

# Delleman–Oorthuys syndrome (oculocerebrocutaneous syndrome) in a Nigerian child: a case report

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## Abstract

**Background:** Delleman–Oorthuys syndrome, also known as oculocerebrocutaneous syndrome, is a rare congenital anomaly with ocular, cerebral and cutaneous manifestations. So far, only 40 cases have been described.

**Clinical case:** A 3-year-old female Nigerian child with no identifiable left eyeball, multiple left-sided facial skin defects and delayed developmental milestones but otherwise uneventful medical and family history was evaluated at the Ophthalmology and Paediatric Neurosurgery in Ibadan, Nigeria. Besides the mentioned defects that were present since birth, brain imaging revealed several brain abnormalities including intracranial cysts. Global hyperreflexia and bilateral flexor plantar response were observed upon clinical examination. Left microphthalmia and orbital mass were detected. A histological assessment of the orbital mass revealed it to be rudimentary ocular tissue. The diagnosis of Delleman–Oorthuys syndrome was made based on the clinico-radiological features. The patient underwent a left-sided posterior fossa cystoperitoneal shunt. The left orbital mass was enucleated and the patient is currently awaiting left eyelid reconstruction and an orbital implant and repair of the left alar nasi cleft.

**Conclusion:** To our knowledge, this is the first published report of Delleman–Oorthuys syndrome in a female child of West African descent. Given the variable manifestations of Delleman–Oorthuys syndrome, and overlap with other syndromes, the Delleman–Oorthuys syndrome may be underreported. Neuroimaging of patients with cutaneous tags, orbital cysts and micro-ophthalmia could reveal more cases.

**Keywords:** Delleman–Oorthuys syndrome, intracranial cysts, micro-ophthalmia, oculocerebrocutaneous syndrome, skin tags

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## Introduction

Delleman–Oorthuys syndrome (also known as oculocerebrocutaneous syndrome and Delleman’s syndrome) is a rare congenital anomaly characterised by ocular, cerebral and cutaneous abnormalities. It was first described by J.W. Delleman and J.W. Oorthuys in 1981.<sup>1,2</sup> The syndrome is sporadic and has no known aetiology or risk factors.<sup>3,4</sup> Very few cases, mostly affecting male patients, have been reported from different regions of the world including Europe, North America, South America, Asia and Middle East.<sup>4–9</sup>

Although there has been a previous report of this syndrome in a male child from South Africa, to the best of the authors’ knowledge, there is no published report of Delleman’s syndrome in a female child of West African descent.<sup>10</sup>

## Case report

A 3-year-old female Nigerian child, third of three siblings, the product of a term pregnancy born to a healthy non-consanguineous couple, presented with ‘absent left eye’, left orbital mass, left alar

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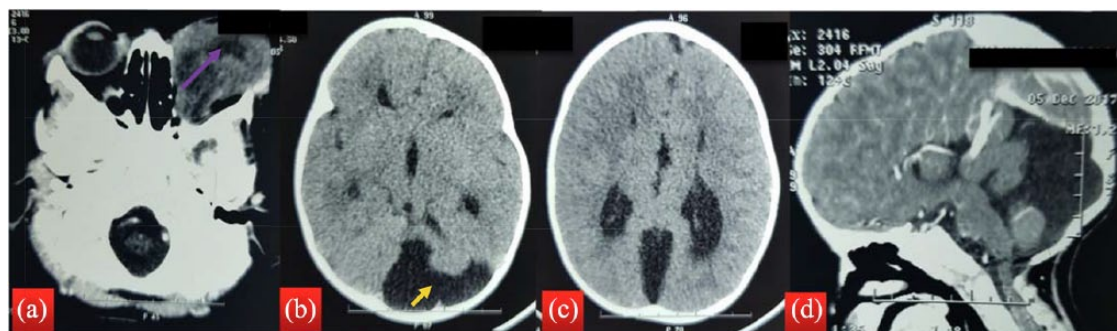
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**Figure 1.** (a–d) Clinical photographs: (a, b) pre-operative, (c) post-operative and (d) orbital soft tissue mass.



**Figure 2.** (a–c) Cranial CT scan axial cuts; (d) sagittal reconstruction. (a) Left orbital mass; the purple arrow on the remnant of the left eye. (b) Left-sided posterior fossa cyst communicating with the fourth ventricle (yellow arrow). (c) Colpocephaly. (d) Note the absence of the corpus callosum.

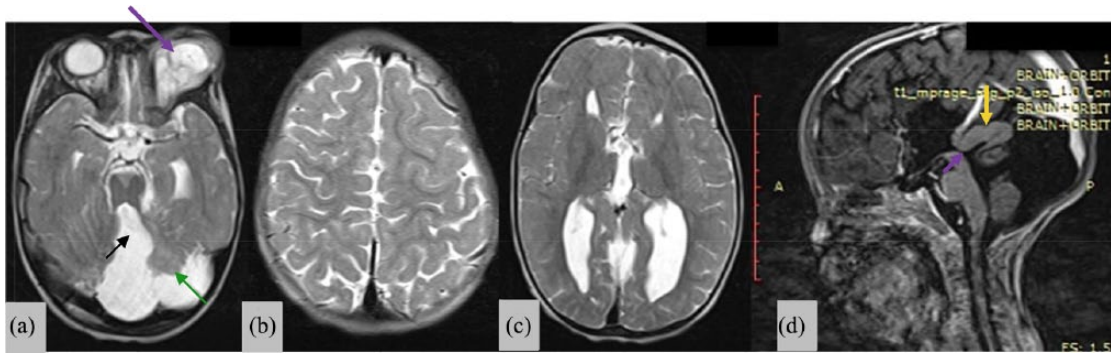
nasi cleft and left peri-ocular skin tags since birth. She had delayed developmental milestones achieving neck control at 6 months, walking at 3 years of age, and was still unable to talk. There was no history of seizure and no family history of a similar condition. Her pregnancy, birth and neonatal history were uneventful, but the mother admitted to ingestion of herbal concoctions during pregnancy.

Examination findings following evaluation at the Ophthalmology and Paediatric Neurosurgery clinics in Ibadan, Nigeria, include an appropriate social response, right horizontal nystagmus and normal right pupillary size and response to light. She had global hyperreflexia and bilateral flexor plantar response. She also had left peri-ocular nodular swellings, multiple left-sided facial skin defects, left lateral canthal tag/cyst, left alar nasi cleft and a left orbital mass with no identifiable left eyeball (Figure 1(a)–(c)). Other examination findings were normal.

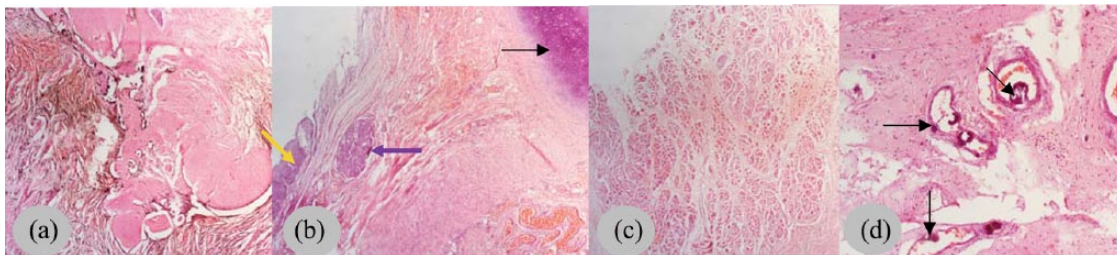
Cranial computerised tomography scan and magnetic resonance imaging showed a left orbital mass, left micro-ophthalmia, colpocephaly, corpus callosal

agenesis, giant dysplastic tectum, anteverted mid-brain, near horizontal aqueduct of Sylvius, hypoplastic left cerebellar hemisphere, vermian aplasia, large left retrocerebellar cyst communicating with the fourth ventricle (Figures 2(a)–(d) and 3(a)–(d)). The left orbital ‘cyst’ represented remnant eye tissue surrounded by mixed density/intensity orbital mass (Figures 2(a) and 3(a)).

A diagnosis of Delleman–Oorthuys syndrome was made based on the clinico-radiological features. She underwent a left-sided posterior fossa cystoperitoneal shunt and later excision of the peri-ocular skin tag and enucleation of the left orbital mass with placement of an orbital implant and a conformer. A firm well-circumscribed tissue with a long stalk was enucleated and sent for histopathological examination (Figure 1(d)). Histology of the orbital mass (Figure 4(a)–(d)) revealed fragments of fibrocollagenous tissue, rudimentary glial tissue, nests of pigmented cells and prominent vascular spaces within the stroma reminiscent of the uveal tract. There was a poorly formed retinal tissue and disorganised optic nerve tract. These were supported by skeletal muscle and nerve bundles of orbital tissue. One of the fragments was lined by



**Figure 3.** Brain MRI scans. (a–c): T<sub>2</sub>-weighted images; D: T<sub>1</sub>-weighted image. (a) Left orbital mass; left microphthalmia (purple arrow); note the extension of the posterior fossa cyst to the quadrigeminal cistern (black arrow), the left cerebellar hemispheric hypoplasia (green arrow) and the vermian agenesis. (b) More sulcation in the right frontal lobe compared to the left. (c) Colpocephaly. Note the prominence of the occipital horns of the lateral ventricles (left > right). (d) Large tectum (yellow arrow), anteversion of the midbrain and near horizontal placement of the aqueduct of Sylvius (purple arrow).



**Figure 4.** (a–d) Photomicrographs of H&E sections of left orbital soft tissue mass. (a) Uveal tract with hamartomatous features. (b) Stratified squamous epithelium of the conjunctiva (yellow arrow), focus of chondroid metaplasia (black arrow) and an apocrine gland (purple arrow). (c) Bundles of skeletal muscle. (d) Section showing blood vessels with foci of calcification of the tunica intima (black arrows).

stratified squamous epithelium with fibrocollagenous stroma showing focal chondroid metaplasia. There was calcific sclerosis in the tunica intima of some of the vessels in the orbital soft tissue. The features were assessed to be consistent with rudimentary ocular tissue, most probably microphthalmia. The patient presently awaits a staged reconstruction of the left eyelid, insertion of a prosthetic eye and repair of the left alar nasi cleft.

### Discussion

Delleman–Oorthuys syndrome is a rare congenital anomaly with about 40 cases reported since its first description in the literature by Delleman and Oorthuys 37 years ago.<sup>9</sup> Some authors posited the genetic basis of the disease as X-linked because of the male preponderance and prominent mes/metencephalic aberrations, and others have suggested a lethal autosomal-dominant mutation able to survive only via mosaicism and autosomal-recessive inheritance in phenotypically

normal consanguineous parents.<sup>3,6,11</sup> There is usually a negative family history of Delleman–Oorthuys syndrome in affected individuals as in our patient, and no racial bias has been identified.

The clinical manifestations of the syndrome are typically related to anomalies of the eye(s), brain and skin. The eye and skin anomalies associated with this syndrome have been fairly well described and include anophthalmia or micro-ophthalmia (unilateral or bilateral) with or without orbital cysts, colobomas of the iris, upper or lower eyelids, epibulbar dermoids, skin appendages or tags (periocular/cheek/peri-auricular) and focal cutaneous defects.<sup>6,12,13</sup> A number of publications have identified intracranial anomalies such as interhemispheric cysts, hydrocephalus, complete or partial corpus callosal agenesis, colpocephaly, meningoencephaloceles, frontal polymicrogyria, nodular periventricular heterotopia and mid/hindbrain defects.<sup>3,6,13</sup> Mid and hindbrain anomalies defined as typical of Delleman–Oorthuys syndrome are anteversion of

the midbrain, near horizontal aqueduct, large dysplastic tectum, absent cerebellar vermis, hypoplastic cerebellar hemispheres and huge posterior fossa cyst (communicating with the fourth ventricle), and these were all present in our patient.<sup>6,9</sup> The last three of these features could be confused with those of Dandy–Walker malformation, which some authors believe is one of the brain manifestations of Delleman’s syndrome.<sup>6,13</sup> However, the co-existence of ocular and cutaneous anomalies in our patient favoured the diagnosis of Delleman–Oorthuys syndrome over Dandy–Walker malformation. Indeed, the pathology in Delleman–Oorthuys syndrome is more devastating and complex than those of Dandy–Walker malformation.<sup>6</sup> Bony abnormalities associated with the condition include underdeveloped orbit, skull defect, micrognathia, malformation of the ribs or vertebrae and scoliosis.<sup>13</sup> Mahomed and Rikhotso described this condition in a 12-year-old African boy who had a forehead cutaneous defect and left-sided craniofacial lesions (like our patient), and a nasal bridge dermal lesion, anophthalmia and a huge supratentorial cyst. He also had the rare presentation of an ossifying fibroma (previously unreported in Delleman–Oorthuys syndrome). Our patient had the classical mid and hindbrain anomalies of Delleman’s syndrome (known to be more common in males), a large infratentorial cyst and multiple skin lesions. Other features of Delleman–Oorthuys syndrome described in the literature are unilateral alopecia, craniofacial clefts, facial  $\pm$  generalised asymmetry, cryptorchidism, complex splenic cyst and intra-abdominal neurofibroma.<sup>4,6,12,13</sup>

All of the above features need not be present for the diagnosis of Delleman–Oorthuys syndrome to be made. The minimum diagnostic criteria suggested by some authors on the subject are microphthalmia or orbital cysts, central nervous system cyst or hydrocephalus and focal skin defects which were met by our patient.<sup>14</sup> Clinical features of Delleman’s syndrome have been known to overlap with those of other established syndromes sometimes constituting a diagnostic dilemma.<sup>15</sup> Some of these conditions are Goldenhar (oculo-auriculo-vertebral) syndrome, Goltz–Gorlin syndrome (also named Goltz syndrome; this condition is characterised by focal dermal hypoplasia), Hallermann–Streiff syndrome (oculomandibulodyscephaly), encephalo-cranio-cutaneous lipomatosis (ECCL or Haberland or Fishman syndrome), Aicardi syndrome, periventricular nodular heterotopia–polymicrogyria syndrome.<sup>3,6,14–16</sup> The peri-ocular location of the skin tags (rather than preauricular)

and the lack of vertebral anomalies make Goldenhar syndrome unlikely in our patient.<sup>3,4,9</sup> The characteristic intracranial lipomatosis of ECCL as well as nevus psiloliparus was absent in our patient thus ruling out this diagnosis. Brain anomalies are rare in Goltz–Gorlin syndrome, the skin is usually normal in Aicardi syndrome, and the unilaterality of the micro-ophthalmia, absence of bird-like facies, sparse hair, mandibular hypoplasia, dental anomalies and short stature in the index patient are not in keeping with Hallermann–Streiff syndrome.<sup>6,17</sup> The mes/metencephalic abnormalities of Delleman–Oorthuys syndrome described by Moog and colleagues<sup>6</sup> have not been reported in any of these closely related differential diagnosis of the condition. Lesions are notably asymmetric and mostly left-sided as in our patient where the ocular abnormalities (micro-ophthalmia and orbital cyst), cerebellar hypoplasia, retrocerebellar cyst, periocular skin appendages, cysts and nasal defect were all located on the left side of the patient.<sup>10</sup> It is also known that individuals with this condition may experience seizures, intellectual disability, delayed developmental milestones or psychomotor retardation.<sup>3,4,12,13</sup> Brisk tendon reflexes and a positive Babinski sign on the side opposite the eye lesion have also been reported.<sup>4,14</sup> However, seizures and cerebral anomalies may be absent and neurologic examination findings are normal in this condition.<sup>4</sup> Seizures were conspicuously absent in our patient despite the plethora of brain anomalies documented in her.

Neuroimaging which includes computerised tomography scan and brain magnetic resonance imaging is key to the diagnosis. These were sufficient in establishing the diagnosis in our patient. Electroencephalogram is useful in those who manifest with seizures. Electrocardiogram, echocardiography, abdominopelvic ultrasound scan and spine roentgenogram may be required to evaluate other associated conditions or to rule out or confirm the differential diagnoses. Prenatal diagnosis with foetal magnetic resonance imaging is valuable and has been previously reported.<sup>18</sup>

The management of Delleman–Oorthuys syndrome is multidisciplinary and could be symptomatic or supportive. Medical management in the form of anti-seizure medications may be implemented for the treatment of seizures when present.<sup>14</sup> Conservative management of the orbital cyst with aspiration and sclerotherapy using ethanalamine oleate has been described.<sup>3</sup> Other

treatment options include excision of the orbital cyst, removal of the skin tags, repair of the eyelid coloboma, cleft lip or palate and insertion of a shunt (ventriculoperitoneal or cystoperitoneal) when hydrocephalus is present.<sup>9</sup> Anaesthetic implications of this condition is an important part of the management.<sup>19</sup> Our index patient underwent neurosurgical and oculoplastic procedures under general anaesthesia and endotracheal intubation. She awaits future reconstruction to achieve acceptable aesthetic appearance. The placement of an implant into the orbit, and a conformer in the fornix, would ensure continuous development of the bony and soft tissue orbit while awaiting definitive eyelid reconstruction. Other management modalities including physiotherapy, occupational or speech therapy and neurobehavioral therapy serve as adjuncts to care. Long-term follow-up of neurologic status is mandatory for patients with Delleman–Oorthuys syndrome.<sup>4</sup>

In conclusion, the clinical and imaging features of this case are consistent with Delleman–Oorthuys syndrome. It is possible that this syndrome is underreported, or the diagnosis is missed entirely and that neuroimaging of patients with cutaneous tags, orbital cysts and micro-ophthalmia will reveal more cases. This requires a high index of suspicion.

#### Conflict of interest statement

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#### Informed consent

A written informed consent to publish clinical patient information and photographs was obtained from the patient's parents.

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