# Pompe Disease in children and A Case Report


## 中文摘要

龐貝氏症是位於第十七對染色體上的基因缺陷導致體內負責轉化肝糖為葡萄糖的酵素 acid α -glucosidase 活性降低，人體無法獲得正常之能量供給而日益虛弱。全身的細胞都會受到影響，尤其以心臟及肌肉系統最嚴重。嬰兒型患者症狀在前幾個月就會出現，包括四肢軟弱、呼吸困難和心臟衰竭，但其智能發展正常，通常患者在一歲前會死亡。而晚發型患者，相對於嬰兒型患者，則可能到成年後才出現肌肉無力的症狀。本病例為一位兩歲六個月診斷為龐貝氏症的女童，因接受語言治療時按摩臉頰會痛才由母親帶來本院兒童牙科就診。檢查後發現口內多顆乳牙嚴重齲齒及殘根。經診斷及相關評估後，在全身麻醉下進行全口齲齒治療及乳牙套復形，目前仍定期回診檢查。

## Abstract

Pompe disease is the gene defect located on the seventeenth of chromosome, leading to the reduction of enzyme acid α-glucosidase activity which is responsible for conversion of glycogen to glucose. The affected ones will become weaker due to insufficient supply of energy. Body cells could be affected, especially the cardiac and muscular system. Infantile symptoms occur in the first few months, including limb weakness, breathing difficulties and heart failure, but intellectual development is normal, such patients usually die before their first birthday. The late-onset patients, compared with the infantile ones, symptom of muscle weakness may not appear until adulthood. This case is a two-and-a-half years old girl diagnosed with Pompe disease brought by her mother to our pediatric dental clinic, complaining of pain when massaging the cheeks during speech therapy. From the oral and dental examination, multiple primary tooth deep caries and residual roots were noted. After the diagnosis and evaluation, full mouth dental caries treatment and stainless steel crown restoration were performed under general anesthesia. The patient still regularly returned for check up visit at present.


## Introduction

Pompe disease is anautosomal recessivegenetic disorder caused by mutation in the gene located on chromosome 17 (17q25.2-q25.3) encodes for the production of acid alpha-glucosidase (GAA), an enzyme

responsible for the breakdown of glycogen to glucose inside lysosomes.[1],[2] The result is intralysosomal accumulation of glycogen, primarily in muscle cells, that leads to a progressive loss of muscle function. It was first defined in 1932 by Dutch pathologist Joannes C. Pompe in a seven-month-old infant who died of idiopathic cardiac hypertrophy and was found to have massive glycogen accumulation in many tissues, but predominantly skeletal and cardiac muscles.[2],[3] Pompe disease affects both sexes equally, and its incidence is estimated at approximately 1 in 40,000 live births.[4],[5]Pompe disease also referred as **Glycogen storage disease (GSD) type II, Acid alpha-glucosidase deficiency, Lysosomal alpha-glucosidase deficiency**.[6]

All patients with Pompe disease exhibit progressive muscular weakness. Proximal limb and respiratory muscles are the most commonly affected across all ages, while cardiomyopathy is the hallmark sign in infants.[2]Infants typically present with pronounced hypotonia and severe cardiomegaly.[7]Other signs include frequent respiratory infections, failure to reach motor milestones, and difficulty feeding. Children and adults show much greater heterogeneity. The most common clinical manifestations are progressive proximal muscle weakness and respiratory insufficiency,[8],[9],[10]ultimately leading to loss of ambulation and the need for ventilation support. Cardiac involvement is rare in this patient population.

In general, earlier presentation of Pompe disease usually correlates with a more aggressive disease course, and most patients who present as infants progress rapidly and die by age one from cardiac or cardiorespiratory failure.[6],[7],[11],[12]

## Case report

The patient was two-and-a-half years old, came to our OPD clinic with her mother and complained about pain when massaging the cheek during speech therapy. According to her mom, she was a patient of Pompe disease and mental retardation which was diagnosed in National Taiwan University Hospital and have received speech and rehabilitation therapies.

From the clinical intraoral examination, we found 51, 52, 61, 62, 74, 75, 81, 84, 85 were residual roots due to extensive decay; 53, 54, 55, 63, 64, 65, 82, 83 had large and deep decay involving pulp; 71, 72 had mild to moderate decay; full mouth gingival inflammation due to poor oral

hygiene(Fig.1&Fig.2).

Therefore, the diagnosis were residual roots of 51, 52, 61, 62, 74, 75, 81, 84, 85; chronic pulpitis of 53, 54, 55, 63, 64, 65, 82, 83; dental caries of 71, 72 and gingivitis.

Because of the patient's compromised systemic condition, full mouth multiple and severe dental caries, and uncooperation due to young age and mental retardation, we advised her mother to let the patient have full mouth dental treatment under general anesthesia. In that time, we also arranged appointments of consultation of Pediatric endocrinologist and anesthesiologist for her. Moreover, the physical evaluation including chest xray, blood examination and coagulation test were necessary for general anesthesia.

The treatment plan was pulpectomy for 53, 54, 55, 63, 64, 65, 82, 83; SSC fabrication for 54, 55, 64, 65; composite resin filling for 53, 63, 82, 83, 71, 72, 73; extraction for 51, 52, 61, 62, 74, 75, 81, 84, 85; full mouth teeth cleaning, fluoride gel application and oral hygiene instruction; admission right after general anesthesia for vital signs and systemic check up(Fig.3&Fig.4).

After the treatment was done under general anesthesia, the patient was transferred to pediatric intensive care unit immediately and taken over by pediatric endocrinologist. The endotracheal tube was removed in the PICU about 1 hour after the oral surgery. The patient discharged on the fifth day, and came to our OPD clinic for follow up examination every three months.

## Discussion

The American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) has issued diagnostic guidelines for Pompe disease.These guidelines recommend testing for Pompe disease should the following constellation occur[13]:

**1.Limb-girdle (especially pelvic) weakness**

**2.Weakness of the paraspinal muscles**

**3.Mild scapular winging**

**4.Orthopnea**

Once the clinical suspicion of Pompe disease is raised, confirming the diagnosis requires demonstration of absent or reduced acid alpha-glucosidase (GAA) enzyme activity.[14]

Technology allows the measurement of residual GAA enzyme activity in a variety of sample types, including minimally invasive blood-based samples such as dried blood spots, lymphocytes, or fibroblasts.[15],[16],[17],[18] These tests are quick and inexpensive, minimizing diagnostic delays for this progressive disease.

Historically, muscle tissue obtained from a biopsy was used to evaluate intracellular glycogen content and/or measure GAA activity. However, absence of glycogen accumulation in muscle tissue does not rule out Pompe disease, since glycogen content can vary in muscle tissue.[8] Therefore, muscle biopsy alone cannot be used for confirmatory diagnosis of Pompe disease.[8] Diagnosis should always be confirmed by enzyme assay demonstrating low GAA enzyme activity or by genetic analysis.

Although the underlying basis of Pompe disease is progressive muscular degeneration, the disease can affect different organs and systems. Therefore patient care and management of this multisystemic disorder is best handled by a multidisciplinary team of healthcare providers.[19],[20],[21]

Patients with Pompe disease have deficient or absent acid alpha-glucosidase (GAA) activity. ERT(enzyme replacement therapy) provides an exogenous source of GAA.

Respiratory support is one of the most critical forms of management for Pompe disease, as most patients experience some form of respiratory compromise, and respiratory failure is the most common cause of premature death among children and adult patients.[2],[8]

Infants often require frequent cardiac assessment and management of symptoms. These patients are at risk for cardiomyopathy, cardiomegaly, congestive heart failure, arrhythmias, and cardiac arrest during surgery. Pharmacologic treatment should be based on the stage of cardiomyopathy.[19]

The need for any surgery in infants with Pompe disease should be carefully weighed against the significant risks of anesthesia in these patients. Therefore, anesthesia should be used only when absolutely necessary, and always overseen by experienced pediatric and/or cardiac anesthesiologists.[19]

## Conclusion

Pompe disease is a congenital genetic disorder which could affect

multiple organ and system. Although there are no specific anomalies in dental aspect, oral hygiene and dental care could be more important than other healthy patients. Early childhood caries could happen if the parents or care givers ignore the necessity of tooth cleaning, and improper diet or eating habits would make the condition even worse. General anesthesia for these patients receiving full mouth dental treatment would be more risky due to the compromised systemic condition. Therefore, to avoid what it could happen, the parents and care givers should develop good oral hygiene and tooth cleaning habit for the patients, besides, take the patients to the dentist routinely for oral and dental check up is a must.

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Fig.1
Pretreatment
photographs

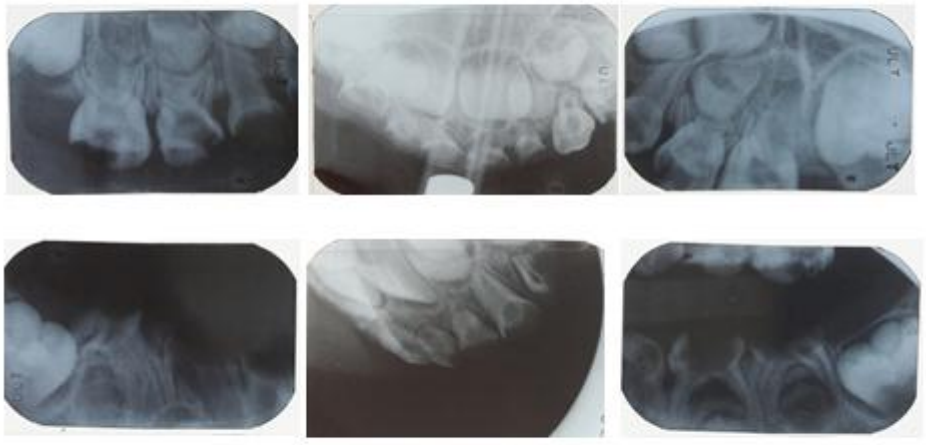

Fig.2 Pretreatment
periapical films

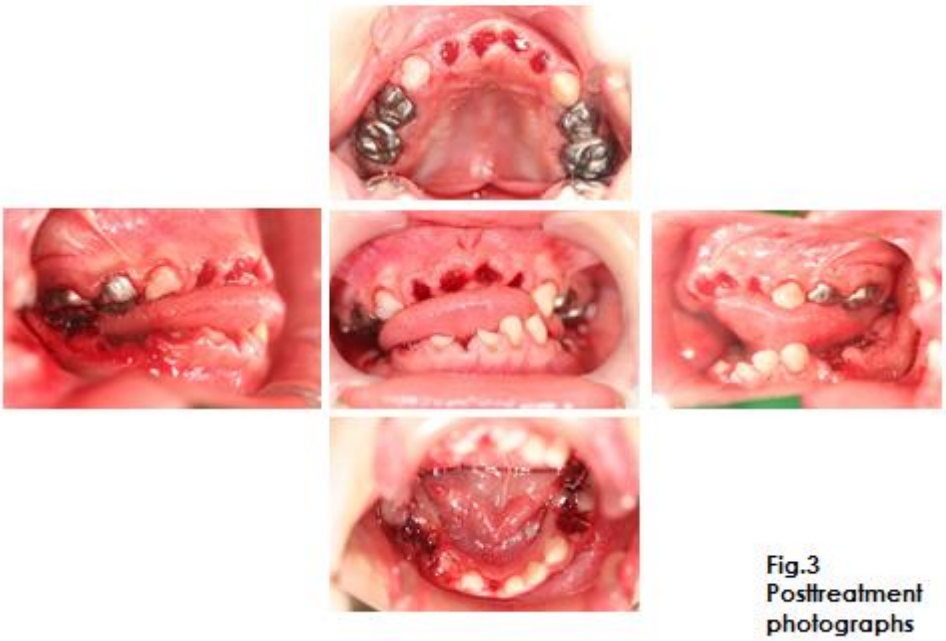

Fig.3
Posttreatment
photographs

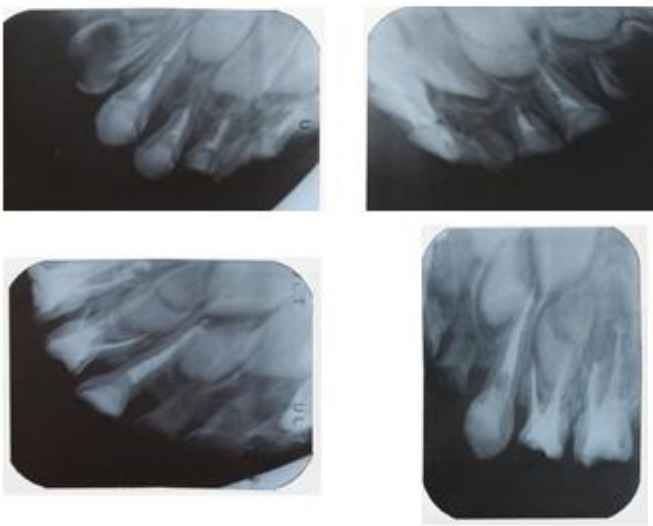

Fig.4
Posttreatment
periapical
films