Acquired Chiari I Malformation Secondary to Spontaneous Intracranial Hypotension Syndrome and Persistent Hypoglycemia: A Case Report

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Abstract
Spontaneous intracranial hypotension (SIH) is a rare and potentially serious condition in childhood. Cerebrospinal fluid (CSF) volume depletion is thought to be the main causative feature for intracranial hypotension, results from spontaneous CSF leak, often at the spine level. SIH is increasingly diagnosed in clinical practice, although it manifests into a variegated symptomatology. Indeed, downward displacement of the brain, sometimes mimicking a Chiari I malformation, but concomitant presentation of these syndromes has rarely been reported.
We present herein a case of a SIH with Chiari 1 malformation accompanied with an unusual clinical presentation of persistent hypoglycemia.

Key words: Intracranial hypotension, hypoglycemia, vagotomy

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What is already known on this topic?
Spontaneous intracranial hypotension (SIH) is a rare and potentially serious pathological syndrome in childhood. Concomitant presentation of Chiari I malformation with SIH has rarely been reported. Diagnostic criteria are more broadened spectrum due to variable manifestations. Myelography computerized tomography and epidural blood patch are reliable diagnostic and treatment modalities.

What this study adds?
Chiari I malformation may mimic SIH and ideal therapy requires recognition of SIH. Persistent hypoglycemia was an early central feature of our patient; indeed this symptom is far from rare in SIH. We discussed here some possible causes of hypoglycemia in SIH and vagotomy as a new treatment modality.

Introduction

Spontaneous intracranial hypotension (SIH) is a rare condition with estimated prevalence is only one in 50,000 individuals. The clinical spectrum of SIH is quite variable and includes headache, neck stiffness, cranial nerve dysfunction, radicular arm pain, and symptoms of diencephalic or hindbrain herniation (1,2). Intracranial hypotension is a well-recognized sequel of a spontaneous cerebrospinal fluid (CSF) leak, particularly in cases in which the leak involves the thoracic spine (3). The cause for these CSF leaks remains unclear, but authors have postulated minor trauma, weakness of the dural sac or a combination of both (4,5). More cases are getting diagnosed with the advances in the imaging, but the diagnosis is still challenging because of the number of atypical, unconfirmed, and doubtful cases. Actually the existing diagnostic criteria are more broadened spectrum due to variable manifestations, the diagnosis of SIH mainly include orthostatic headache with the presence of at least one of the following; low CSF pressure, sustained improvement of symptoms after epidural blood patching, demonstration of an active spinal cerebrospinal fluid leak and cranial magnetic resonance imaging (MRI) changes of intracranial hypotension (6). Myelography computerized tomography is the most reliable method for

the accurate localization of the CSF leak. (7). In most cases, epidural blood patch is the main treatment modality (8).

Chiari I malformation is defined radiographically as a simple displacement of the cerebellar tonsils 5 mm or greater below the foramen magnum and is distinguished from Chiari II and Chiari III malformations occurring with myelodysplasia and cervical encephalocele respectively (9). Spontaneous CSF leakage with development of SIH and acquired Chiari I malformation due to lumbar spinal CSF diversion procedures have both been well described. However, concomitant presentation of both syndromes has rarely been reported. Not to be confused with idiopathic Chiari I malformation, ideal therapy requires recognition of the syndrome and treatment directed to the site of the spinal CSF leak (10).

This article reports on a 13 year-old girl with acquired Chiari I malformation secondary to SIH with a unique coexistence of persistent hypoglycemia.

Case

A 13-year-old girl was admitted to Kanuni Sultan Suleyman Research and Training Hospital suffering from hypoglycemia, syncope and convulsive seizures. She had no notable health problem in her past medical history by 11.5 years of age. Thereafter, she had six subsequent hospital admissions in previous 1.5 years, mostly at emergency services for hypoglycemic convulsions and syncope attacks. She was born at term, weighing 3100 gr from non-consanguineous parents after an uncomplicated delivery. In evaluation of her records, we found that she had hypoglycemic periods 2-3 times per day, but syncope attacks were independent from hypoglycemia. She was diagnosed with hyperinsulinemia with serum glucose level of 29 mg/dl with matching serum insulin of 25 IU/L. Positron emission tomography and abdominal ultrasonography were performed for the etiology of hyperinsulinemia, but revealed normal anatomic findings. Electroencephalography showed bilateral delta waves with spikes at neurological counseling and cranial MRI revealed a 7 mm herniation of the cerebellar tonsils from the foramen magnum (Fig 1). Further work-up with brainstem auditory evoked potentials and somatosensory evoked potentials, cardiac evaluation with echocardiography and holter monitoring were normal. Hypoglycemia episodes were resolved in the following weeks, but although reduced in number, syncope persisted. Therefore, pediatric psychiatry counseling was performed with normal psychiatric examination at her previous discharge. At 13 years old, she was admitted to our pediatric emergency service with hypoglycemic convulsion. Her body weight was 55 kg (90 percentile) and height was 145 cm (25 percentile). Laboratory investigations figured out hypoglycemia (serum glucose level: 30 mg/dl) with high insulin level (serum insulin level: 50 IU/L), serum C-peptide of 5 pmol/ml (N: 0,15-1,30 pmol/ml), cortisol of 23µg/dL (N: 6,2-19,4µg/dL). After intravenous glucose, intramuscular glucagon and methylprednisolone treatment, glucagon infusion was initiated; glucose levels were 40 to 65 mg/dl during 24 hour, but surprisingly, glucose levels of 80-90 mg/dl were detected after stopping infusion. Hypoglycemia was not recorded in fasting glucose level for 24 hours. Oral glucose tolerance test (OGTT) showed us hypoglycemia at 30 th minute (glucose: 25 mg/dl) with insulin level of 300 IU/L. We monitored our patient's daily glucose levels by continuous glucose monitoring system [CGMS System Gold® (Medtronic Minimed, Northridge, CA)]; 14 hypoglycemia episodes were noted mostly occurring at sleep or during toilet and postprandial period with the maximum glucose level of 70 mg/dl in three days of follow-up. We measured glucose levels before and after defecation; results were 85 mg/dl and 29 mg/dl respectively. Any adrenergic symptoms were not observed during hypoglycemic episodes. Treatment of diazoxide (40 mg/kg) and octreotide (40 µg/kg) had no medical efficiency and disartria was recognized at the first month of hospitalization with frequent hypoglycemia episodes. During this period, syncope attacks were observed 4 times, but independent from hypoglycemia. Additionally, she had severe biparietal headache not related to hypoglycemia in the morning lasting for two hours, and then anisocoria was observed. Myelography was performed for SIH and verified with 2 CSF leaks originating at lumbar 2 levels. She had a procedure of autologous epidural blood patch at the CSF-leak site (Fig 2). This gave good clinical results including complete control of her episodes of syncope, headache and hypoglycemia. Thereafter, hypoglycemia repeated with disartria after two months of healthy period; we figured out displacement of the cerebellar tonsils, due to an epidural patch failure. Although the patient remains in good clinical condition after two subsequent epidural patch surgery, neurologic problems and hypoglycemia repeated with failure of the procedures. Truncal vagotomy and partial pancreatectomy were planned for persistent hypoglycemia, because glucose levels were continuously under 29 mg/dl. Surgery was started with serum glucose of 25 mg/dl with 0.9% sodium chloride. Glucose level spontaneously normalized and was about 100 mg/dl during anesthesia. Truncal vagotomy was performed firstly and due to test the efficiency of vagotomy, dextrose 10% solution infusion was initiated instead of 0.9% sodium chloride, and serum glucose level increased to 180 mg/dl. Distal partial pancreatectomy performed additionally, due to not to take secondary surgery risk. Post operative diabetes mellitus presented. An informed consent was taken from the parents. She was discharged with single-dose insulin glargine treatment and her follow-up has been successful for 4 years.

Discussion

In clinical practice, SIH may be manifested as a loss of the prepontine cistern due to leak of CSF, with flattening of the brainstem and downward herniation of the cerebellar tonsils, which may mistakenly lead to a diagnosis of

Chiari I malformation (10,11). Our case was diagnosed initially Chiari I malformation, but thereafter it was noticed to be resulting of SIH with evaluation of symptoms and laboratory investigations.

The diagnosis of SIH is initially suspected on the basis of presenting signs and symptoms as headache, syncope and some neurological problems as in the patient reported here. However, in our patient, hypoglycemia was the leading clinical feature and this symptom is far from rare in SIH patients. Indeed, hyperinsulinism is seems to be responsible for the cause of hypoglycemia. Rekate et al (12) reported four cases diagnosed with Chiari malformation were suffering from intermittent hyperinsulinemic hypoglycemia and proposed that vagal hypertonia caused by variations in intracranial pressure affected the pancreas leading to hypoglycemia in their patients. Tarani et al (13) proposed that the brainstem compression due to hindbrain herniation leads to dysfunction of the normal homeostatic mechanisms to correct the hypoglycemia and direct stimulation of the vagal nuclei stimulates pancreatic islet cells to secrete insulin. Actually, hypoglycemia mostly occurred with parasympathetic activities such as postprandial, defecation or asleep in our clinical observation. Moreover, adrenergic activities had never been observed even with severe hypoglycemic episodes, so this condition may be resembled to autonomic failure related to parasympathetic dominancy due to vagal stimulus. Actually, vagal efferent activity starts with stimulus on oropharyngeal receptors by oral intake and increases gastrointestinal peristaltic activity and then leads to insulin release, inhibition of norepinephrine from splanchnic nerves, gluconeogenesis and activation of glycogen synthesis (14). Vagal stimulus also produces early phase of insulin response with postprandial insulin release (15,16). Hypoglycemia at 30 th minute with high insulin level in OGTT has a worthy of interest for vagal effect. Moreover, we thought that syncope in our patient may be related to this unbalanced reflexes of sympathetic system (17).

Spontaneous intracranial hypotension in childhood is rare (18). Orthostatic head ache in the morning directed us for a diagnosis of SIH and myelogram showed us two dural puncture at lumbar region (Fig 2). We observed patch procedure efficiency on hypoglycemia and other symptoms with resolving caudal displacement of cerebellar tonsil. Actually, Rekate et al (12) used continuous-drip feeding for hypoglycemia in their cases with Arnold Chiari syndrome. Unfortunately, persistent hypoglycemia presented concomitant to an epidural patch procedure failures in our patient. Truncal vagotomy and partial pancreatectomy were planned for persistent hypoglycemia as a radical therapy for our patient in concordance with our estimation of parasympathetic dominancy. Surgery was stated with glucose level of 25 mg/dl, and surprisingly serum glucose level normalized with anesthesia induction; the outcome may be related to anesthesia due to possible changes in sympathetic-parasympathetic balance during anesthetic administration (19). Additionally, glucose response after vagotomy procedure during surgery verified the role of vagal effect on hypoglycemia with increased glucose level with glucose infusion. Diabetes mellitus presented after the surgery due to partial pancreatectomy and our patient continues to take single-dose glargine insulin treatment.

Intracranial hypotension syndrome may result into a variegated symptomatology in clinical practice, one of which could be persistent hypoglycemia. The authors' experience is reported here, along with some pathophysiological considerations, diagnostic processes and a possible treatment modality for persistent hypoglycemia in SIH.

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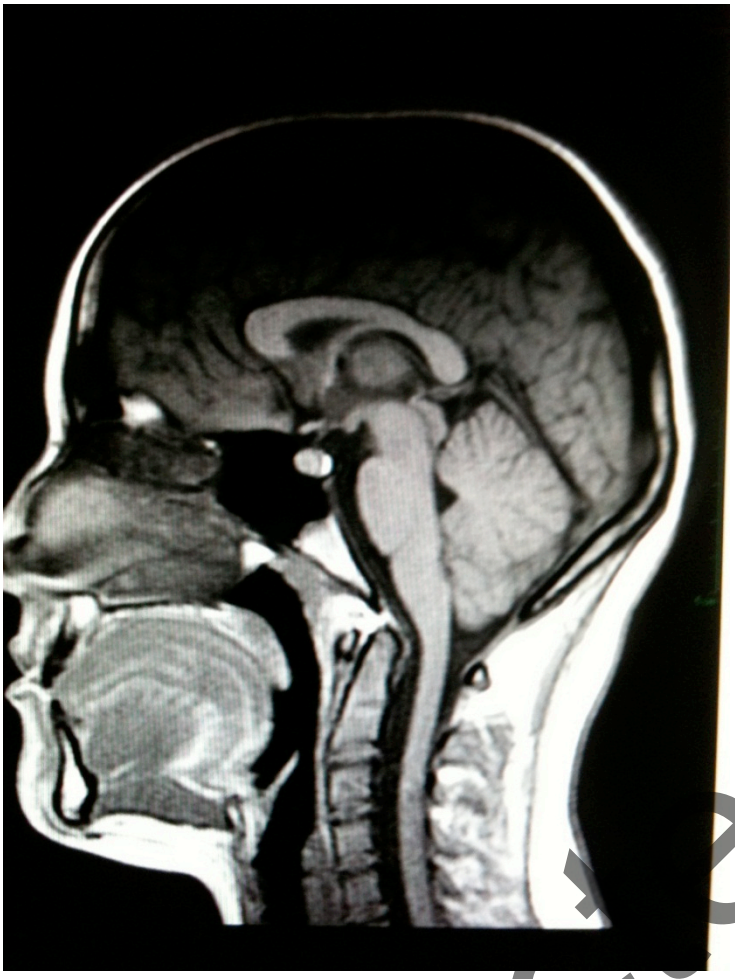

Figure 1. A simple displacement of the cerebellar tonsils 7 mm below the foramen magnum compatible with Chiari I malformation

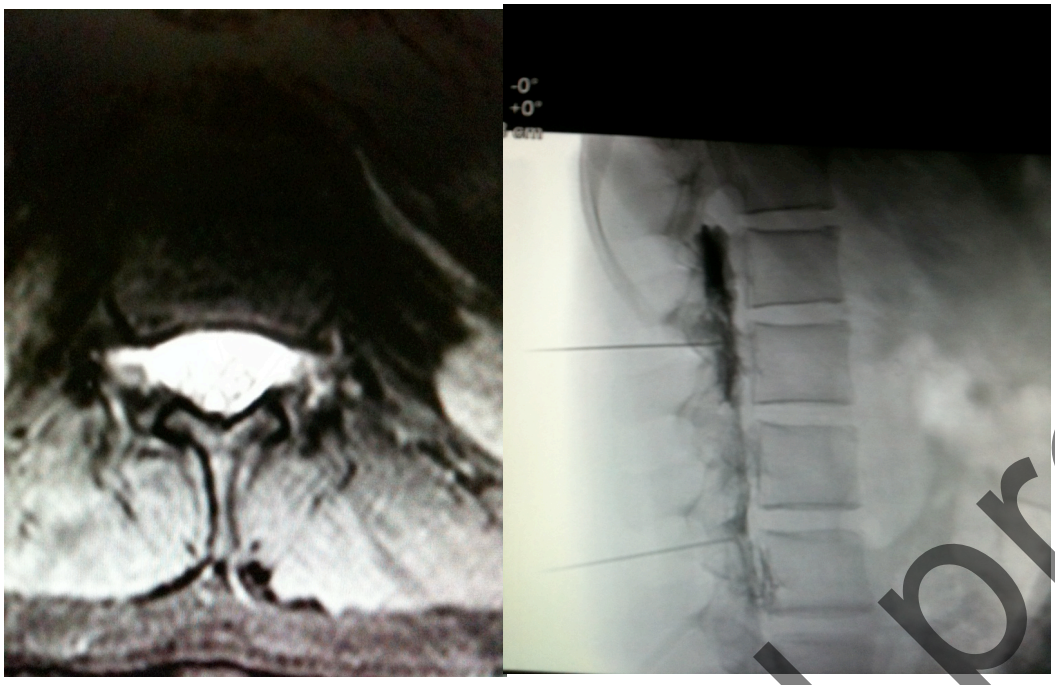

Figure 2. Two cerebrospinal fluid leak at the lumbar 2 level and the procedure of autologous epidural blood patch