



## Case Report

# Challenges of Managing Advanced Retinoblastoma in a 4 Year Old Nigerian Girl: Case Report and Review of Literature

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### Abstract

Retinoblastoma is the most common childhood ocular malignancy. It is possible to save life and vision in many patients with retinoblastoma due to advances in management and care. In Sub-Saharan Africa, management is marred by challenges including poverty and late presentation. This was a case report of advanced right eye retinoblastoma in a four year old girl. The patient had modified exenteration and was scheduled for adjuvant chemotherapy; however, the patient defaulted and only returned to eye clinic with tumor recurrence four months after initial intervention. Patient had four courses of cytotoxic medications at monthly intervals. The tumour regressed one month after the third course, and again defaulted from further follow up due to lack of fund. The current report underscores the need for health education of children's caregivers, availability of resource for eye care and subsidized care for retinoblastoma in developing countries.

### Keywords

Advanced retinoblastoma; Childhood cancer; Cytotoxic therapy; Poor compliance

## Introduction

Retinoblastoma is the commonest malignant intraocular tumour among children accounting for 3% of all cancer cases in developed countries [1]. In developing countries, the diagnosis is often made late and patients are seen at advanced metastatic disease [2-4] with resultant high mortality rates [1].

Metastatic retinoblastoma is rare in developed countries, with a reported range from 4.8% in the United States to 5.8% in the United Kingdom [5]. However, the frequency reported in developing countries varies from 9 to 11% at presentation [5]. Medical care has been shown to improve the survival rate of patients with advanced retinoblastoma especially multiagent chemotherapy in combination with radiation therapy [5,6]. Surgical interventions such as enucleation or exenteration have been combined in some advanced cases following chemoreduction [7].

There are peculiar challenges in managing tumours in developing countries. The challenges include ignorance, poverty, late

presentation and poor compliance to follow up schedule [8,9]. This was a case report of a four year old girl with advanced retinoblastoma who presented with management challenges.

## Case Report

A four year old girl presented in our clinic on account of three months history of cat eye reflex, progressive protrusion, tearing, eye discharge and vision loss involving her right eye (RE). The initial treatment comprised over-the-counter eye drops and traditional eye medication, both without any improvement. The child was a product of a consanguineous marriage with no positive family history.

Examination at presentation revealed a normal general clinical condition with no palpable preauricular or cervical lymphadenopathy and no hepatomegaly. The visual acuities were Nil Light Perception (NPL) RE and 6/9 Left Eye (LE). The LE was essentially normal. RE had marked proptosis with conjunctival hyperemia, chemosis and exposure keratopathy. The patient was admitted and found to have normal haematological parameters. Ocular ultrasound suggested advanced retinoblastoma with features of optic nerve involvement. The patient could not afford Magnetic Resonance Imaging (MRI) or Computed Tomographic (CT) scan of the brain which were only available at a hospital some kilometers away. Furthermore, there were no financial resources to perform further investigations such as cerebrospinal fluid (CSF) cytology, liver and bone marrow-aspirates/biopsies to detect distant metastases.

The patient subsequently had modified exenteration of the RE within five days of admission and was then discharged home on request to return two weeks later. The patient was to commence adjuvant chemotherapy upon histological confirmation. Histology report confirmed poorly differentiated retinoblastoma of the RE.

The patient reported back four months after discharge with tumour recurrence (Figure 1). The patient was re-admitted and co-managed with Paediatricians. Rehydration and allopurinol were initiated after haematological and electrolyte parameters were found to be essentially normal. The patient had the first course of cytotoxics commenced within one week of re-admission using intravenous (IV) Vincristine 0.05 mg/kg day 1, IV Carboplatin 18.6 mg/kg day 1 and IV Etoposide 5 mg/kg day 1 and 2. She then had two other courses of cytotoxics at monthly intervals using the same regimen/protocol as in the first course. The swelling regressed one month after the third course (Figure 2); however, parents again defaulted from follow up schedule due to lack of funds.



Figure 1: Right eye recurrent tumour at four months after modified exenteration.

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**Figure 2:** Regressed right eye re-growth a month after the third course of chemotherapy.

## Discussion

This case report highlights the challenges of managing advanced retinoblastoma in a resource-limited setting. These challenges are multifaceted and include ignorance, poor compliance with medications, lack of drug availability and diagnostic and therapeutic challenges (Table 1).

### Ignorance and late presentation

The initial challenge was late presentation to the hospital which accounted for the presence of advanced disease (orbital involvement) at the time of diagnosis. The delay in presentation was attributed to use of over-the-counter eye drops and to the application of traditional medications. Lack of knowledge of parents and health workers about the early signs of the disease also contributed to late presentation. Several studies have demonstrated that orbital extension is often associated with late presentation and diagnosis [2-4]. In developed countries diagnosis is often made before the age of two years, while in developing countries diagnosis is typically made at 50 months and above in most unilateral cases [1,10].

### Poor compliance and poverty

Another challenge faced in the management of this patient was poor compliance to follow up schedule. The patient was discharged home on request to return for follow up two weeks later by which time the histology report was available. Notably having to wait for at least two weeks to get the histology report is an added challenge. The need to commence cytotoxic therapy was discussed with the parents before discharge; however, patient was brought back four months later with a tumour recurrence involving the right orbit and the right upper eyelid. The parents were in the low socio-economic cadre of the society and could not afford the cost of treatment. In our hospital, most patients bear their hospital fee and fee waiver is enjoyed only by selected few indigent patients. Such patients' fees are settled using social welfare funds. However, in some countries there are social security systems that help cushion the effects for needy patients [1]. In addition to socioeconomic status, the observed poor compliance to follow up schedule might be related to the societal perception of cancer as an incurable deadly condition. Once parents are informed of a cancer diagnosis, many choose to go home rather than waste their scarce resources in the hospital [8].

Although the tumour appeared to have regressed, the need for more cytotoxic courses was discussed with the parents, however, they defaulted from bringing the child for further follow up citing financial constraint as the reason for their action. The poor follow up culture or non-compliance to treatment schedule makes it difficult to have statistics on retinoblastoma survivors in developing countries.

The medical social services department of the hospital was contacted for assistance but could not render financial assistance due to lack of funds.

### Availability of anti-cancer drugs

There were challenges associated with the procurement of anti-cancer drugs. The regimen that was used in the index case was highly effective as evidenced by the regression of the recurred tumour after three courses. However, the drugs are expensive and are not readily available in our environment. The cost and non-availability of the drugs added to the challenge of effective management of retinoblastoma in developing countries. The cytotoxic medications used in this patient were procured from a pharmacy store in a city located about 700 kilometres away from our hospital. The local pharmacy outlets hardly stock current anti-cancer drugs due to their low turnover rates.

### Diagnostic and therapeutic challenges

The patient was evaluated clinically for the presence of distant metastases, but could not afford MRI or CT of the brain which was only available at a hospital some kilometers away. Furthermore, there was no financial resources to do further investigations such as CSF cytology, liver and bone marrow-aspirates/biopsies to detect distant metastases. Retinoblastoma can metastasize to the regional lymph nodes, Central Nervous System (CNS) and distant organs, usually the bone and bone marrow. CNS involvement is not only through the optic nerve, but also through haematogenous spread [11]. Systemic workup for suspected metastatic disease should therefore include MRI of the brain and orbit with and without contrast. Lumbar puncture for CSF cytology, abdominal CT, bone scan and bone marrow biopsy should also be conducted. The laboratory workup should include complete blood and differential counts, liver function test, renal function test and serum lactate dehydrogenase (LDH) levels [11]. Proper evaluation of these patients would enable the attending physician to properly stage these patients at diagnosis as this would help adjust the interventions more appropriately. Patients with extraorbital disease (CNS or systemic) are not curable and are only amenable to palliative care. Palliative care services are scarcely available in countries with limited resources [12].

A biopsy, followed by cytoreductive chemotherapy, enucleation, and radiation therapy (RT) is usually a better approach in patients with advanced orbital disease [11]. However, because RT was not readily available in our environment, a primary exenteration was considered in this patient.

Another challenge encountered in the management of this patient was the lack of standardized protocol for managing retinoblastoma in our environment. This challenge can be overcome through training of staff in the management of retinoblastoma. There is the need to train pediatric and ocular oncologists as is the practice elsewhere. This would ultimately lead to increase survival rate of patients with retinoblastoma as the mortality rate is currently high in developing countries [3,4].

## Conclusion

Measures that can be adopted to ensure effective treatment of retinoblastoma in developing countries would include proper health education of health personnel and patients' caregivers on retinoblastoma and its managements. There is also the need to establish retinoblastoma centres with strong collaborative efforts

**Table 1:** Challenges of managing Retinoblastoma in Resource Limited Setting.

SN	Challenges	Possible Solution
1	Patient <ul style="list-style-type: none"> <li>• Inability to afford cancer care (Poverty)</li> <li>• Wrong beliefs (traditional/superstitious)</li> <li>• Illiteracy/Ignorance</li> <li>• Use of traditional medication</li> <li>• Consanguineous marriage</li> <li>• Late presentation</li> </ul>	<ul style="list-style-type: none"> <li>• Public enlightenment / awareness</li> <li>• Subsidized/free treatment</li> </ul>
2	Government/ Society <ul style="list-style-type: none"> <li>• Lack of health policy on retinoblastoma</li> <li>• Scarcity of anticancer drugs</li> <li>• Tariffs on anticancer drugs/equipments</li> <li>• Poor social welfare/subsidized treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Enactment of specific health policy on management of retinoblastoma.</li> <li>• Provision of highly subsidized/free anticancer drugs.</li> <li>• Duty free anticancer drugs/equipments</li> </ul>
3	Hospital <ul style="list-style-type: none"> <li>• Inadequate equipment</li> <li>• Inadequate infrastructure /material resources</li> <li>• Inadequate manpower</li> <li>• Hospital bureaucracy/hostile environment</li> <li>• Non affordable hospital fee</li> </ul>	<ul style="list-style-type: none"> <li>• Provision of needed cancer equipments/ infrastructure</li> <li>• Appointment of skilled manpower</li> <li>• Decentralisation of hospital procedures to minimize bureaucracy</li> <li>• Patients' hospital friendly culture</li> <li>• Subsidized care for retinoblastoma</li> </ul>
4	Health care Personnel <ul style="list-style-type: none"> <li>• Inadequate very skilled personnel to deliver retinoblastoma care</li> <li>• Inadequate training</li> <li>• Poor condition of service</li> <li>• Poor attitude of health carers</li> </ul>	<ul style="list-style-type: none"> <li>• Manpower training as ocular oncologists/assistants</li> <li>• Regular refresher courses for personnel</li> <li>• Enhanced condition of service for personnel</li> <li>• Improved attitude of health personnel to patient care</li> </ul>

with donor agencies to co-ordinate and subsidize the treatment of retinoblastoma in our environment.

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**Conflicts of Interest**

The authors/ contributors indicate no conflicts of interest.

**Ethical Approval/ Informed Consent**

This study was approved by the Ethical Research committee of the Federal Medical Centre, Birnin-Kebbi. An informed consent was obtained from patient's father.

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