Turkish Neurosurgery 2008, Vol: 18, No: 2, 172-176

Macrocephaly and Bitemporal Arachnoid Cysts not Associated with Glutaric Aciduria Type I in a Child

Bir Çocukta Glutarik Asidüri Tip 1 ile İlişkisiz Makrosefali ve Bitemporal Araknoid Kist

Yurdal SERARSLAN[1]
İsmet Murat MELEK[2]
Özlem SANGÜN[3]
Bülent AKÇORA[4]
Gökhan AKDEMİR[5]

[1,5] Mustafa Kemal University, Tayfur Ata Sökmen Medical School, Department of Neurosurgery, Hatay/Turkey
[2] Mustafa Kemal University, Tayfur Ata Sökmen Medical School, Department of Neurology, Hatay/Turkey
[3] Mustafa Kemal University, Tayfur Ata Sökmen Medical School, Department of Pediatrics, Hatay/Turkey
[4] Mustafa Kemal University, Tayfur Ata Sökmen Medical School, Department of Pediatric Surgery, Hatay/Turkey

ABSTRACT

A 45-month-old child who had bitemporal arachnoid cysts and macrocephaly unrelated to glutaric aciduria type 1 (GA 1) was reported. The patient was admitted to the emergency unit after head trauma at 11 months of age. CT and MRI showed bitemporal arachnoid cysts (BACs). Acylcarnitine profile was normal in serum using tandem mass spectrometry. Urine and blood screening tests were within normal range for metabolic disorders. There were no unusual organic acids in urine and blood samples. No additional clinical findings of metabolic disorders such as GA 1 developed during follow-up. The majority of children affected with GA 1 have macrocephaly and BACs on CT or MRI. These signs should alert neurosurgeons to the possibility of GA 1. Neurosurgeons evaluating patients with head trauma or suspected non-accidental head injury should include GA 1 in the differential diagnosis of BACs associated with macrocephaly, and an evaluation should be performed.

KEY WORDS: Arachnoid cyst, Bitemporal arachnoid cysts, GA 1, Glutaric aciduria type 1, Head trauma, Macrocephaly, Metabolic disorder

ÖZ

Glutarik asidüri tip 1 (GA 1) ile ilişkisiz, bitemporal araknod kist (BAK) ve makrosefalli, kırkbeş aylık bir erkek çocuk sunuldu. Hasta, 11 aylık iken, kafa travması sonrası acil serviste muayene edildi. Beyin BT ve MRG'de BAK saptandı. Tandem mass spektrometri ile ölçülen serum açilkarnitin profili normaldi. Metabolik hastalıklar için yapılan idrar ve kan tarama testleri normal sınırlar içerisindeydi. İdrar ve kanda anormal organik aside rastlanmadı. Takiplerde, GA 1 gibi metabolik bozukluklara ait ilave klinik bulgu gelişmedi. GA 1'e sahip çocukların büyük çoğunluğunda, makrosefali ve BT veya MRG'de BAK vardır. Bu bulgular, nöroşirürjiyeni GA 1 olasılığı konusunda uyarmalıdır. Nöroşirürjiyenler, kafa travmalı veya kaza dışı şüpheli kafa travmalı hastaları değerlendirirken, makrosefali ile ilişkili BAK'ın ayırıcı tanısı GA 1'i içermelidir. Bu yönde bir araştırma yapılmalıdır.

Received: 19.02.2008
Accepted: 21.04.2008

Correspondence address:
Yurdal SERARSLAN
Altınçay Mah. Mehmet Kafadar Cad.
128 Sk. TOKI Konutları, A Adası,
DGA-1 Blk. Kat:3, Daire:8,
31020 Antakya, Hatay, Turkey.
GSM: +90 532 482 34 67
E-mail: yserarslan@yahoo.com

INTRODUCTION

Bitemporal arachnoid cysts (BACs) and macrocephaly are the most common features of infants and children with glutaric aciduria type 1 (GA 1). The diagnosis of GA 1 is based on the detection of a high concentration of glutaric acid in the urine and a low plasma carnitine level (10). Expanded newborn screening using tandem mass spectrometry for detection of glutarylcarnitine can enable presymptomatic detection and pre-emptive management of affected children (13).

GA 1 is an organic aciduria of autosomal recessive origin with an estimated prevalence of 1/100,000 neonates (12). There is deficiency of the mitochondrial enzyme glutaryl-CoA dehydrogenase, which is involved in the metabolism of tryptophan, lysine, and hydroxylysine. GA 1 is diagnosed by demonstration of pathologically high levels of glutaric acid in the urine of the patient. Clinically, the disease course is usually determined by acute encephalopathic crises precipitated by infectious diseases, immunizations, and surgery during infancy or childhood (11). The clinical picture typically shows varying degrees of muscular hypotonia, motor delay, dystonia, dysarthria and dyskinesia beginning acutely or gradually in the first few years of life in often macrocephalic children (6,22). Micrencephalic macrocephaly (the reduced amount of brain tissue within an enlarged head) at birth is the earliest sign and an enlarged head circumference is the only presenting sign of GA 1 in the majority of neonates (23).

Cerebral MRI demonstrates hyperintensity on T2-weighted images in the basal ganglia. The putamen is most commonly involved, followed in incidence by the caudate nucleus and globus pallidus. The basal ganglia atrophy and sulci enlarge with progression (22). Myelination is delayed (2). Large frontotemporal cerebrospinal fluid (CSF) spaces and bilateral temporal arachnoid cysts are found (3). Enlargement of the Sylvian fissure is considered to correlate with the severity of the enzyme deficiency (6,15). The major and typical neuroradiological features are temporal hypoplasia with bilateral temporopolar arachnoid cysts (15,20,23). However, enlarged head and bitemporal arachnoid cysts may occur unrelated to GA 1.

A general anaesthesiological procedure usually triggers severe catabolic state in children with GA 1, and thus causes a dramatic worsening of the patient's neurological condition. Children with bitemporal cysts and macrocephaly should be screened for GA 1 before any surgical procedure as bitemporal cysts and macrocephaly are the major signs of GA 1 (8,14).

CASE REPORT

An 11-month-old male child was admitted after head trauma to the emergency department of the hospital. He was the second and youngest child of phenotypically normal parents and had one healthy sister. He was born at term gestational age after an uncomplicated pregnancy. On examination, macrocephaly and cephal hematoma were noted (head circumference: 48 cm, >95 percentile). There were no focal central nervous system signs. CT revealed enlarged Sylvian fissures and BACs (Figure 1). GA 1 was suspected based on the clinical and neuroradiological findings. After the management of head trauma, the patient was referred to the Department of Pediatrics to investigate metabolic disorders. Acylcarnitine profile was normal in serum using tandem mass spectrometry (MS/MS). Urine and blood screening tests were within normal range for metabolic disorders. There were no unusual organic acids in urine and blood samples. Repeated urinary and blood organic acids and acylcarnitine profile analyses were normal. All laboratory tests

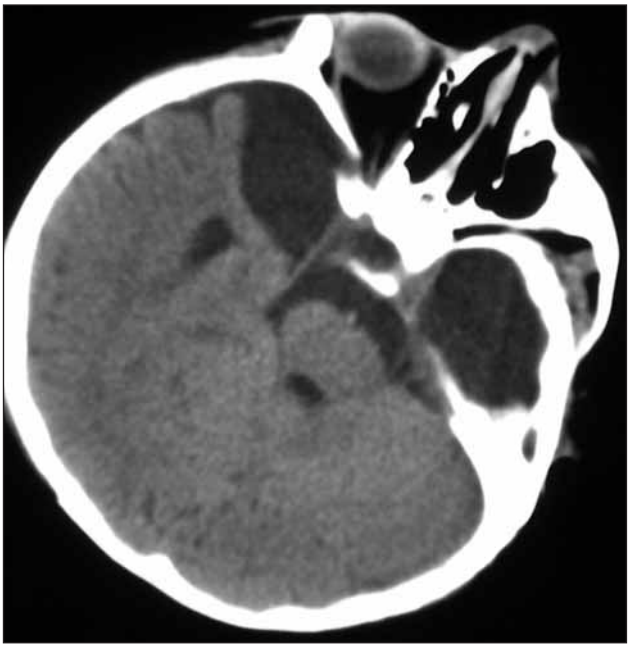
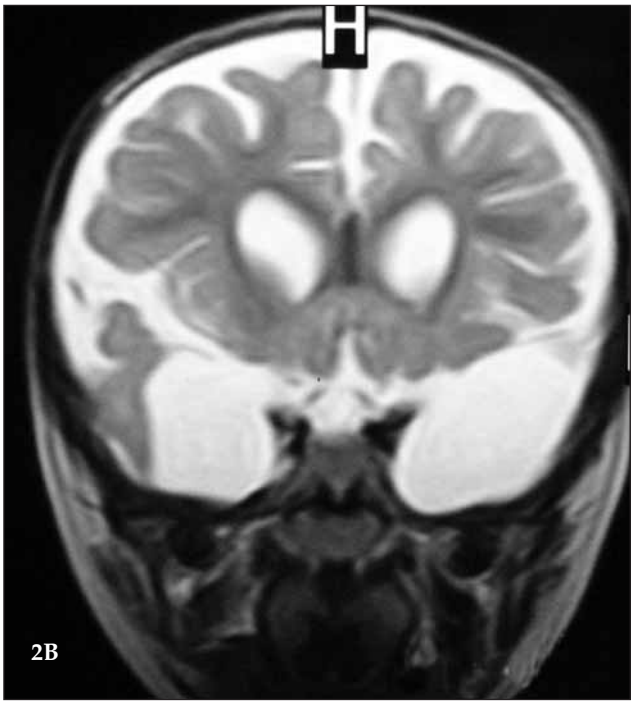


Figure 1: *Axial CT showing bitemporal arachnoid cysts.*

also were within normal range. At 24 months of age, the head circumference was over 97 percentile. The Denver II test demonstrated that the child's development was within normal range. Repeated screening tests for metabolic disorders (MD) were normal. MRI revealed no additional features (Figure 2 A and B). There were no new clinical signs or symptoms regarding MD such as GA 1 during 32-month follow-up. The patient had one episode of acute gastroenteritis and several episodes of upper respiratory tract infections in this period. Routine childhood immunizations were performed according to the schedule of national immunization programme. No signs of metabolic decompensation, unexplained clinical worsening or encephalopathy were observed during this period.

DISCUSSION

Arachnoid cysts are congenital collections of CSF contained within the arachnoidal membrane and subarachnoid space of the cisterns and major cerebral fissures (19). Overall, arachnoid cysts account for approximately 1% of all intracranial mass lesions (1). Most cysts are incidentally diagnosed during neuroimaging after head trauma (18). Bitemporal cysts occur in 5.4% of all the arachnoid cyst patients. Bilateral temporal arachnoid cysts are common in patients with GAT 1 (7,14). In our patient, serum amino acids and acylcarnitines were analyzed by tandem mass spectrometry, and reported as normal. Organic acid screening in urine was reported within the normal range.



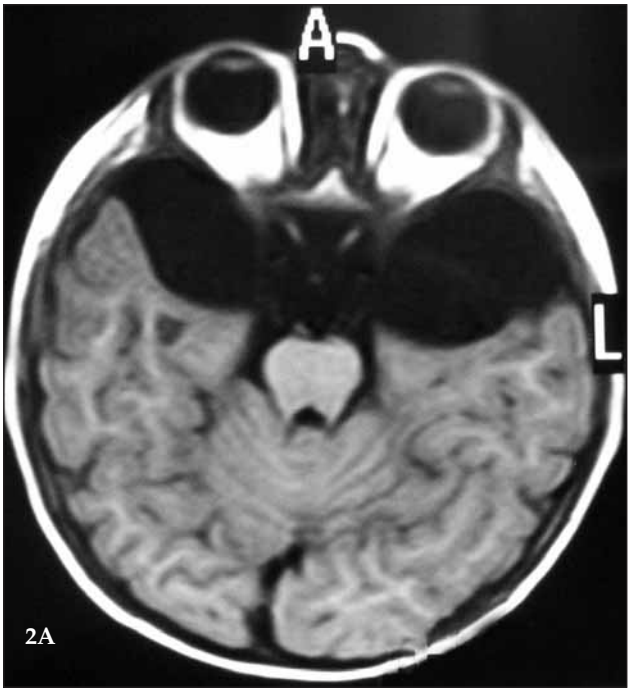


Figure 2: *Axial T1-weighted (**A**) and coronal (**B**) T2-weighted MRI demonstrating bilateral arachnoid cysts.*

Mild to moderate metabolic acidosis and ketosis may occur during acute episodes such as infections or immunizations. Hypoglycemia, hyperammonnemia, and elevation of serum transaminases have been seen in some patients. Laboratory findings may be unremarkable between attacks (21). The biochemical analyses were repeated in this patient during the acute episodes of gastroenteritis and upper respiratory tract infections and also between the attacks. However, they showed unremarkable plasma amino acid and acylcarnitine levels, urinary organic acids and acylcarnitine profile.

Early diagnosis of GA 1 is necessary for a positive outcome. No specific or even pathognomonic clinical sign or symptom that helps to identify patients before the onset of neurological disease exists. The most common presenting symptom of GA 1 is macrocephaly that occurs within the first 6 months of life. Macrocephaly is found in 75–80% of patients and is most pronounced during infancy, but is a nonspecific sign (9,13). BACs are common in patients

with GA 1, but they are nonspecific as well (3,6,10). According to the literature, the most characteristic neuroimaging feature of GA I is the symmetric widening of the Sylvian fissure with poor operculization. This finding is found in approximately 93-95% of all patients (4,5,9,17,23,24) and is usually referred to as widened Sylvian fissures or less commonly as 'bat wings appearance'. The widened Sylvian fissures are accompanied by an expansion of external CSF spaces anterior to the temporal lobes on MRI. The finding of very widely open opercula suggests GA 1, and if combined with abnormalities of the basal ganglia and white matter is almost pathognomonic, especially in a child with macrocephaly (5,24) The finding of bilateral enlarged Sylvian fissures or BACs on CT or MRI examination should alert surgeons and clinicians to the possibility of GAT 1. Our patient had neuroimaging hallmarks of GA 1 including BACs with macrocephaly but neuroradiological tools revealed no other GA 1 findings on CT or MRI.

Hald et al. (7) demonstrated that four out of five GA 1 patients had BACs, and therefore suggested that patients with bitemporal cysts should be investigated for this metabolic disorder. Jamjoom et al. (10) reported that surgically confirmed bilateral arachnoid cysts of the Sylvian region in female siblings with GA 1. This was the first report to provide clear radiological and surgical evidence of the association between GA 1 and bilateral arachnoid cysts of the Sylvian region. Lütcherath et al. (14) reported that seven GA 1 patients had BACs. All the patients were operated on to obtain a decompression of the cysts. They verified that these lesions are true cysts and not a passive accumulation of fluid due to atrophy of the temporal lobes. Two of these patients have no pre-operative metabolic evaluations, and surgery deteriorated the clinical condition in both infants. The authors recommended that even simple surgical approach may be extremely hazardous procedure in this disorder, and all pediatric patients with BACs should be screened for GA 1.

BACs are rare disorders and case reports are mainly in children with GA 1. BACs not associated with other systemic or genetic disorders are extremely rare. Clinicians should be aware that a patient with bitemporal arachnoid cysts and macrocephaly may have GA 1, and the risks of encephalopathic crises and metabolic decompensation may be present in these patients during anesthesia. The surgical and postsurgical periods should not be ignored for his aspect (16). It is also reported that GA 1 may present as bilateral subdural hematomas mimicking nonaccidental trauma (4,9). However, BACs and macrocephaly may occur unrelated to GA 1. Neurosurgeons and others medical care providers evaluating patients with head trauma or suspected non-accidental head injury should include GA 1 in the differential diagnosis of BACs associated with macrocephaly.

CONCLUSION

It is important to remember that children with macrocephaly and BACs may have GA 1. A surgeon should know that operative intervention may induce severe a catabolic state in patients with GA 1, and will almost inevitably cause a devastating neurological worsening. GA 1 should be considered in the differential diagnosis of macrocephaly and BACs. Patients with bitemporal cysts and macrocephaly should be screened for GA 1. However, enlarged head and bitemporal arachnoid cysts may also occur unrelated to GA 1.

REFERENCES

1. Albuquerque FC, Giannotta SL: Arachnoid cyst rupture producing subdural hygroma and intracranial hypertension: case reports. Neurosurgery 41: 951–956, 1997
2. Altman NR, Rovira MJ, Bauer M: Glutaric aciduria type I: MR findings in two cases. Am J Neuroradiol 12: 966–968, 1991
3. Barkovich AJ: Pediatric Neuroimaging. Philadelphia: Lippincott Williams & Wilkins, 2000
4. Bishop FS, Liu JK, McCall TD, Brockmeyer DL: Glutaric aciduria type 1 presenting as bilateral subdural hematomas mimicking nonaccidental trauma. Case report and review of the literature. J Neurosurg (Pediatrics) 106: 222-226, 2007
5. Brismar J, Ozand PT: CT and MR of the brain in glutaric acidemia type I: a review of 59 published cases and a report of 5 new patients. AJNR 16: 675-683, 1995
6. Faerber EN, Poussaint TY: Magnetic resonance of metabolic and degenerative diseases in children. Top Magn Reson Imaging 13: 3-21, 2002
7. Hald JK, Nakstad PH, Skjeldal OH, Strømme P: Bilateral arachnoid cysts of the temporal fossa in four children with glutaric aciduria type 1. AJNR 12: 407-409, 1991
8. Hoffmann GF, Zschocke J: Glutaric aciduria type I: from clinical, biochemical and molecular diversity to successful therapy. J Inherit Metab Dis 22: 381-391, 1999
9. Hou LC, Veeravagu A, Hsu AR, Enns GM, Huhn SL: Glutaric acidemia type I: a neurosurgical perspective. Report of two cases. J Neurosurg (Pediatrics) 107: 167–172, 2007

10. Jamjoom ZA, Okamoto E, Jamjoom AH, al-Hajery O, Abu-Melha A: Bilateral arachnoid cysts of the sylvian region in female siblings with glutaric aciduria type I. Report of two cases. J Neurosurg 82: 1078-1081, 1995

11. Kölker S, Christensen E, Leonard JV, Greenberg CR, Burlina AB, Burlina AP, Dixon M, Duran M, Goodman SI, Koeller DM, Müller E, Naughten ER, Neumaier-Probst E, Okun JG, Kyllerman M, Surtees RA, Wilcken B, Hoffmann GF, Burgard P: Guideline for the diagnosis and management of glutaryl-CoA dehydrogenase deficiency (glutaric aciduria type I). J Inherit Metab Dis 30: 5-22, 2007

12. Lindner M, Kolker S, Schulze A, Christensen E, Greenberg CR, Hoffman GF: Neonatal screening for glutaryl-CoA dehydrogenase deficiency. J Inherit Metab Dis 27: 851–859, 2004

13. Lindner M, Ho S, Fang-Hoffmann J, Hoffmann GF, Kölker S: Neonatal screening for glutaric aciduria type I: strategies to proceed. J Inherit Metab Dis 29: 378-382, 2006

14. Lütcherath V, Waaler PE, Jellum E, Wester K: Children with bilateral temporal arachnoid cysts may have glutaric aciduria type 1 (GAT1); operation without knowing that may be harmful. Acta Neurochir (Wien) 142: 1025-1030, 2000

15. Mandel H, Braun J, el-Peleg O, Christensen E, Berant M: Glutaric aciduria type I. Brain CT features and a diagnostic pitfall. Neuroradiology 33: 75-78, 1991

16. Martinez-Lage JF: Neurosurgical treatment for hydrocephalus, subdural hematomas, and arachnoid cysts in glutaric aciduria type 1. Neuropediatrics 27: 335–336, 1996

17. Neumaier-Probst E, Harting I, Seitz A, Ding C, Kolker S: Neuroradiological findings in glutaric aciduria type I (glutaryl-CoA dehydrogenase deficiency). J Inherit Metab Dis 27: 869-876, 2004

18. Pradilla G, Jallo G: Arachnoid cysts: case series and review of the literature. Neurosurg Focus 15: 22(2): E7, 2007

19. Rengachary SS, Watanabe I: Ultrastructure and pathogenesis of intracranial arachnoid cysts. J Neuropathol Exp Neurol 40: 61–83, 1981

20. Renner C, Razeghi S, Uberall MA, Hartmann P, Lehnert W: Clinically asymptomatic glutaric aciduria type I in a 4 5/12-year-old girl with bilateral temporal arachnoid cysts. J Inherit Metab Dis 20: 840-841, 1997

21. Rezvani I: Defects in metabolism of aminoacids. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics 17th edition. Philedelphia: Saunders, 2004: 398-432

22. Ruggieri PM: Metabolic and neurodegenerative disorders and disorders with abnormal myelination. In: Ball WS Jr, ed. Pediatric Neuroradiology. Lippincott-Raven Philadelphia, 1997: 175–237

23. Strauss KA, Puffenberger EG, Robinson DL, Morton DH: Type I glutaric aciduria, part 1: natural history of 77 patients. Am J Med Genet C Semin Med Genet 121: 38-52, 2003

24. Twomey EL, Naughten ER, Donoghue VB, Ryan S: Neuroimaging findings in glutaric aciduria type 1. Pediatr Radiol 33: 823-830, 2003