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Unilateral Retinoblastoma in a Homozygous Sickle Cell Disease Patient: A Coincidental Occurrence with a Fatal Outcome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Retinoblastoma (RB) is the most common ocular malignancy. Presentation of this embryonal tumour in association with homozygous Sickle cell disease (HSCD) is seen for the very first time in a region with the highest prevalence of sickle cell disease and has also never been reported in the literature. The aetiology of RB remains unknown with unilateral disease occurring in about 60% nonhereditary form, and 15% hereditary. Here we present RB in association with HSCD. A 6-year-old HSCD child developed progressive swelling of the left eye for 2-months. Physical examination of the eye showed proptosis and inability to move the eyeball, loss of vision and absent red-light reflex. Histopathology of enucleated eye macroscopically revealed a distorted eyeball. Microscopy revealed a section of a malignant neoplasm composing dense and loose masses of small round cells with hyperchromatic nuclei and scanty cytoplasm, cells were arranged in sheets with few

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Flexner-wintersteiner rosettes. Presentation of RB in a patient with HSCD may lead to management challenges in our settings with the paucity of voluntary blood donors.

Keywords: Enucleation; Flexner-wintersteiner; homozygous; malignant; rosettes.

ABBREVIATIONS

RB : Retinoblastoma
HSCD: Homozygous sickle cell disease
UMTH: University of Maiduguri Teaching Hospital
SS : Sickle haemoglobin
SC : Sickle cell
CBC : Complete blood count
PCV : Packed cell volume
RFT : Renal function test
EUA : Examination under anaesthesia
CSF : Cerebrospinal fluid
CT : Computed tomography
HbSS: Haemoglobin SS
SCD : Sickle cell disease
SCT : Sickle cell trait
MRI : Magnetic resonance imaging
CNS : Central nervous system

1. INTRODUCTION

Retinoblastoma (RB) is the most common primary ocular malignancy of childhood. Retinoblastomas are primary malignant intraocular neoplasms of childhood displaying photoreceptor differentiation [1]. Peter Pawius of Amsterdam first described a tumour resembling retinoblastoma where he wrote about the malignant invasion of the orbit, the temporal region, and the volt of the cranium, a picture which was strongly suggestive of the natural history of RB [2]. No racial predilection appears to exist for RB, and there is also no significant difference in its incidence by sex. Retinoblastoma is diagnosed in patients at an average age of 18 months, with about 90% of cases diagnosed in children younger than 5-years. Histologically, RB appears as a small round blue cell tumour with rosette formation. It may arise in any of the nucleated retinal layers, and exhibits various degrees of differentiation, it tends to outgrow its blood supply, resulting in necrosis and calcification [1]. Homozygous sickle cell disease (HSCD) is the commonest hereditary hemoglobinopathy predominantly in people of African descent. Although the majority of the global population of HSCD patients resides in Africa [3]. To the best of our knowledge, this is the first case presentation of a child with HSCD proven to have developed RB. The only case we found in the literature to the best of our vigorous search was Intraocular Hemorrhage After Intra-Arterial Chemotherapy for retinoblastoma in Sickle Cell Trait (SCT) [4]. This reported case was in an SCT which is not in the spectrum of sickle cell disease (SCD). The presentation with an embryonal tumour at the age of six years in association with HSCD prompted the report. The child was followed up in the paediatric outpatient clinic of the State Specialist Hospital Maiduguri for his HSCD from the age of six months and has since had recurrent infections, infarctions and repeated blood transfusions.

2. CASE REPORT

The child was a six-year-old Negro boy, of African descent, that presented with complaints of progressive swelling of the left eye of 2-months duration. It was initially seen as a whitish patch within the left eye which gradually increased in size. There was associated history of redness and excessive lacrimation with occasional pain and double vision which progressed to the blurring of vision about 2-months prior to presentation. A month prior to presentation blurred vision progressed to inability to see completely with the left eye. The right eye was normal with no similar problem. No history of fever, weight loss, convulsions or loss of consciousness. No family history of similar presentation or any malignant disease, and no prior history of exposure to ionizing radiation. The marriage between the parents of the patient was not consanguineous.

While examination of the right eye revealed normal findings, the left eye examination, however, showed proptosis with corneal opacity and dryness with no discharge but was unable to move the eyeball with loss of vision and absent red-light reflex in the left eye.

Other systemic examinations were essentially stable except for the HSCD facie. Full blood count done at presentation revealed blood filmed with dysmorphic blood picture and features of haemolysis suggesting sickle cell (SC). A repeat haemoglobin genotype done at the University of Maiduguri Teaching Hospital (UMTH) revealed haemoglobin SS (HbSS).

Renal and liver function tests were done which were found to be within normal limits.

He was transferred to the Paediatric Haemato-Oncology unit and admitted where he received two cycles of neoadjuvant chemotherapy with Cyclophosphamide at 800 mg/m^2 and Cisplatin at 100 mg/m^2. Complete blood count (CBC) before the commencement of the chemotherapy showed packed cell volume (PCV) was 16% which necessitated transfusion with packed cells and PCV was optimized to 25%. Renal function tests (RFT) before and after the chemotherapy were unremarkable.

He was also placed on prophylactic Cotrimoxazole, Proguanil and Allopurinol but the Folic acid which he should have been on (as an HSCD patient) was withheld because it may enhance the growth of the tumour. Computed tomography (CT) and/or Magnetic resonance imaging (MRI) was requested but unfortunately, the two were non-functional in our facility and the patient-caregiver was not able to afford referral to centres where it was available. The patient was left with the option to schedule him for examination under anaesthesia (EUA) and enucleation of the eye and the optic nerve a month after neoadjuvant chemotherapy following review by both ophthalmologists and anaesthesiologists. However, the industrial dispute in our facility resulted in the patient having the surgical procure three weeks later in another facility. However, the patient represented two weeks after surgery back to our facility following enucleation of the eye with histopathology report which was as follows: Macroscopy revealed a distorted eyeball measuring 4 X 3 X 3cm, cornea ulcerated and the optic nerve was not identified (Fig. 1A). Cut surface appear grey white with brown and black areas (Fig. 1B). Microscopy revealed the section to be a malignant neoplasm composing dense and loose masses of small round cells with hyperchromatic nuclei and scanty cytoplasm. The cells are mostly arranged in sheets with few Flexner-wintersteiner rosettes. Haematoxyphillic deposits in and around blood vessels are present. There is through and through penetration of the sclera with subconjunctival deposits. The optic nerve was not identified (Fig. 1C).

He was readmitted in preparation for adjuvant chemotherapy and was in stable condition. Complete blood count done showed PCV of 24%, other parameters were normal and he was transfused with packed cells and post-transfusion PCV was 36% while, RFT was normal. He was commenced on adjuvant chemotherapy using the regimen: Vincristine at 1.5mg/m^2 day 1, Etoposide 150mg/m^2 day 1 and 2 and Carboplatin 560mg/m^2, these were given in a 28-day cycle. After receiving two cycles of chemotherapy, he was brought before being due for the third cycle with convulsion and loss of consciousness without associated fever which he succumbs before planned evaluation which included lumbar puncture for cerebrospinal fluid (CSF) analysis and CT scan. Being an HSCD patient he might probably have a cerebrovascular accident from sickling in the cerebral arteries as there was no fever to suggest Central nervous system (CNS) infection. The patient's caregiver denied consent to having an autopsy for ascertaining what led to the demise of the patient.

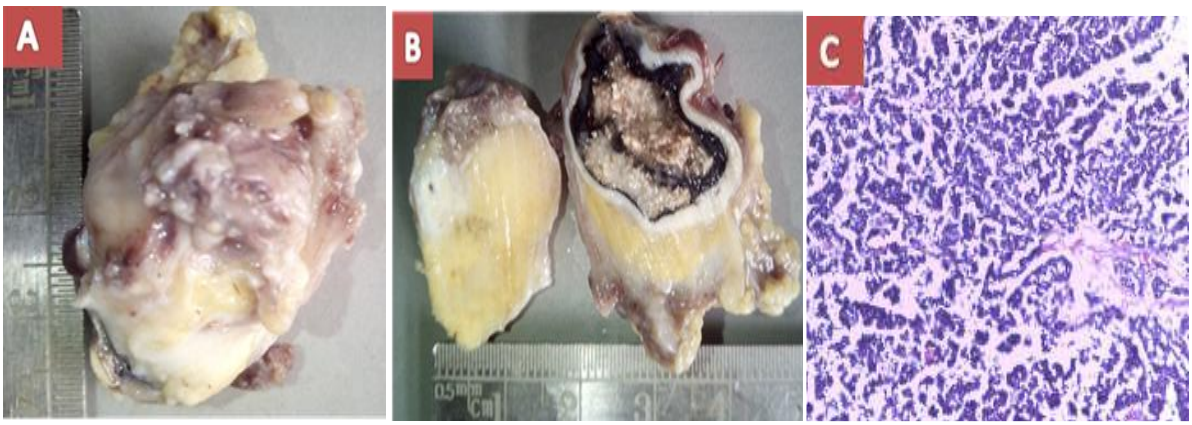

Fig. 1. A- Gross picture of enucleated left eye; B- Cut section of the eyeball showing friable grey-white tumour invading the choroid layer and focally extending to the sclera; C- Photomicrograph showing small round blue cell tumour with few Flexner-Winter Steiner rosettes and frequent mitoses, (H & E x100)

3. DISCUSSION

This report demonstrates the fact that embryonic tumours such as RB may have delayed presentation beyond the age of five years as is seen in our patient at the age of six years. Eighty per cent of the cases are diagnosed before the age of 3 to 4 years [5,6]. Retinoblastoma is the most common intraocular malignancy in children and usually presents with leukocoria, a white pupillary reflex, which often is first noticed when a red reflex is absent at routine well-child examination or a flash photograph of the child. Strabismus is often the initial presenting complaint. Orbital inflammation, hyphema, or pupil irregularity occurs with advanced disease. Pain is usually a feature if secondary glaucoma is present. Our patient presented with most of these features. In the setting of developing countries like ours, RB is mostly diagnosed at the advanced stage, usually when extraocular dissemination has occurred and the prognosis is unfavourable [7]. Late referrals might account for the delay in diagnosis until the tumour is advanced [8]. However, it has also been suggested that the tumour might present more aggressively at a later age in developing countries [9]. Late age presentation beyond five years and association with HSCD were important factors that probably led to the early demise of our patient, this is similar to the report of late diagnosis of RB in the documentation from developing countries like ours (Buenos Aires, Argentina) by Chantada et al. [7]. Although unilateral presentation does not vary with race or sex, age older than 5-years at diagnosis is usually associated with unilateral tumours as is the case of our report. Associated congenital anomalies with RB has been reported as a rare event but not HSCD. Congenital cardiac defects, Bloch-Sulzberger syndrome, cleft palate, and infantile cortical hyperostosis have been reported [5,10]. In contrast with the Indian series were 10.5% were associated with various congenital anomalies, non was associated with HSCD as in our patient [11].

Even though, we do not postulate a causative link between retinoblastoma and HSCD rather a coincidental co-occurrence. The presence of the two diseases with retinoblastoma requiring blood transfusion from marrow suppression following the cycles of cytotoxic chemotherapy and recurrent transfusion from anaemic crises of HSCD may lead to management challenges in the settings of the paucity of voluntary blood donors, although this has not proven to be the case. His management of HSCD remains supportive with lack of facility for marrow transplantation and that of retinoblastoma remains cytotoxic chemotherapy with radiotherapy still at infancy stage in our facility and yet to be in use.

4. CONCLUSION

Presentation of RB in association with HSCD poses a huge demand for recurrent transfusion protocols and a gloomy prognosis were the salient features of this report. Here exist inherent difficulties in the management of RB coexisting with HSCD in entirety in developing countries with the paucity of voluntary blood donors where blood and blood products for transfusion are difficult to come by. Given the late age presentation with HSCD, perhaps there exist the potential of difference in the biology of the tumour in this patient.

CONSENT

Written informed consent was obtained from the patient's caregiver (Biological father) for the publication of this report but denied consent for a facial image with left eye proptosis and sickle cell habitus.

ETHICAL APPROVAL

Approval was obtained from the hospital research and ethics committee of the University of Maiduguri Teaching Hospital (UMTH/REC/21/ 902) for this submission.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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