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CASE REPORT

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Living with chronic progressive external ophthalmoplegia alongside cataract, peptic ulcer disease, diabetes and hypertension in Ghana

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Key Clinical Message

This is the case of a 51-year-old woman with chronic progressive external ophthalmoplegia (CPEO) alongside some comorbidities in a low-resource setting. This report seeks to sensitise clinicians about this rare condition in order to increase their index of suspicion and avoid misdiagnosis.

KEYWORDS

chronic, diabetes, external, hypertension, ophthalmoplegia, progressive

1 | INTRODUCTION

Chronic progressive external ophthalmoplegia (CPEO) is a rare autosomal dominant/recessive disorder, (genetic mutations such as polymerase subunit gamma-1, adenine nucleotide translocase type 1, and Twinkle are sometimes implicated) characterized by progressive myopathy usually involving the extraocular muscles and sparing the ciliary and iris muscles. Chronic progressive external ophthalmoplegia is a mitochondrial disorder with a global prevalence rate of 11.5 cases per 100,000.[1] The incidence rate of CPEO was stated to be 1–2 in 100,000, which shows the rareness of the disease.[2]

Chronic progressive external ophthalmoplegia sometimes has maternal inheritance because the mitochondrial genome is inherited from the mother. Therefore, the disorder can be transmitted only through females when this is the mode of inheritance.[3] Not much is known of sex distribution in this disease, but patients with Kearns–Sayre syndrome (KSS) have equal male-to-female distribution.

Patients with CPEO commonly have progressive, bilateral, and symmetrical ptosis which is subsequently followed by ophthalmoparesis within a couple of months or years. Some symptoms of CPEO include exercise intolerance, muscle weakness, impaired gait, dysarthria, mild peripheral neuropathy, and sometimes respiratory insufficiency.[3] This disorder can be clinically diagnosed, but a muscle biopsy is the gold standard. Polymerase chain reaction (PCR) is also diagnostic.

In our literature search, we did not find any case report in Ghana of a patient with CPEO. There was also no case of a patient with CPEO found with the following comorbidities – glaucoma, cataract, uveitis, peptic ulcer disease, diabetes, and hypertension.

2 | CASE REPORT

A 51-year-old woman diagnosed of hypertension at age 32 years and Type II diabetes mellitus 2 years later was apparently well until she started experiencing left upper eyelid ptosis at age 17. It became progressively worse and was followed by right upper eyelid ptosis, after which there was progressive ophthalmoparesis years later with sparing of both pupillary muscles. The patient had frozen globes bilaterally (downward gaze not spared) as of 2022. None of the following symptoms were present: eye pain, diplopia, exercise intolerance, muscle weakness in other parts of the body except extraocular muscles, impaired gait, dysarthria, dysphagia, mild peripheral neuropathy, thyrotoxicosis, or symptoms of thyroid dysfunction and respiratory insufficiency. There was no known family history of CPEO. Myasthenia gravis was ruled out by an ice-pack test and also clinically, as the patient presented many times to the eye clinic exactly the same way. She was diagnosed with CPEO clinically. There was no nystagmus, and pupillary reaction to light was normal. She never did a visual-field test or pinhole test because she did not cooperate. Patient had poor glycemic control (glycated hemoglobin as at 2020 was 8.2%) with dyslipidemia.

Initial assessment of visual acuity for right eye was 6/12 + 3 while left eye was 6/9 + 3 with intraocular pressure in the right eye being 39 mmHg and that of the left being 41 mmHg (all done in 2020). As her cup-to-disc ratio was normal, 0.3 in both eyes, she was diagnosed with ocular hypertension (OHT). Her high eye pressures were persistent over the years, and in 2020, the patient was placed on Timolol 0.5% drops twice daily in both eyes to prevent her from developing glaucoma. Selective laser trabeculoplasty (SLT) for both eyes was also offered as an alternative to drops, but patient refused due to the cost of treatment and/or fear of laser. Cup to disc ratio remained at a constant 0.3 in both eyes over the years. Fundoscopy did not reveal any pigmentary retinopathy.

In 2021, visual acuity was reduced to 6/36 in the right and 6/18 in the left eyes respectively, secondary to cataracts, and intraocular pressure was reduced to 21mmHg in the right and 20mmHg in the left on Timolol drops.

On general examination, patient had complete bilateral drooping of the eyelids (dense ptosis) as seen in Figure 1. All other systems were normal – respiratory, gastrointestinal, cardiovascular, throat, and ears (though patient complained of itchiness and poor hearing but no tinnitus or vertigo). The neck, however, had a soft and tender left tonsillar node, but no other masses were detected. She was diagnosed with peptic ulcer disease after complaining of epigastric pain and had a positive *Helicobacter pylori* stool antigen test. An upper gastrointestinal endoscopy could not be done due to unavailability of equipment to perform the procedure.

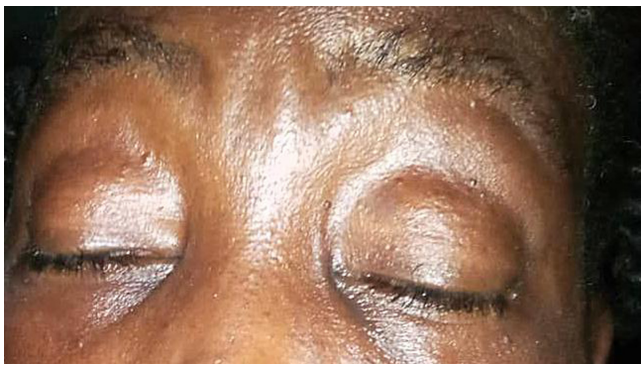

FIGURE 1 Showing bilateral complete ptosis.

In the first quarter of 2022, patient's vision decreased to counting fingers at 1 m in both eyes. She was diagnosed with dense cataract of both eyes and underwent small-incision cataract surgery. Vision in the right eye improved to 6/18 and the left eye to 6/12 without correction.

On review, intraocular pressures were 24 mmHg for the right and 27 mmHg for the left on Timolol 0.5% drops so she was offered SLT again for both eyes as well as ptosis surgery. She is still in the decision-making process. Crutch glasses were not offered because the glasses were not readily available and the optometrists in our region are not familiar with these glasses.

The patient's reasons for rejecting ptosis surgery (bilateral frontal sling surgery) were because she had both functional and cosmetic concerns of not being able to close her eyes in the hot weather despite being offered artificial tears to compensate for this. Her other co-morbidities were managed medically on subsequent follow-up visits.

3 | DISCUSSION

The diagnosis of CPEO in this patient was entirely clinical due to cost and unavailability of genetic testing in our part of the country, Northern Ghana. The age at which the disease started (17 years) is in concordance with the usual age of onset for the disease which is either before age 20 or after age 50.[4]

This patient had a slow progression of palpebral ptosis, which is often asymmetric (progression of ptosis was also asymmetric in this case; left occurred first) and symmetrical extraocular muscles weakness, which was followed by ophthalmoparesis. In our case, there was no diplopia, which is expected because it is an uncommon symptom. The ptosis in this patient was severe, and she was offered ptosis surgery over the years, but she declined due to fear of surgery, even though it was offered to her at no cost. She was later diagnosed of ocular hypertension and started on

treatment to prevent the development of glaucoma. Visual field assessment was unsuccessful as the patient's dense ptosis contributed to her lack of cooperation.

In cases of autosomal dominant or recessive CPEO (which usually presents in adulthood), it may have systemic involvement such as ataxia, tremor, neuropathy, parkinsonism, depression, hypogonadism, pigmentary retinopathy, deafness, and cataracts because of the multiple mitochondrial deoxyriboneucleic acid deletions that are usually from a mutation in PLOG1.[4] CPEO-plus was ruled out because other neurological symptoms associated with the syndrome were absent. Cataract and hearing loss (ear examination proved normal but the patient was symptomatic) were present in this situation.

Kearns–Sayre syndrome (KSS) can be ruled out because, though she presented before age 20, pigmentary retinopathy, cerebellar ataxia, heart block, and/or elevated cerebrospinal fluid (CSF) protein >100 mg/dL (the triad) were not present. CSF protein was not assessed here due to the lack of need for the level of invasiveness. Also, the lack of progressive limb myopathy or usual short stature also further reduces the probability of this patient having KSS.

This patient had possible cardiac involvement (hypertension) but not heart block though the existence of hypertension could have also been a coincidence. There was no ocular pain; therefore, ocular myositis was ruled out. Myasthenia gravis (ocular myasthenia gravis) was ruled out by the negative ice-pack test and by the clinical presentation.

Tolsa-Hunt syndrome was also ruled out due to the lack of suggestive symptoms. Severe periorbital headaches, painful eye movements (ophthalmoplegia), and ophthalmoparesis are also present in this syndrome. Extraocular muscles are usually the first or only muscles to be paralyzed in CPEO because of their small motor unit sizes, higher volume of mitochondria in comparison with skeletal muscles, higher blood flow rate, and higher discharge rate of motor neurons.

The diagnosis of type II diabetes mellitus was not surprising due to the fact that CPEO is often associated with impaired glucose effectiveness. A study on insulin sensitivity index, insulin secretion, and glucose effectiveness in patients with CPEO found a significant difference in glucose effectiveness between CPEO patients and control patients, which meant impaired effectiveness of glucose in CPEO patients. Therefore, the study concluded that the incidence of impaired glucose tolerance and diabetes mellitus is higher in people with CPEO, which may play a major role in early pathogenesis[5] as in this case.

In this patient, a genetic study could not be done due to cost and unavailability of equipment. In absence of a genetic study, other options could be PCR or a muscle biopsy for histological examination. This is likely to show ragged red fibers, while electron microscopy may reveal abnormal mitochondria containing paracrystalline inclusion bodies, which would be diagnostic as was seen in a study by Shin et al.[6] However, these were not done due to unavailability of equipment and financial constraints on the patient's part.

There was one case report in which CPEO was detected in a patient with glaucoma of 10 years duration, bilateral cataracts and associated hyperlipidemia and hypertension (both well-controlled on oral medication) through thorough history and examination. She had a positive family history of CPEO – 4 members of her family.[7]

There is no well-established link between CPEO and glaucoma, but there is the need for further studies to find out if there is a link or if this is an incidental finding among these two patients. Also, in the aforementioned case report, the patient had ocular hypertension (a precursor of glaucoma), cataract (bilateral also in our case), hyperlipidemia, and hypertension, which were well-controlled on oral medication but were not well-controlled in our case report. Also, the patient in our case study had no known family history of CPEO, while the one mentioned above had four family members with CPEO. This means the one with no family history is likely to be a sporadic case of CPEO. Throughout our literature review, we did not find any associations of CPEO with peptic ulcer disease. Also, the *Helicobacter pylori* isolated explains the pathogenesis of her diagnosis of peptic ulcer disease.

The patient did not want to go through surgery for the ptosis, but after her successful cataract surgeries, she seemed to be more eager to accept it. She is in the decision-making process on the selective laser trabeculoplasty (SLT) for the ocular hypertension. This is most likely due to the fatigue she developed from the chronicity of her condition. Hence, counselling is important to ensure adherence to management and to enlighten patients concerning the chronicity of the illness in the case of CPEO and possibility of not needing to chronically use eye drops if SLT for glaucoma works.

It is important to rule out other diseases, especially myasthenia gravis, which can either be done via the ice-pack test (like in this case), Tensilon test, biomarkers such as acetylcholine receptor antibodies, muscle-specific kinase antibodies, or through single-fiber electromyography. KSS must also be ruled out by using the triad (pigmentary retinopathy, cerebellar ataxia, and heart block) and/or genetic testing. It is also important to rule out thyroid eye disease, ocular muscular dystrophy (which manifests later after 40 years), and other differentials to be sure that it is indeed CPEO. There is no well-established link between CPEO

and ocular hypertension (OHT) or glaucoma but there is the need for further studies to find out if there is a link or if this is an incidental finding among these two patients mentioned. On the other hand, since no associations were found between CPEO and peptic ulcer disease, this may just be an incidental finding. Also, CPEO patients can be afflicted with any other illness just like other patients without CPEO.

However, there has been a strong link between diabetes and hypertension in patients with CPEO, but there was only one case report found in which the patient had hyperlipidemia, glaucoma, and CPEO.[7] Adequately counselling patients about the diagnosis and comorbidities is essential since this is a chronic condition. It is very important to ensure adherence to management.

4 | CONCLUSIONS

This is the first known case report of CPEO in Ghana. In a low-resource setting like ours in Ghana, the diagnosis of CPEO can be clinical, and a high index of suspicion is required not to miss such cases. This was a case of a 51-year-old woman who was clinically diagnosed of CPEO alongside other comorbidities, and multidisciplinary management should be the rule.

AUTHOR CONTRIBUTIONS

Naa Adzoa Adzeley Boi-Dsane: Conceptualization; writing – original draft; writing – review and editing. **Anwar Sadat Seidu:** Writing – review and editing. **Judith Simon:** Writing – review and editing. **Gilbert Batieka Bonsaana:** Writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

All authors in this study have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All data in this case report have been made available.

CONSENT

Written informed consent was obtained from the patient for the medical records and photos of this patient.

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