

Bilateral Pallidotomy for Dystonia with Glutaric Aciduria Type 1

Hyung-Sik Hwang, M.D.,¹ Antonio De Salles, M.D., Ph.D.²

Department of Neurosurgery,¹ College of Medicine, Hallym University, Seoul, Korea

Division of Neurosurgery,² University of California, Los Angeles, California, USA

Glutaric aciduria type 1 is an inborn error of lysine, hydroxylysine, and tryptophan metabolism caused by deficiency of glutaryl-coenzyme A dehydrogenase. The disease often appears in infancy with encephalopathy episode that results in acute basal ganglia and white matter degeneration. The majority of patients develop a dystonic-dyskinetic syndrome. This reports 6-year-old boy who had been done previous gastrostomy due to swallowing difficulty underwent bilateral pallidotomy with intraoperative electromyography(EMG) monitoring for disabling dystonia. Intraoperative EMG was used to assess stimulation thresholds required for capsular responses and muscle tone. Surface EMG electrodes were placed on the face and cricopharyngeal muscles. Exact target were directly modified according to MRI-visualized anatomy. EMG response was consistently seen prior to visual observation of muscle activity. The surgery improved dystonic symptoms without swallowing difficulty.

KEY WORDS : Glutaric aciduria · Dystonia · Pallidotomy.

Introduction

Type 1 glutaric aciduria(GA1) is an inborn error of organic acid metabolism.

Affected children cannot completely degrade the two essential amino acids lysine and tryptophan due to deficiency of the flavin-dependent mitochondrial matrix enzyme glutaryl-CoA dehydrogenase(GCDH). Although the tryptophan oxidation occurs in the liver and kidney, the brain is the principal organ affected^{12,13}. Between birth and 18 months of age, with a peak at 14 months, 90% of untreated children with GA1 suffer an acute neurological crisis precipitated by an infectious illness. Acute episodes of vomiting, ketosis, hyperammonemia, elevation of serum transaminase, seizures and coma with hepatomegaly, a combination of symptoms that resemble Reye syndrome, may occur during an intercurrent infection or stress. Recovery is slow and incomplete, with marked residual dystonic and choreoathetotic movements and the development of mental retardation. Some affected children are asymptomatic and some symptomatic individuals may remain undiagnosed. The natural history of the disease is remarkable and ranges from acute infantile encephalopathy and sudden death to static

extrapyramidal cerebral palsy to normal adult^{10,13,14}. GA1 is a progressive disorder and causes severe disability and pain due to dystonia. Carnitine deficiency and malnutrition develop in patients with severe dystonia and dysphagia, which necessitates gastrostomy.

Dystonia is very difficult to manage in these patients. Baclofen, benzodiazepines and botulinum toxin administration can occasionally improve dystonia, but the majority of the patients have minimal benefit^{2,3,8,15}. There are multiple reports of pallidotomy for generalized dystonia, and few case report of GA1 treated with staged bilateral pallidotomy^{6,8,9,11-13,15}. We report a 6-year-old boy with severe generalized dystonia secondary to GA1 treated with staged bilateral pallidotomy and intraoperative EMG monitoring to avoid swallowing difficulty.

Case Report

The patient is a 6-year-old little boy with a diagnosis of glutaric aciduria type I that was diagnosed at Childrens hospital of Los Angeles at 6 months of age when he presented with decreased strength, low tone, and seizures. The seizure

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• Address for reprints : Hyung-Sik Hwang, M.D., Department of Neurosurgery, College of Medicine, Hallym University, 94-200 Yeongdeungpo-dong, Yeongdeungpo-gu, Seoul 150-030, Korea Tel : +82-2-2639-5450, Fax : +82-2-2676-0980, E-mail : hyungsik99@yahoo.co.kr

resolved within 1 year. Since he has been given a special formula, but other than that, he does not take any medications. He is extremely hypertonic with episodic of dystonia refractory to baclofen. He had been with G-tube placement, G-tube was removed at three years old. He was born from a 17-year-old female, full term and 7 pounds at birth, but C-section for failure to progress. He took a formula at home with carnitine. On family history there was negative for any neurologic disorder, any kinetic or degenerative disorders. His family was originally from Mexico. On developmental history he was globally delayed, he was unable to walk and functionally use his upper extremities. His parents felted that he seemed to understand somethings, cried and looked at something when he wanted it but had no speech. He attended school with special education.

He exhibited reduced facial expression and jaw opening dystonia. He could not support his head unassisted, rollover or reach out for objects with his extremities. He had continuous dystonic posturing in the neck, forearm, and hand flexion. Axial muscle dystonia resulted in opisthotonus posturing. Dystonia also resulted in extensor posturing of the legs on attempts to sustain antigravity postures and with agitation. He could not sit or stand independently.

He was brought to the MRI scanner and placed on general anesthesia. While in the anteroom of the MRI scan, his forehead and occipital region are prepared and distended in sterile fashion, local anesthetic agent (lidocaine) was injected in two points in the forehead and two another points in occipital regions, where screw pins are applied to hold the Leksell frame in place. The frame was placed parallel to the anterior commissure, posterior commissure line based on the infraorbital meatal line. The frame was well adjusted and centered, the patient was transferred to the MRI scanner. The images were downloaded into the Brainlab software (@Target, Germany). The anterior and posterior commissures were marked and calculations were made for globus pallidus interna(GPi) on the left side. The planning MRI coordinates of the target were 2.7mm below AC-PC plane, 1.5mm anterior to the midcommissural point and 18.4mm lateral. The Leksell arc angle was 97.7° and the ring angle was 53.8° . The planning MRI target was adjusted using the images to ensure it was in the posteroinferior edge of the GPi just above optic tract. Leksell coordinates were obtained and the patient was transferred to the table in the 0.25 tesla MRI scanner. Here, his head was held in place by a Mayfield adapter. He was prepped in the standard sterile fashion from the frontal region, all the way to the parietal and temporal area. A 2cm incision was placed over the coronal suture. On this side, a burr hole locates 3cm from the midline.

A radionics electrode and radiofrequency with 2mm exposed

tip with 1.5mm diameter, was introduced in the direction of the target. Impedence was used for guidance. We proceeded by giving antegrade stimulation. The retrograde stimulation was given to try to identify the relationship of the tip of the electrode with the internal capsule. In all sites 10volts with pulses of 1.00msec duration and 2Hz did not elicit any motor response. We made 3 lesions sparse 2mm apart. Lesions were made at 75° for 60s. There were in the same trajectory of the electrode. Postoperative MRI measurements were made by using the lesion artifact tip in the relation to intercommissural line. For the left brain there was no distinct margin between the lesioning tracts. On postoperative MRI the lesion tip was measured as anterior 1.5mm, lateral 18.4mm and inferior 2.7mm. It was not expected that there would be a one-to-one relationship between the lesioning electrode tip location and the extent of the radiofrequency lesion. No complications related to the lesion.

The patient had significant right side improvement of dystonia as well as axial symptoms including jaw opening and facial expression following the surgery. Tone on the right was improved. There were also reduced spontaneous movements on the left side, improved to turn the neck toward directions what he wanted to see and also improved to reach the object by usage of right upper extremity. He continued to have left side dystonia, interfering with his motor functions. He still had problems with balance and speech.

After 3months later from the initial surgery, the patient had right side pallidotomy with EMG monitoring of pharyngeal and facial muscles by electrophysiologist (Fig. 1). After assurance of good position of Leksell stereotatic frame, the patient was transferred to the 1.5-tesla MRI scanner coil (Sonata). This MRI scan was obtained in 1mm slices of T1WI and T2WI. The planning MRI coordinates were 19.2mm lateral, 0.5mm anterior to the midcommissural point and 4.3mm inferior to

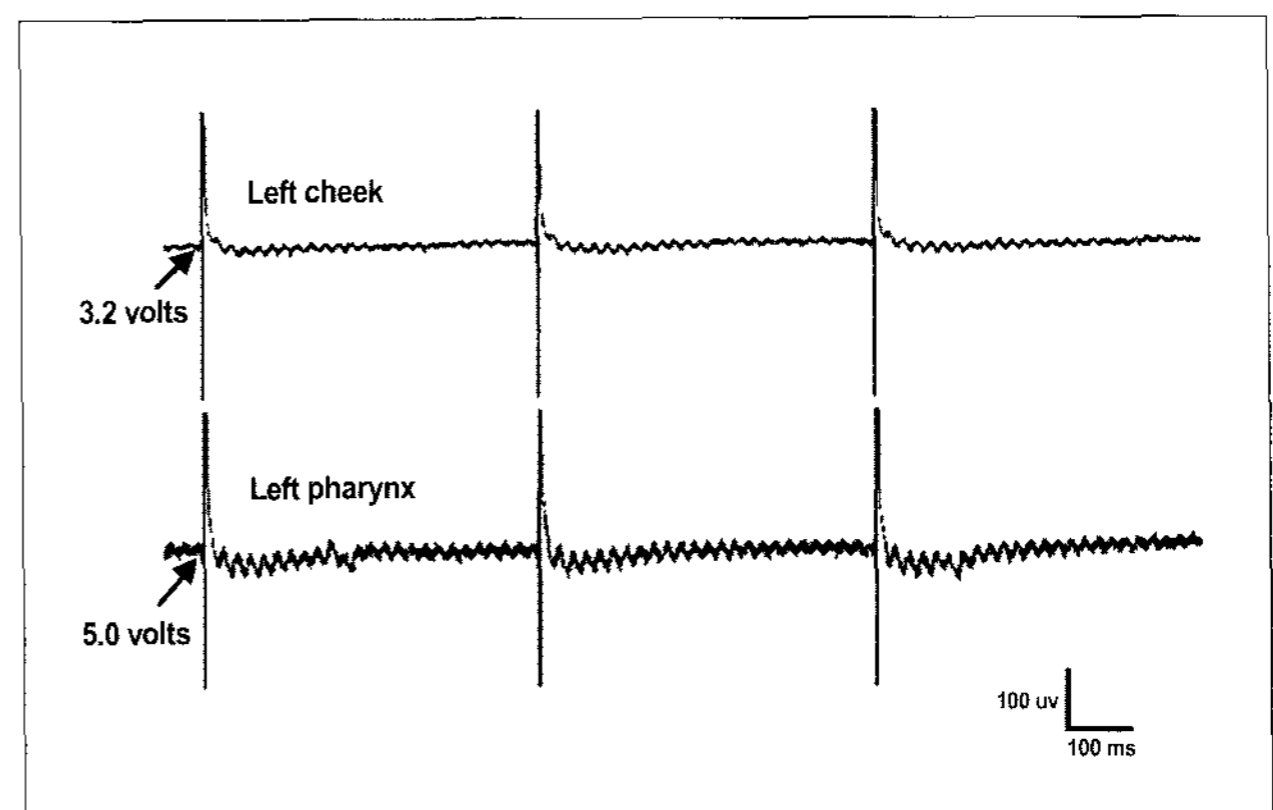


Fig. 1. Intraoperative electromyogram(EMG) shows that the threshold for initiation of any response in the EMG is 2.75 volts on left pharynx and 3.2 volts on left cheek and showing more prominent potential change around 5 volts. Visualization of contractions in the face was possible only with 7.5volts.

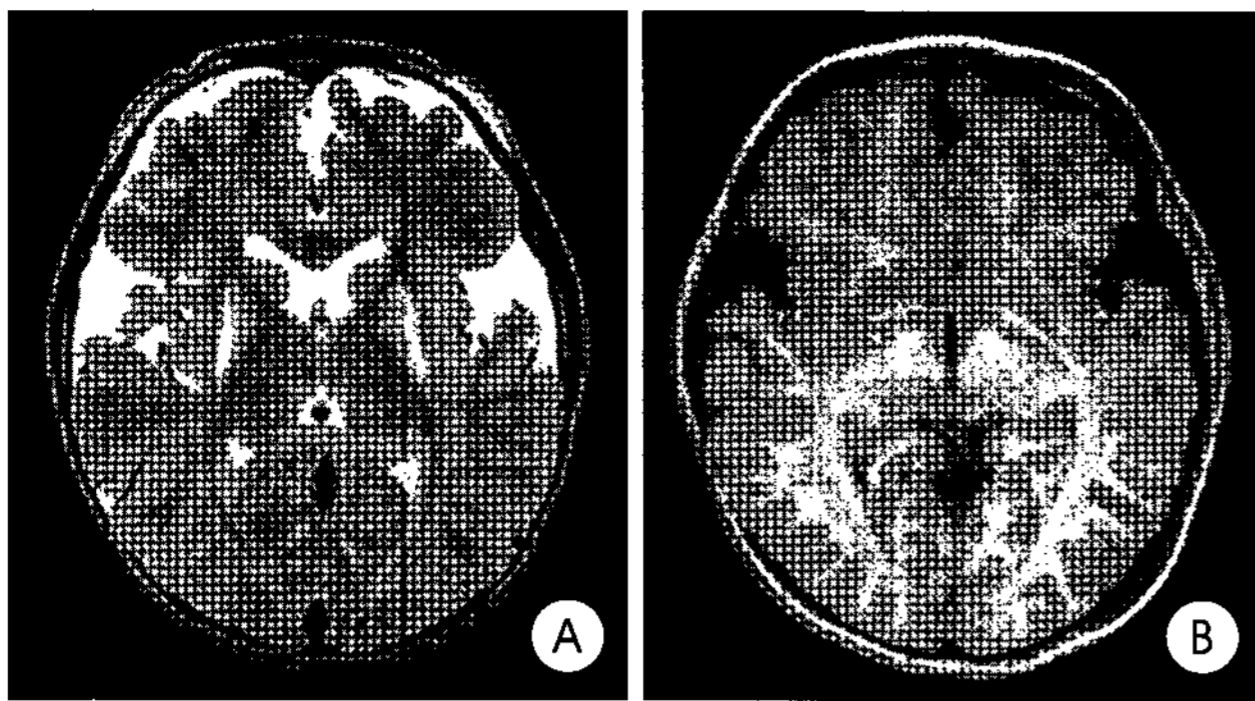


Fig. 2. A : Bilateral putamens are observed hyperintense and atrophic on magnetic resonance MR image T2WI, B : Bilateral pallidotomy are demonstrated on T1W MR image.

the AC-PC plane. The Leksell arc angle was 82.5° and the ring angle was 58.2° . The radiofrequency electrode with 2mm exposed 1.8mm diameter was used. Once all impedances were recorded and matched with CSF, cortex, white mater, and the gray mater of the pallidum, and then electrical stimulation was started after we had placed EMG electrodes in the cricopharyngeal and circumoralis muscle. The recordings were defined to show thresholds for electrical stimulation with 2Hz and 1.00msec. The threshold for initiation of any response in the EMG was 2.75volts. Visualization of contractions in the face was possible only with 7.5volts. We suspect whether the tip of electrode locates in the internal capsule or Gpi, how much close to internal capsule by subthreshold facial and cricopharyngeal contraction with each voltage levels. Actually, even though EMG changed below 3volts, we could make lesions because the muscles contracted around 7.5volts on monopolar stimulation. We performed 3 lesions each of 75 degree celcius held for 60 seconds and were 2mm apart in the track of electrode as before. On the postoperative MRI the lesion tip was measured as anterior 2.8mm to the mid commissural line, lateral 19.5mm to the AC-PC line and inferior 2.9mm on the AC-PC plane. MRI of the brain after the second surgery is shown in Fig. 2.

The patient showed immediate postoperative neurologic improvement and did not complicate the swallowing function. Six month after second surgery, marginal improvement was seen in the BFMDRS and GDS scores (BFMDRS Score : 15% and GDS Score : 20% compare to preoperative condition BFMDRS Score : 115 and GDS Score, 98). On neurologic examination, the axial symptoms including opisthotonus, jaw and cervical dystonia were markedly improved and also can lie flat on the bed with slight hypotonia of all extremities. Even though he never gained purposeful use of his hands and arms and could not sit without support nor stand on his own, his parents satisfied this improvement because the patient looked more comfortable appearance with intermittent smile expression on his face.

Discussion

This is a case of an 6-year-old boy with generalized dystonia secondary to GA 1. The patient had tried all pharmacological therapies since 6months old and continued to have significant disability due to dystonia. Bilateral pallidotomy with usage of EMG monitoring improved the dystonic symptoms without complication of swallowing function (Fig. 1). There were reports of improvement in generalized dystonia with pallidotomy but it was difficult to predict which patient improved after surgery and the degree of that improvement. Primary dystonia have much better response than secondary dystonia because the presence of basal ganglia abnormalities on the preoperative MR images is an indicator of a lesser response to pallidal interventions for dystonia^{4,7)}. But they mentioned that even patients who did not satisfy these criteria might have dramatic benefit with pallidotomy¹⁵⁾.

They described the 12year-old child with GA1 with presenting severe axial and limb dystonias with postural deformities (preoperative BFMDRS Scores, 113) had only marginal improvement, with improvement in axial dystonia and relief of the arching posture allowing him to lie flat (BFMDRS Score, 99) similar to our patient⁴⁾. According to another case report, the youngest patient who was 18-month-old and initially presented his metabolic disorder at 10months of age improved dystonic symptoms after surgery, especially pain with minor eye deviation¹¹⁾. In the literatures, the complication rate among dystonic patients was also low and this included lethargy and mild unilateral weakness in their series of 12patients¹⁵⁾, 2 of 15patients who were not diagnosed GA1 and both treated with bilateral pallidotomy developed persistent speech impairment : hypophonia (n=1) or dysphonia (n=1)⁴⁾.

EMG recording has potential for use in modern stereotatic surgery for movement disorder. And facilitation of corticospinal tract function was identified¹⁾. Motor responses evoked by capsular stimulation may be obscured by tremor until the stimulation current and the reponse reach higher amplitude. EMG recordings enable more sensitive and reliable detection of motor reponses prior to visualization of gross movement. Three instances of minimal postoperative facial paresis were noted after the patients had left the operating room and may have been related to perilesional edema.

These patients did not display particularly low stimulation threshold, and the EMG results did not predict these neurologic findings⁵⁾. We could identify the changes of intraoperative cricopharyngeal muscle on EMG before gross muscle contraction with higher voltage, which might be helpful to make safe lesions in case of bilateral pallidotomy combined with previous gastrostomy due to swallowing difficulty.

Conclusion

Bilateral pallidotomy is some effective to control dystonia with glutaric aciduria and intraoperative EMG monitoring is also helpful to determine lesions without postoperative swallowing difficulty.

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