

Oral Findings in a Patient with Pompe Disease: A Case Report

Bimbola Opeyemi **AKINDELE***, Omolade Ademiposi **OSIBOGUN***, Adeola Rafeeat **MAJEKODUNMI***, Adesuwa **ABE***, Oladipupo Solomon **AYEDUN*,****, Omolola Olubunmi **ORENUGA*,****, Folakemi Adenike **OREDUGBA*,****

* Department of Child Dental Health, Lagos University Teaching Hospital, Lagos State, **Department of Child Dental Health, Faculty of Dental Sciences, College of Medicine, University of Lagos, Lagos State.

Correspondence

Dr Bimbola O. Akindele

Department of Child Dental Health
Lagos University Teaching Hospital, Lagos.
Email Address: bimope10@yahoo.com

Bimbola O. Akindele

<https://orcid.org/0009-0001-0500-0902>

Omolade A. Osibogun

<https://orcid.org/0009-0006-0588-4855>

Adeola R. Majekodunmi

<https://orcid.org/0009-0004-5545-3928>

Adesuwa Abe

<https://orcid.org/0000-0002-8242-3351>

ABSTRACT

Background: Pompe disease, also called glycogen storage disease type II, is a rare metabolic disease due to deficiency of acid alpha-glucosidase enzyme leading to accumulation of lysosomal glycogen within the tissues. Pompe disease can be classified into infantile and late-onset according to the age of onset. Clinical features include cardiomegaly, muscle weakness, hepatomegaly, recurrent pneumonia and dysphagia. Orofacial features include facial hypotonia, midface hypoplasia and mandibular prognathism, macroglossia, gingival hyperplasia, taurodontism, fusion of primary incisors and delayed eruption.

Case Presentation: A 7-year-old boy presented with complaints of several missing teeth. On general physical examination, the patient was hyperactive with an ataxic gait. Intraorally, oligodontia of the primary dentition, macroglossia and mild ankyloglossia were found. An orthopantomogram, however, revealed the presence of permanent tooth buds. The patient was counselled and extraction of a mobile, necrosed and retained primary tooth (71) was done.

Conclusion: Effective diagnosis and treatment of patients with Pompe disease requires a multidisciplinary team approach.

Key words: Infantile-onset Pompe Disease (IOPD), Late-onset Pompe Disease (LOPD), macroglossia, Acid alpha-glucosidase enzyme (GAA)

Oladipupo S. Ayedun

<https://orcid.org/0000-0002-7278-7522>

Omolola O. Orenuga

<https://orcid.org/0000-0001-6363-4949>

Folakemi A. Oredugba

<https://orcid.org/0000-0001-9863-9686>

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INTRODUCTION

Pompe disease, also known as glycogen storage disease type II, is a rare metabolic disease belonging to the lysosomal storage disorders.¹ The incidence of Pompe disease varies in different regions with a combined incidence of 1:40,000.²⁻⁴ Pompe disease is the deficiency of acid alpha-glucosidase enzyme (acid maltase) due to chromosomal mutation at 17q25.2-17q25.3, which has an autosomal recessive inheritance pattern.^{1,5,6} Acid alpha-glucosidase enzyme (GAA) is responsible for the breakdown of alpha-1,4- and alpha-1,6- glycosidic bonds of lysosomal glycogen to glucose.⁷ Deficiency of GAA leads to accumulation of glycogen within the lysosome.⁸⁻¹⁰

Pompe disease can be classified into Infantile and late-onset according to the age of onset.^{6,11} Infantile-onset Pompe Disease (IOPD) occurs during the first year of life and is further divided into classical and non-classical. The classical IOPD was first described in 1932 by a Dutch pathologist called Pompe after the death of a 7-month-old child with cardiomegaly.¹² This classical IOPD is a more severe form, but the non-classical, as first described by Hers is a less severe form with slower progression of cardiomegaly.^{13,14} Late-onset Pompe disease (LOPD) occurs any time after the first year and can be grouped into childhood, juvenile and adult-onset Pompe disease.^{8,15}

The severity is usually inversely proportional to the amount of acid alpha-glucosidase enzyme present.¹⁵ In IOPD, there is an absence or <1% of acid alpha-glucosidase enzyme activity, hence an increased level of severity, while LOPD has <30% of acid alpha-glucosidase enzyme activity, and they present with less severity.^{7,16} Enzyme replacement therapy with recombinant GAA is the treatment given to reverse cardiac abnormalities; however, it is expensive and not readily available in developing countries.^{17,18}

Clinical features of IOPD are progressively debilitating cardiomegaly, hepatomegaly, muscle weakness, developmental delay of motor skills, cardiomyopathy, recurrent pneumonia, dysphagia, organ failure or death.^{7,8,15,18} There is usually failure to thrive in the classic IOPD if untreated.^{8,10,15,18} LOPD presents with skeletal muscle weakness, respiratory insufficiency, less severe cardiac hypertrophy, chronic hypoxia, abdominal pain, hypothyroidism and dysphagia.^{8,15,19}

Facial features may include facial hypotonia, midface hypoplasia and mandibular prognathism^{18,20} while oral findings include macroglossia, gingival

hyperplasia, taurodontism, fusion of primary incisors, delayed eruption and malocclusion.^{10,20-22} The multisystem involvement in Pompe disease requires a multi-disciplinary team approach for management.^{9,13,15,18}

CASE REPORT

A 7-year-old boy, DG, presented to the paediatric dental clinic at Lagos University Teaching Hospital, Lagos State, Nigeria, with complaints of multiple missing teeth in the lower jaw and discolouration of a lower anterior tooth. The mother was the informant. The patient was referred from the paediatric neurology clinic, the Lagos University Teaching Hospital due to the missing teeth.

Dental history revealed that a mobile neonatal tooth was extracted from his lower anterior region when he was five weeks old. A history of recurrent falls due to his ataxic gait was also reported. The mother noticed discolouration of the lower anterior tooth two years before this presentation. There was no history of swelling around the tooth or spontaneous pain. However, the patient complained of mild pain and tooth mobility.

The patient was born through caesarean operation at full term, with a birth weight of 3.25kg and no history of perinatal illness. Mother, however, noticed some delayed developmental milestones as he did not crawl until one year and did not walk until two years old.

The patient, DG, had two episodes of seizure at three years of age, which prompted an investigation using a cranial computed tomography (CT) scan. He was subsequently diagnosed with Dandy-Walker Syndrome at a private hospital by a neurosurgeon. There was no family history of any disease or syndrome, and the parents' marriage was non-consanguineous. There was mild intellectual disability as he was a Nursery 2 pupil in a regular school. There was no history of visual or hearing impairment. No history of dysphagia.

The patient was managed by a paediatric neurologist for ataxic gait and hyperactivity, a paediatric endocrinologist for growth hormone deficiency, and conservatively managed by the otolaryngologist for tonsillitis.

At the time of the first presentation (7 years old) to the dental clinic, the patient was on oral Methylphenidate 5mg, 12 hourly for three months by the paediatric neurologist and Augmentin by the otolaryngologist. He had no known drug allergies.

On general physical examination, the patient had an ataxic gait and was hyperactive with a short attention

span. Extraoral picture of DG with Pompe disease (Figure 1) and other intraoral findings like discoloured 71 (Figure 2) and tooth in occlusion (figure 3).

Gingiva appeared normal.

Teeth present: 55,54,53,52,51,62,63,64,65,71,84

Missing teeth: 61,75,74,73,72,81,82,83,85

Discoloured tooth: 71

Retained tooth 71 with grade II mobility

Investigation: Orthopantomogram (OPG) showed erupted teeth: erupted

55,54,53,52,51,62,63,64,65,71,84. Unerupted tooth germs of 17,16,14,13,12,11,21,22,23,24,26,27,37,

36,35,34,33,32,31,41,43,44,45,46,47. (Figure 4)

Congenitally missing: 61,75,74,73,72,81,82,83,85, tooth germs of 15,25 and 42. Some unerupted teeth seems to have displacements and other dental anomalies like microdontia and Supernumerary. (36,35,33,34,44,45,46)

Diagnosis of oligodontia (Congenitally missing teeth 61,75,74,73,73,81,82,83,85,15,25 and 42 in a patient with Dandy-Walker Syndrome). Also noted at the first visit was pulpal necrosis of 71 secondary to trauma and retained primary teeth 71.

The treatment plan included counselling and reassurance of the concerned mother, scaling and polishing, oral hygiene education and fluoride therapy during the first visit.

On subsequent visits, pulpally necrosed retained tooth 71 extraction was done post-operative instruction was given and an intraoral post-opt picture was taken (Figures 5 and 6) A week later, the extraction site was satisfactorily healed. Oral hygiene education was re-emphasised and the patient was given a three-month appointment. Post-treatment orthopantomogram and pictures were taken at 8 years. (Figures 8-10)

Subsequent investigations by the paediatric endocrinologist revealed a deficient activity of acid alpha-glucosidase of 0.9 nmol/h/mg protein in peripheral blood leukocytes (reference interval: 42-123 nmol/h/mg). A chromogenic assay using glycogen substrate with acarbose inhibitor was used to measure leukocyte enzyme activity. The patient was diagnosed with Pompe disease nine months after the initial presentation. DG's mother travelled to India, where the diagnosis of Pompe disease was reconfirmed after several investigations. Endoscopic coblation adenoidectomy with tonsillectomy was carried out by the otolaryngologist 11 months after initial presentation and stainless steel crowns were placed on teeth 54 and 64 in the Society for

Rehabilitation of Crippled Children (SRCC) hospital, Mumbai.

Recent brain Magnetic Resonance Imaging (MRI) revealed generalised hypomyelination, thinning of the corpus callosum and exaggerated hypointensity in the putamina and thalami with severe cerebellar atrophy. The patient is being managed by the paediatric neurology and paediatric endocrinology units in Lagos University Teaching Hospital and is currently on Ticstop (tetrabenazine) 25mg, Bexol (trihexyphenidyl hydrochloride) 2mg, Inspiral (methylphenidate) 10mg, Cholecalciferol syrup 100ml (Ultra D3) and Nordilet (somatropin injection) 15mg/1.5ml. The patient could not afford the enzyme replacement therapy. DG has also been consistent with his three monthly dental preventive care at the paediatric dental clinic for scaling, polishing and fluoride therapy. A prosthesis was not considered as there is ongoing active eruption of his permanent teeth.



Figure 1: Extraoral picture of DG with Pompe disease



Figure 2: Intraoral pre-operative picture of DG showing oligodontia (multiple missing teeth) and pulpal necrosis of 71



Figure 3: Intraoral picture of the teeth in occlusion

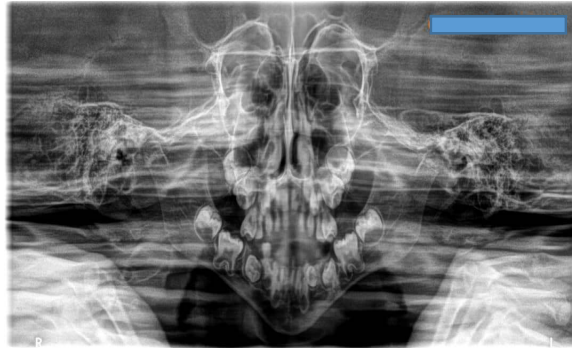


Figure 4: Orthopantomogram (OPG) of DG at 7 years



Figure 5: Immediate postoperative picture after extraction of 71 also showing mild ankyloglossia according to kotlow's classification



Figure 6: Extracted 71 showing resorbed root



Figure 7: 1-week post-operative picture after extraction of 71



Figure 8: OPG of DG at 8 years
55,54,53,52,62,63,64,65,33,84. Unerupted tooth germs of 17,16,14,13,11,21,22,23,24,26,27,37,36,35,34,32,31,41,42,43,44,45,46,47 Unerupted teeth seem to have displacements and other dental anomalies like microdontia and supernumerary (36,35,33,34,44,45,46)



Figure 9: Intraoral picture of DG at 8 years showing eruption of 33



Figure 10: Intraoral picture of DG at 8 years showing exfoliation of 51. Stainless steel crown on 54 and 64

DISCUSSION

Pompe disease is an autosomal recessive metabolic disorder, which shows there is an increased incidence of consanguineous marriage.^{21,23} However, in the case presentation above, there was no history of Pompe disease in the family and parents' marriage was non-consanguineous. All forms of mutation of the GAA gene are possible in Pompe disease with missense mutation being the commonest form of mutation occurring in about half of individuals with Pompe disease.^{8,24} Males have been reported to show more severe symptoms of the disease.²⁵

Clinical features of Pompe disease are dependent on the classification. In this case, childhood LOPD was diagnosed as there were no symptoms before the age of 1. This case did not present with the classic muscle weakness or cardiomyopathy associated with Pompe disease. However, there was central nervous system involvement, such as severe cerebellar atrophy, thinning of the corpus callosum and ataxic gait which have been reported in other studies due to excessive accumulation of glycogen in the nervous system in individuals with Pompe disease.^{13,15}

Cognitive function is usually normal in most cases of Pompe disease. However, few cases have shown mild impairment, which is like that reported in this case, with the patient showing mild intellectual disability.^{9,11,15} There have been reports of developmental delays in childhood.²⁶ This is also seen in this case presentation where the patient did not crawl until one and did not walk until two. Problems with growth can be seen in children with Pompe disease, as was evident in this case, where the paediatric endocrinologist placed him on growth hormones.^{11,15,27}

The commonest oral feature seen in infantile and LOPD is macroglossia, which was seen in this case report.^{7,8,15,18,21,22,28,29} Other oral findings in this case report, such as taurodontism and problems with tooth eruption, have also been reported in other studies.²⁰⁻²² Features such as oligodontia, mild ankyloglossia and a history of a neonatal tooth were observed in this case presentation.

Genetic counselling should be offered to affected individuals and carriers. Also, prenatal diagnostic testing and newborn screening should be done when available.^{3,8,9}

CONCLUSION

The present case illustrates the presence of ataxia, mild intellectual disability, macroglossia, mild ankyloglossia and oligodontia in a 7-year-old boy with Pompe disease. Early diagnosis and the need for

a multidisciplinary team approach to management is essential. This patient had no severe morbidity and could carry out his daily activities and oral hygiene practices with assistance. He was advised to regularly maintain good oral hygiene practices and attend three-monthly periodic reviews at the dental clinic.

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Source of Support

Nil

Conflict of Interest

None declared

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