# Dandy–Walker Syndrome with Giant Cell Lesions and Cherubism

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## Abstract

It has been very aptly quoted, "Variety is the spice of life"; and so variations exist in all forms and kinds good or bad, and for the worst or the best! Mother nature in all her glory and beauty has been very generous, but what when she fails to provide? It is this very character of nature that gives us variations which sometimes manifest in a cruel way on the human body and gives us the eponym of syndromes. Dandy–Walker malformation is an abnormality of the central nervous system, which leads to hydrocephalus and is associated with other abnormalities. Neurologic symptoms are the norm in afflicted patients due to the inherent nature of the disease in that it affects the very center of human function-the brain. This article brings to you a very unique, challenging and rare case of a young patient with this debilitating disorder who was also affected with giant cell lesions of the maxilla and mandible along with cherubism. It highlights the unpredictable course and progression of the disease in a child and our unique protocol employed for the management of the same. It adds providence and a new perspective to the still ambiguous nature of this disorder and the unprecedented maxillofacial anomalies, i.e., giant cell lesions and Cherubism associated with the same.

**Keywords:** Cherubism, Dandy–Walker syndrome, dexamethasone injections, giant cell lesions, surgical curettage

## Introduction

Dandy–Walker malformation (DWM) is an abnormality of the central nervous system (CNS), which leads to hydrocephalus and is associated with other abnormalities. Inheritance of the disorder remains controversial, with the majority perceived to be sporadic cases.[1] The difficulty in prognosticating the clinical and intellectual outcome of fetuses presenting with a DWM comes from the great variety of cystic, median, and retrocerebellar malformations that probably have nothing in common and the variability of the definitions given to these lesions. In addition, many of these lesions can mimic each other. A correct diagnosis cannot be made without a good quality magnetic resonance imaging (MRI) including sagittal views of the vermis and T2-weighted images.[2] This case report describes the clinical manifestations, treatment protocol, and it's outcome in a case of multiple giant cell lesions and cherubism associated with the "Dandy-Walker syndrome."

## Case Report

An 11-year-old boy was brought to the Department of Oral, Maxillofacial and Plastic surgery, Nair Hospital Dental College, Mumbai, with the complaint of multiple swellings on the face. It was seen that he had a wobbly gait, peculiar facies, and spoke with difficulty. A detailed history revealed the following facts about his general health. He was the first and only child of his parents and was born prematurely at the 7$^{th}$ month of life by cesarean section. It was observed that his milestones were delayed. He started to sit at the age of one and a half years and walked at 2 years. At this time, he developed seizures for which physician consultation was obtained and he was started on anti-epileptic medication (tablet Tegretol and tablet Gardenal). Following this regimen, the frequency of seizure episodes decreased but was persistent at regular intervals. At the age of 4 years, the anti-epileptic medications were withdrawn. He was scholastically fair. At age 6 years, a swelling was noticed on his chin. In addition, similar swellings were seen on the lower jaw posteriorly and on the upper face. In addition, he encountered difficulty in seeing distant objects.

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Consent for pre, intra- and postoperative facial photographs was obtained from the patient and his father.

Examination findings revealed that the boy had difficulty in balance, spasticity, and fine motor control movements. Intermittent tremors were seen in relation to his hands and fingers as well as whole body tremoring was noted. The presence of squint was noted in both eyes with fluctuant movements of the eyeballs. Pigmentation in the form of freckles was seen on his skin and especially so on the facial skin [Figure 1]. He could comprehend things, however, understood what was spoken to him with difficulty. His intelligence was thus judged to be subnormal. His head size was larger than normal. Facial examination revealed swellings at the mandibular symphysis and at the angle region bilaterally. In addition, similar swelling was observed in the region of the right Maxilla [Figure 1]. The masses were hard on palpation; however, no tenderness was elicited. Intraoral examination revealed masses obliterating the mandibular labial and buccal vestibules bilaterally. In addition, the right maxillary buccal vestibule was obliterated. The palatal cortical plate was expanded by the mass. Orthopantomographic examination revealed the presence of multiple, multilocular lesions in the symphysis, and left- and right body-angle region of the mandible with similar lesions in the right and left maxilla [Figure 2]. Plain and contrast-enhanced computed tomography (CT) of the paranasal sinuses, mandible, and maxilla was performed in the axial and coronal planes and color volume-rendered three-dimensional-CT images were obtained with audio video interleaved files [Figures 3 and 4]. The entire mandible showed a multilocular cystic appearance extending up to the subcondylar region of the rami. Variable areas of buccal and lingual cortical breaks were seen with extraosseous extension into the soft tissue. Similar lesions were seen involving the left maxillary alveolus and hard palate partly extending into the right maxillary alveolus. The right-sided lesion encroached into the right maxillary sinus. The parapharyngeal and masticator spaces were normal. No adenopathy was seen. A biopsy procedure was carried out for the lesions of the maxilla and the mandible and was suggestive of multiple giant cell tumors with odontogenic keratocysts and Cherubism [Figure 5].

He was then referred for neurological and ophthalmic consultations. Neurologic examination was suggestive of dysdiadokokinesia with past pointing and hydrocephalus. Ophthalmologic examination was suggestive of slight optic atrophy of the right eye with sluggishness of the right eye, decreased vision, and nystagmus. A plain MRI of the brain was performed, using PD T1W and T2W coronal sequences. Inferior vermis agenesis was seen with a widened vallecula and prominence of the cisterna magna. The ventricles were found to be prominent. Mild ventricular dilatation was seen which was out of proportion to the sulcal prominence and suggestive of extraventricular obstructive hydrocephalus. Overall features were suggestive of Dandy–Walker syndrome. A pediatric consultation was also obtained in view of a V-P shunt.

An endocrine consultation was obtained in view of the perplexity of the lesions involved. Serum calcium, phosphate, and alkaline phosphatase levels were obtained and were found to be normal. There was no evidence of hyperparathyroidism. After a thorough review of the literature and endocrine consultation, it was decided to start the patient on calcitonin therapy. However, since human calcitonin is not available, the patient was given salmon calcitonin as per the following schedule.

Before the start of the regimen, the patient was given a test dose of salmon calcitonin 1 IU

(Caltine injection, Ferring pharma) subcutaneously to check for any adverse reactions.

- First 10 days: 10 IU salmon calcitonin (SC)
- Day 11– Day 20: 20 IU SC
- Day 21– Day 30: 30 IU SC
- Day 31– Day 40: 40 IU SC

For the next 1 month, he was kept on a dose of 50 IU. This was well tolerated by the patient, and the dose was further stepped up to 80 IU which was maintained for the next 4 months. Salmon calcitonin does not exert any additional effect after a period of about one and a half years. A fresh set of radiographs were obtained, and it was found that the lesions had reduced in size with evidence of new bone formation. Suddenly after 18 months, the patient developed increase in the size of the lesions and it was decided to plan an excision surgery for the same.

The patient was prepared for general anesthesia with nasal intubation and was scrubbed and draped as per the standard surgical protocol. The lesions in the right and left maxilla, right, left half and anterior mandible were exposed [Figures 6 and 7] and curetted thoroughly, and the cavities in bone were filled with decalcified freeze-dried bone powder [Figures 8-12]. Postoperative recovery of the patient was uneventful, and there was a significant improvement in the facial appearance 6 months postoperatively [Figure 13]. There was a significant reduction in the size of the lesions postcalcitonin therapy as reflected in the postoperative OPG [Figure 14].

## Discussion

DWM is a rare congenital malformation and involves the cerebellum and fourth ventricle. The condition is characterized by agenesis or hypoplasia of the cerebellar vermis, cystic dilatation of the fourth ventricle, and enlargement of the posterior fossa. A large number of concomitant problems may be present, but the syndrome exists whenever these three features are found. Approximately 70%–90% of patients have hydrocephalus, which often develops postnatally. DWM may be associated with atresia of the foramen of Magendie and possibly, the foramen of Luschka.

DWM first was described by Dandy and Blackfan[3] in 1914. Since the original description, additional studies have reported

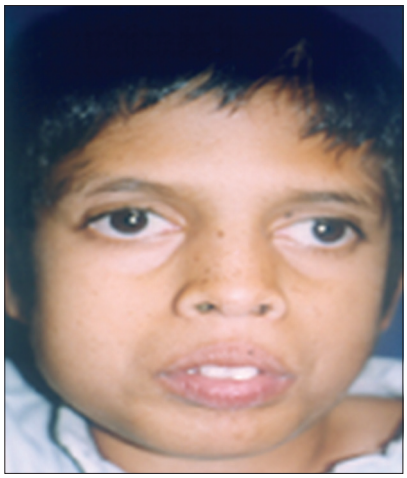

**Figure 1:** Preoperative view showing facial swellings and skin pigmentation

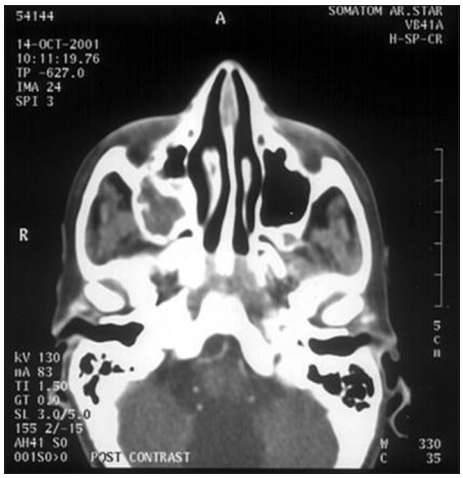


**Figure 3:** Computed tomography scan - Axial view

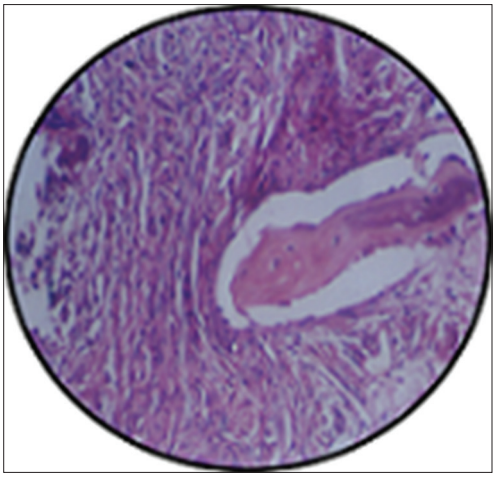

**Figure 5:** Histopathology slide suggestive of Giant cell lesions

on the various morphologic features of the syndrome. Not until 1954 did Benda[4] first emphasize that atresia of the cerebellar outlet foramina is not an essential feature of the condition and suggested the now widely accepted term DWM.

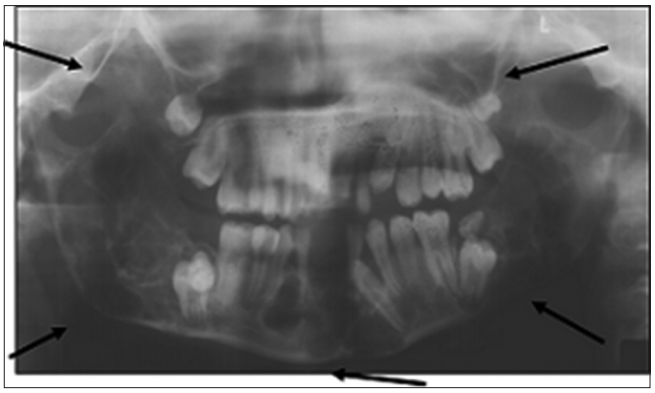

**Figure 2:** Preoperative OPG showing the maxillary and mandibular lesions

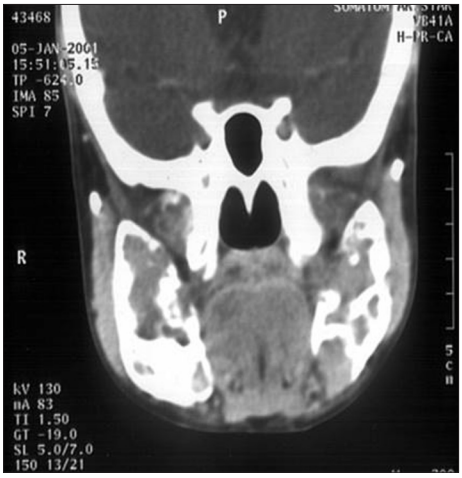


**Figure 4:** Computed tomography scan - Coronal view

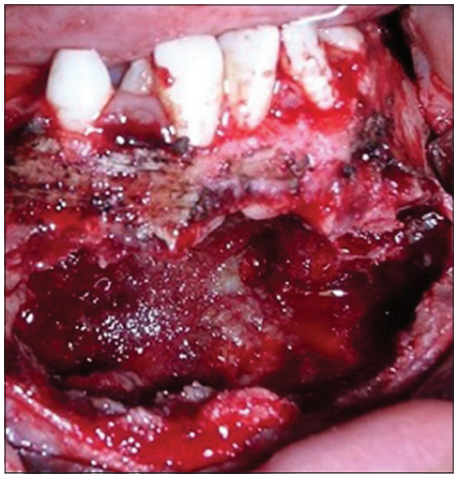

**Figure 6:** Lesions exposed for curettage

Studies by D'agostino *et al*.,[5] in 1963 and Hart *et al*.[6] In 1972 further defined the characteristic triad of DWM as consisting of (1) complete or partial agenesis of the vermis, (2) cystic dilatation of the fourth ventricle, and (3) an enlarged posterior fossa with upward displacement of lateral sinuses, tentorium, and torcular herophili. The triad typically is found in association with supratentorial hydrocephalus, which

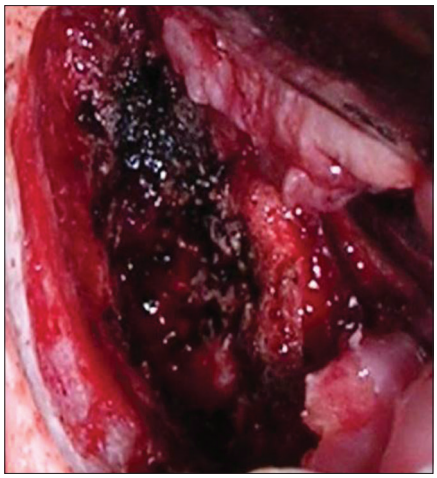

**Figure 7:** Lesions exposed for curettage

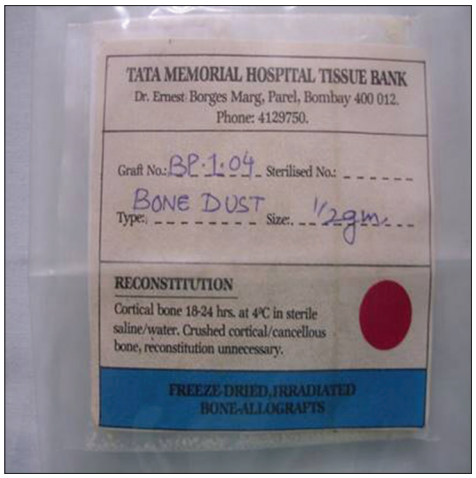


**Figure 8:** Decalcified freeze-dried bone powder used for filling the surgical defects

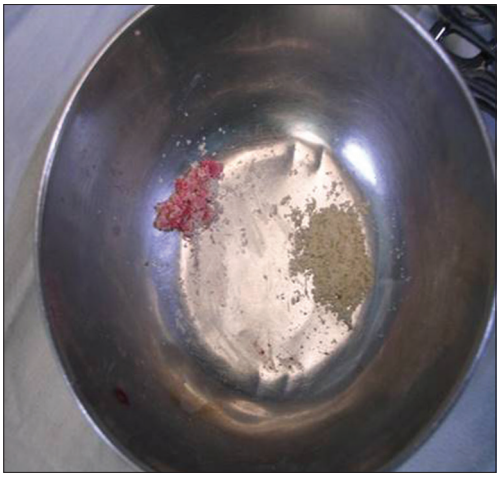

**Figure 9:** Decalcified freeze-dried bone powder

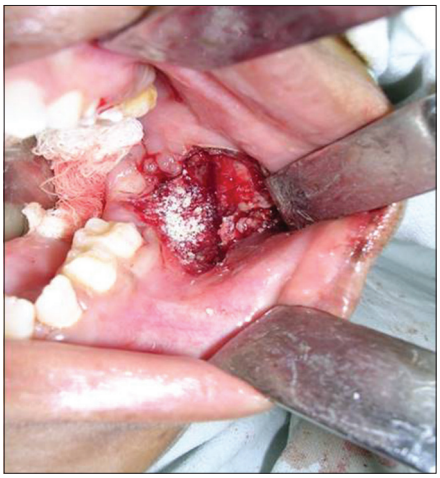

**Figure 10:** Mandibular defects filled with bone powder postcurettage

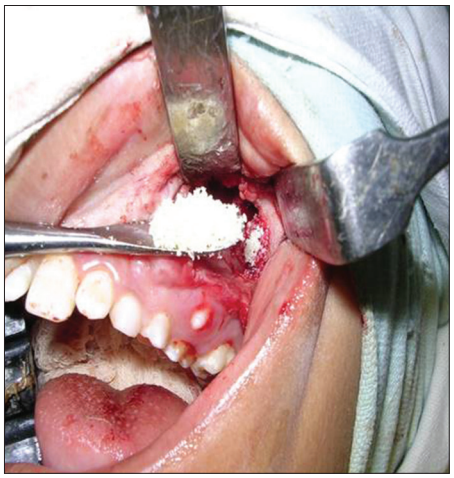

**Figure 11:** Maxillary defects filled with bone powder postcurettage

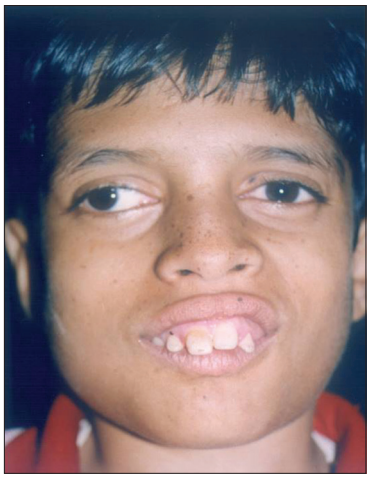

**Figure 12:** Postoperative OPG: At 2-week postenucleation

should be considered a complication rather than part of the malformation complex.

Dandy and Blackfan[3] and Taggart and Walker believed that the massive dilatation of the fourth ventricle originates in a congenital obstruction of the outlets of Luschka and Magendie. This theory includes the presence of a developmental cerebellar defect that begins before the embryologic differentiation of the

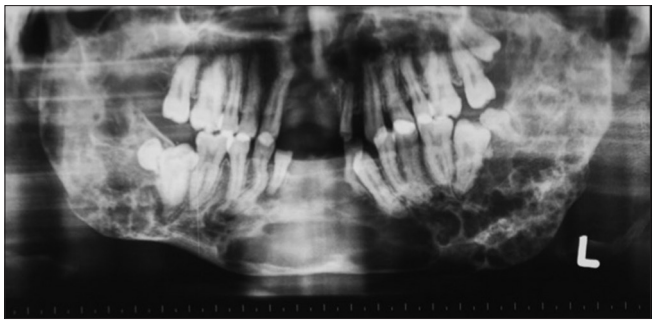

**Figure 13:** Six months postoperative view

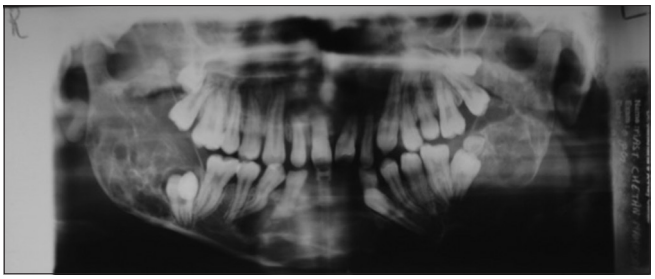

**Figure 14:** Postoperative OPG: At 15 months postcalcitonin therapy

fourth ventricle foramina and results in blockage or atresia of the foramina of Magendie and Luschka. This, in turn, results in cystic transformation of the roof of the fourth ventricle and in an obstructive (noncommunicating) hydrocephalus, in which a cyst arises from compromised absorption of cerebrospinal fluid.

The etiology is heterogeneous, and familial occurrence also has been reported. A few cases resulting from autosomal recessive genes have been reported, although in most patients, the cause of DWM is not known. Genetic counseling is critical to estimate the risk of recurrence of genetic disorders in family members.[7]

Etiologic heterogeneity and low-recurrence risk in siblings (1%–5%) for DWM have been reported. Increased frequency of an association with congenital heart disease, cleft palate, and neural tube defects appear to exist.

Predisposing factors include gestational (first trimester) exposure to rubella, cytomegalovirus, toxoplasmosis, warfarin (Coumadin), alcohol, and isotretinoin.

## Frequency

In the US: the incidence of DWM is 1 case per 25,000–35,000 live births. DWM accounts for approximately 1%–4% of hydrocephalus cases.

The prognosis is difficult to formulate. The prognosis is only moderately favorable, even when hydrocephalus is treated early and correctly.[8] An extreme range of severity is seen in this malformation. The presence of multiple congenital defects may affect survival adversely. Some people have Dandy–Walker variant their entire lives without any symptoms. Some infants may have it in association with other syndromes, resulting in severe complications or death.

## Sex

DWM occurs more frequently in females than in males.

## Age

Depending on the time of onset and degree of hydrocephalus, the age at diagnosis varies from birth to older childhood. Presentation in adulthood has been reported but is unusual. Patients with Dandy–Walker variant are more likely to present in adulthood than in infancy or childhood.

Associated CNS abnormalities of DWM are reported in 70% of children. Non-CNS–associated malformations are reported in 20%–33% of children such as orofacial deformities and cleft palate, polydactyly and syndactyly, cardiac anomalies, urinary tract abnormalities (polycystic kidneys), cataracts, retinal dysgenesis, and choroid coloboma, facial hemangioma, hypertelorism, Meckel–Gruber syndrome, and neurocutaneous melanosis.

Patients with DWM present with developmental delay, enlarged head circumference, or signs and symptoms of hydrocephalus. The clinical presentation depends to some extent on the combination of the developmental anomalies in the infant.

Difficulty with balance, spasticity, and poor fine motor control are common. The degree of developmental delay appears to be related to the level of control of hydrocephalus and to the extent of supratentorial anomalies. Interference with respiratory control centers in the brainstem may cause respiratory failure. Seizures occur in 15%–30% of patients.

Hearing or visual difficulties, systemic abnormalities, and CNS abnormalities are associated with poor intellectual development. Subnormal intelligence (intelligence quotient <83) is manifested in 41%–71% of patients. More severe intellectual impairment has been observed in patients with agenesis of the corpus callosum.

In our case, the systemic injections of salmon calcitonin proved to be a very wise decision in that they helped regressing the lesions to a fair size over a one and a half year period which were much more convenient to excise; thus rescuing the patient from the agony and trauma that he would have had to face if the excision surgery was planned without a formal calcitonin regimen. The patient is under regular follow-up and no recurrence of the lesions has been observed. Furthermore, he is been advised regular consultations with the neuromedicine and endocrine specialties for monitoring of his systemic status.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest
There are no conflicts of interest.

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