in children with unilateral exophthalmia, between January 2009 and December 2013, in the ophthalmology department of the University Hospital of Brazzaville*

| Visual Acuity | F. C1% | F. C2% | F. C3% |
|---|---|---|---|
| (0.0 – 0.1) | 58.33 | 35.55 | 57.14 |
| (0.1 – 0.2) | 10.41 | 00.00 | 5.71 |
| (0.2 - 0.3) | 6.25 | 28.89 | 11.43 |
| (0.3 – 0.4) | 14.58 | 8.89 | 2.86 |
| (0.4 - 0.5) | 2.08 | 15.55 | 8.57 |
| (0.5 - 0.6) | 8.35 | 11.12 | 14.19 |
| Total | 100 | 100 | 100 |

F . C1 = Frequency in first consultation , F. C2 = Frequency after one month
F. C3 = Frequency after two months
General condition evolution is shown in Table 3.

**Table 3**
*Evolution of general condition in children with unilateral exophthalmia, between January 2009 and December 2013, in the Ophthalmology department of the University Hospital of Brazzaville.*

| General condition | F. C1% | F. C2% | F. C3% |
|---|---|---|---|
| Satisfactory | 33.33 | 44.44 | 51.43 |
| Moderately Satisfactory | 14.58 | 22.22 | 42.86 |
| Bad | 52.09 | 33.34 | 5.71 |
| Total | 100 | 100 | 100 |

Existence of a brain metastasis in a case of retinoblastoma (Figure 2).
At the second consultation:
Deaths: 3 cases (1 cases of retinoblastoma, 2 cases of orbital cellulitis).
At the third consultation:
Deaths: 7 cases of retinoblastoma (total deaths 10).
Complications are presented in Table 4.

**Table 4**
*Main complications in children with unilateral exophthalmoia after one month and two months follow up, between January 2009 and December 2013, in the Ophthalmology department of the University Hospital of Brazzaville*

| Main Complications | M1 | M2 |
|---|---|---|
| Brain metastases | 1 | 0 |
| Lymph node metastases * | 5 | 0 |
| Ophthalmoplegia | 2 | 3 |
| Optic Atrophy | 1 | 2 |
| Cavernous sinus thrombosis | 2 | 0 |
| Meningitis | 1 | 0 |
| Phtisis bulbi | 0 | 4 |
| Eyelid ptosis | 0 | 1 |
| Death | 3 | 10 |

*Lymph node metastasis: cervical and submandibular lymphadenopathy
M1= one month follow up, M2= two months follow up
Table 5 shows the main complications of each etiology.

**Table 5**
*Overall trend unilateral exophthalmia in children at the University Hospital of Brazzaville between January 2009 and December 2013.*

| Complication | Etiology | Effective |
|---|---|---|
| Ophthalmoplegia | Orbital Cellulitis | 2 |
| Optic atrophy | Optic nerve glioma | 1 |
| Ophthalmoplegia | Orbital Haematoma | 1 |
| Aucune | Graves' disease | 0 |
| Metastasis | Retinoblastoma | 6 |
| Optic atrophy | Sarcoidosis | 1 |
| Meningitis | Orbital cellulitis | 1 |
| Thrombosis | Orbital cellulitis | 2 |
| Phtisis bulbi | Orbital cellulitis | 1 |
| Eyelid ptosis | Orbital haematoma | 2 |
| Phtisis bulbi | Orbital haematoma | 1 |
| Death | Retinoblastoma | |
| Death | Orbital cellulitis | |

Statistical test:
Comparison of the evolution of the VA between the first and third consulation:
$\chi 2 = 2.15$ ($p = 0.17$).
Comparison of the evolution of the general condition between the first and third consultation: $\chi 2 = 3.75$ ($p < 0.001$).

## DISCUSSION

Life expectancy in cases of retinoblastoma can be improved. At only if the diagnosis is done at an early stage, ie before the onset of exophthalmia. In almost 80% of cases, before the onset of proptosis, leucocoria and strabismus are present as early signs. These two signs are present respectively in 60 and 20% at the beginning of this disease (6 -9). Leucocoria reflecting a tumour with high vitreous expression and strabismus reflecting a tumour sometimes very small but in macular localisation. In rich countries where the social security system allows even the poorest to have access to better health care system, it is unusual nowadays that retinoblastoma is diagnosed at the stage of complications. The diagnosis is made early, sometimes conservative treatments available to help maintain the eyeball, and the five year survival is generally greater than 90%. In poor countries, because of the sub medicalisation, the situation is completely reversed. The early diagnoses are exceptional. The exophthalmos and burgeoning externalisation represent over 90% of the clinical aspects of retinoblastoma when children are seen for the first time. Almost all African authors recognise the very high death rates of this cancer in their respective departments (6, 10-12).

Orbital cellulitis usually begins abruptly by an unilateral painful proptosis, often accompanied by diplopia and inflammatory signs (eyelid edema, chemosis) in an infectious context (fever and impaired general condition) (13-15). *Streptococci* and *staphylococci* are commonly found germs. The ethmoiditis is most found as causal infection (13, 15-17). In the case of HIV / AIDS this ecology can be different with unusual germs like Pseudomonas in this investigation (18, 19).

Although we do not have exact statistics, it is accepted that before the age of ten injuries are generally due to domestic accidents or domestic violence. The severity of an eye-orbital trauma in children lies not only in the importance of initial lesions, but equally in the risk of secondary amblyopia (20, 21). Surgical decompression (external cantholysis) in case of haematoma allows to release the optic nerve, and reduce the negative effects of possible orbital apex syndrome (20-22).

Sarcoidosis is a systemic granulomatous disease of unknown etiology. It usually manifests as bilateral hilar lymphadenopathy, pulmonary infiltrates, skin and eye damage. Ophthalmological manifestations are inaugural in 7-20% of cases depending on the series (23, 24). The patent orbital events, dominated by reaching the lacrimal glands are even rarer and very little reported in the literature. The simultaneous enlargement of the lacrimal and parotid glands constituting Mikulicz's syndrome is met mainly during sarcoidosis, tuberculosis, Hodgkin's disease and certain leukemias (23, 24).

The optic nerve glioma is a childhood tumour (mean age nine years). Between 15 to 40% of these gliomas are associated with neurofibromatosis.

The clinical presentation is an unilateral painless exophthalmos with optic atrophy or rarely papilloedema. Strabismus or nystagmus are common and can be the first sign (3, 4, 25). The scanner or MRI show a fusiform increase volume of the optic nerve. Surgical excision is reserved to orbital forms accompanied by exophthalmos and blindness. Monitoring, rarely chemotherapy and/or radiotherapy are used in other cases (3, 25, 26).

Graves' disease is a form of hyperthyroidism with ocular (chemosis, keratitis, high ocular tonus), orbital (unilateral or bilateral exophthalmia) and eyelid signs (retraction, edema) (5, 27). It can be acquired or congenital due to a hormonal placental transfer during hypothyroid mother pregnancy. Evolution is satisfactory under treatment (5, 27, 28).

Overall, from the first to the third consultation, there is not a statistically significant difference in the evolution of visual acuity. The severity of the diseases in question, probably explains the importance of eye injuries or any of its related structures as soon as the exophthalmia is installed. As against, the general condition is better at the last visit, because children are cured or in the process of being in most cases.

In conclusion, the paediatric form of exophthalmia almost always reflects a serious clinical situation. Early diagnosis in retinoblastoma, rapid and adapted support in orbital cellulitis, can improve the vital and/or functional prognosis (visual acuity).

## REFERENCES


1. Belmekki M, el Bakkali M, Abdellah H, Benchrifa F, Berrado A. Epidemiology of orbital processes in the child: about 54 cases. *J Fr Ophtalmol.* 1999, **22**: 394-398.
2. Koki G, Sylla F, Traore J. Exophthalmia in children at the African Institute of Tropical Ophthalmology (AITO). *Med Trop.* 2009;**69**:467-70.
3. Nair AG, Pathak RS, Iyer VR, Gandhi RA. Optic nerve glioma: an update. *Int Ophthalmol.* 2014;**34**:999-1005.
4. Rebika S, Bonnin N, Kémény JL, Chiambaretta F, Bacin F. About of 5 cases of optic nerve tumours diagnosed during a 6-year-period. J *Fr Ophtalmol.* 2015;**38**:13-21.
5. Ho YH, Chung EC, Park SA. A 3-year-old girl with Graves' disease with literature review. *Ann Pediatr Endocrinol Metab.* 2014;**19**:154-158.
6. Wang Y, Huang D, Shi J, Ma J, Zhao J, Li B *et al.* Prognostic observation of 465 patients with retinoblastoma with optic nerve invasion. *Zhonghua Er Ke Za Zhi.* 2015;**53**:109-113.
7. Lumbroso-Le Rouic L, Savignoni A, Levy-Gabriel C, Aerts I, Cassoux N, Salviat F *et al.* Treatment of retinoblastoma: The Institut Curie experience on a series of 730 patients (1995 to 2009). J *Fr Ophtalmol.* 2015;**38**:535-541.
8. Ortiz MV, Dunkel IJ. Retinoblastoma. *J Child Neurol.* 2015 May 28. pii: 0883073815587943. (Epub ahead of print).
9. Subha L, Reddy AS, Ramyaa. A clinical study of retinoblastoma. *J Pharm Bioallied Sci.* 2015;**7**(Suppl 1):S2-3.
10. Togo B, Sylla F, Traoré F, Sylla M, Dicko-Traoré F, Sidibé T *et al.* A 30 months prospective study on the treatment of retinoblastoma in the Gabriel Touré Teaching Hospital. *Br J Ophthalmol.* 2010; **94**: 467- 469.
11. Walinjkar J, Krishnakumar S, Gopal L, Ramesh A, Khetan V. Retinoblastoma presenting with orbital cellulitis. *J AAPOS.* 2013;**17**:282-286.
12. Chang Y, Shi J, Zhao J, Xu X, Ma J, Shen L *et al.* Retinoblastoma in Chinese Children Aged Five to Fourteen Years. *Ophthalmologica.* 2015;**233**:222-229.
13. Sharma A, Liu ES, Le TD, Adatia FA, Buncic JR, Blaser S et al. Pediatric orbital cellulitis in the Haemophilus influenzae vaccine era. *J AAPOS.* 2015;**19**:206-210.
14. Davies BW, Smith JM, Hink EM, Durairaj VD. C-Reactive Protein As a Marker for Initiating Steroid Treatment in Children With Orbital Cellulitis. *Ophthal Plast Reconstr Surg.* 2014 Nov 12. (Epub ahead of print).
15. Mathew AV, Craig E, Al-Mahmoud R, Batty R, Raghavan A, Mordekar SR *et al.* Paediatric post-septal and pre-septal cellulitis: 10 years' experience at a tertiary-level children's hospital. *Br J Radiol.* 2014;**87**:20130503.
16. Pérez MG, Castro G, Mansilla C, Kaldzielski C, Salas G, Rosanova MT *et al.* Staphylococcus aureus methicillin-resistant community acquired neonatal orbital cellulitis. *Arch Argent Pediatr.* 2013;**111**:e50-53.
17. Amato M, Pershing S, Walvick M, Tanaka S. Trends in ophthalmic manifestations of methicillin-resistant Staphylococcus aureus (MRSA) in a northern California pediatric population. *J AAPOS.* 2013;**17**:243-247.
18. Atipo-Tsiba PW. Orbital cellulitis due to Chlamydia pneumoniae and HIV/AIDS: a bout a case. *RMJ.* 2014;**71**:17-18.
19. Kok AG, Botes MD. Orbital cellulitis in acquired immunodeficiency syndrome. *SA Ophthalmology Journal.* 2009;**4**:28-29.
20. Ukponmwan CU, Momoh RO. Broomstick Injuries to the Eye; an Emerging Cause of Blindness among Children in Nigeria. *Niger J Surg.* 2015;**21**:13-17.
21. Dhillon M, Dhariwal DK. Acute Haemorrhagic Oedema of Infancy (AHOI): A Case Report. *J Maxillofac Oral Surg.* 2015;**14**(Suppl 1):173-175.
22. Vinuthinee N, Azreen-Redzal A, Juanarita J, Zunaina E. Gunshot-like wound caused by sling shot injury - a case report. *Int Med Case Rep J.* 2015;**13**;8:47-50.
23. Kaes K, Betz PH. Lacrimal gland swelling in a young African woman. *Bull Soc Belge Ophtalmol.* 2011;(318):81-83.
24. Imai T, Yoshihara T. A case of Mikulicz's syndrome associated with sarcoidosis. *Nihon Jibiinkoka Gakkai Kaiho.* 2009;**112**:25-28.
25. Kaufman LM, Doroftei O. Optic glioma warranting treatment in children. *Eye* (Lond). 2006;**20**:1149-1164.
26. Gupta V, Sabri K, Whelan KF, Viscardi V. Rare case of optic pathway glioma with extensive intra-ocular involvement in a child with neurofibromatosis type 1. *Middle East Afr J Ophthalmol.* 2015;**22**:117-118.
27. Jevalikar G, Solis J, Zacharin M. Long-term outcomes of pediatric Graves' disease. *J Pediatr Endocrinol Metab.* 2014;**27**:1131-1136.
28. Harvengt J, Boizeau P, Chevenne D, Zenaty D, Paulsen A, Simon D *et al.* Triiodothyronine-predominant Graves' disease in childhood: detection and therapeutic implications. *Eur J Endocrinol.* 2015;**172**:715-723