7. Edge SB, Compton CC. American Joint Committee on Cancer Staging Manual. 7th ed New York: Springer; 2010.
8. Market Velker BA, Louie AV, Verlker VM, Kwan KF, Franklin JH, Venkatesan VM. Adenocarcinoma not otherwise specified on dorsum of tongue: case report and literature review. Curr Oncol. 2012;19:358–63.

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Hyperammonemic encephalopathy after urinary diversion. Diet therapy☆

Encefalopatía hiperamoniémica tras cistectomía radical y derivación urinaria. Tratamiento nutricional

Radical cystectomy is the standard treatment for infiltrating bladder cancer. This surgery is associated with a high morbidity due to structure resection and to metabolic complications derived from urinary diversion, such as hyperammonemic encephalopathy, an uncommon complication that may occur several years after the surgical procedure.[1]

The case of a 78-year-old female patient with an unremarkable personal and family history diagnosed 5 years earlier with grade III, stage B bladder carcinoma treated with cystectomy, hysterectomy, double adnexectomy, and ureterosigmoidostomy is reported.

Four years after surgery, she was admitted to another hospital for episodes of disconnection from the environment, sucking movements, myoclonic twitching in the head and right limbs, episodes of amnesia, and postictal confusion. Magnetic resonance imaging showed normal results, and an electroencephalogram showed marked bilateral frontotemporal activity. Idiopathic epilepsy was diagnosed, and antiepileptic treatment was started (levetiracetam 500 mg/12 h).

Three months later she was admitted again to the same hospital with fever, and hyperchloremic metabolic acidosis was found. Because of prior urinary diversion, ammonia levels in blood were tested and were found to be 200 μg/dL (normal range, 17–80 μg/dL). The patient had no symptoms of chronic hyperammonemia during the intercritical period.

Tests for autoimmunity, hormones (TSH 2.36 μU/mL [0.27–4.2] and free thyroxine 1.05 ng/dL [0.93–1.7]), and tumor markers, viral serologic testing, and abdominal ultrasonography were performed to rule out a hepatic origin of hyperammonemia with normal results.

Based on a diagnosis of encephalopathy with a non-convulsive status of complex partial seizures of toxic-metabolic origin and hyperchloremic metabolic acidosis secondary to ureterointestinal diversion, the patient was managed with a low-protein diet, hydration with 2 L/day, oral bicarbonate 500 mg/8 h, lactulose 10 g/8 h, and levetiracetam 500 mg/12 h, and was referred to the nutrition unit of our hospital for an adjustment of nutritional therapy.

The patient reported a weight loss of 8% since surgery. She weighed 55 kg and had a body mass index of 27 kg/m^2, a tricipital skinfold of 18 mm, arm circumference of 25 cm, arm muscle circumference of 19.35 cm, and grade B overall subjective assessment. Blood pressure values were 120/80 mmHg, the physical examination was normal, and there was no ankle edema.

After work-up, a total restriction of proteins of animal origin and a supplementation of proteins of vegetable origin were recommended.

An evaluation of dietary intake by means of a dietetic diary on three non-consecutive days was requested. At the control visit, a daily intake of 40 g of protein and 1300 kcal was seen.

Table 1 shows blood test results at diagnosis, after the first visit to the nutrition clinic, and after 1 and 4 years.

The elimination of proteins of animal origin was again emphasized, except for the occasional egg to supplement proteins of vegetable origin, and an individualized nutritional regimen was devised. Treatment with calcifediol 266 μg/month was started when vitamin D deficiency was detected.

After 3 months of individualized diet, the patient had not been readmitted, had maintained her weight, and had normal ammonia levels (36 μg/dL), kidney and liver function, and vitamin D levels.

Normal blood ammonia levels were found in all subsequent measurements, with no clinical or biochemical evidence of protein malnutrition.

In this patient, encephalopathy occurred because the bowel segments used for ureteral diversion retain their absorption and secretion capacity,[2] which results in increased ammonia absorption with saturation of the metabolic capacity of the liver and hyperammonemia. Sodium and bicarbonate secretion, as well as the reabsorption of hydrogen ions and chlorine by the intestinal mucosa, causes hyperchloremic metabolic acidosis.[3]

Under normal conditions, ammonia mainly comes from the bowel, where it is generated by the metabolism of nitrogenated products in the diet, the action of intestinal flora, and glutamine metabolism by intestinal glutaminase. Ammonia is absorbed from the small bowel and reaches portal circulation, finally arriving at the liver, where 90% is metabolized by the urea cycle.[4,5]

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Table 1 Blood chemistry at diagnosis, after the first visit to the nutrition clinic, and 1 and 4 years after the start of nutritional therapy.

Parameter	At diagnosis	Three months after visit to nutrition	At 1 year	At 4 years	Reference range
Glucose	95 mg/dL	83 mg/dL	81 mg/dL	86 mg/dL	64–106 mg/dL
Urea	42 mg/dL	33 mg/dL	50 mg/dL	44 mg/dL	20–50 mg/dL
Creatinine	0.87 mg/dL	0.75 mg/dL	0.61 mg/dL	0.78 mg/dL	0.51–0.95 mg/dL
Albumin	3.0 g/dL	3.3 g/dL	3–5 g/dL	3.7 g/dL	3.5–5.2 g/dL
Ammonia	200 μg/dL	36 μg/dL	63 μg/dL	51 μg/dL	17–80 μg/dL

Protein-rich diets and intestinal bacterial growth with a predominant proteolytic flora increase ammonia synthesis and availability for absorption.

In ureterointestinal diversion, ammonia absorption is promoted by the alkalinization of the bowel lumen, so that urinary ammonia is converted to its ionized form (NH_4^+), which is liposoluble and diffuses more readily through biological membranes,[5] and increased ammonia production resulting from the overgrowth of proteolytic enzymes.[6] In addition, as ammonia is absorbed by distal bowel segments draining to the inferior hemorrhoidal plexus, a direct passage into the systemic circulation with no liver metabolism occurs,[7] promoting hyperammonemic encephalopathy.

The main treatment for hyperammonemia for non-hepatic causes is ammonia reduction in the bowel lumen. Treatments proposed include decreased exogenous protein provision and the use of non-absorbable disaccharides to decrease ammonia formation by flora and to promote intestinal excretion.

As regards protein, no agreement exists regarding the restrictions required by this disease. In the case reported, a protein provision of 0.8 g/kg/day induced no clinical evidence of energy and protein malnutrition. Dietary recommendations were made to achieve maximum protein quality through the combined use of vegetable proteins, because cereals are deficient in lysine, corn is poor in tryptophan, and legumes are poor in methionine and cysteine. In addition, the fiber associated with these foods favors the growth of saccharolytic over proteolytic bacterial flora. The patient was also advised to eat eggs occasionally, as they contain protein of the highest quality. With these changes, the patient has maintained an adequate nutritional state with no reappearance of her neurological symptoms.

As regards drug treatment, non-absorbable disaccharides (such as lactulose) are metabolized by saccharolytic intestinal flora in the colon, generating short-chain fatty acids that decrease intestinal pH and, thus, ammonia absorption. Treatment with antiepileptic drugs for epileptic states secondary to toxic-metabolic causes in patients with no history of epilepsy or cerebral structural organic lesion may be gradually decreased if the patient is free from seizures after the complete correction of the underlying cause. If the recurrence of the metabolic impairment is expected, the prescribed drug may be maintained at the minimum effective dose as prevention.[8]

While uncommon, hyperammonemia for non-hepatic cause may be due to changes in the urea cycle, such as ornithine transcarbamylase (OTC) deficiency. The fact that a deficiency of this enzyme coded in chromosome x first becomes evident in adulthood is usually due to the concurrence in heterozygous subjects of triggering factors (infection, trauma, valproate administration, surgery, stress, or excess protein intake).[9] Clinical suspicion of these deficiencies if neurological symptoms (mental retardation, ataxia, irritability, aggressiveness, confusion, hallucinations) and hyperammonemia occur in the same family is important.

If the clinical signs and symptoms persist, the conversion of urinary diversion to an ileal conduit may be considered, as this has been shown to normalize ammonia levels and to eliminate symptoms in a refractory patient.[1]

Conflicts of interest

The authors state that they have no conflicts of interest.

References

1. Jäger W, Viertmann AO, Janßen C, Birklein F, Thüroff JW, Stein R. Intermittent hyperammonemic encephalopathy after ureterosigmoidostomy: spontaneous onset in the absence of hepatic failure. Cent Eur J Urol. 2015;68:121–4.
2. Pérez-Fidalgo JA, Chirivella González I, Günthner S, Cervera Miguel JI, March Villalba JA, Cervantes Ruipérez A. La encefalopatía hiperamonémica, una posible complicación por derivación urinaria tras cistectomía radical. Revisión de la literatura a proposito de un caso. Actas Urol Esp. 2007;31:394–9.
3. Mundy AR. Metabolic complications of urinary diversion. Lancet. 1999;353:1813–4.
4. García Martínez R, Córdoba Cardona J. Actualización en el tratamiento de la encefalopatía hepática. Rev Esp Enferm Dig. 2008;100:637–44.
5. Téllez Villajos L, Aicart Ramos M, Moreira Vicente V. Hiperamonemia en pacientes adultos sin cirrosis. Med Clin (Barc). 2013;141:494–500.
6. Schwarz S, Georgiadis D, Schwab S, Gehlen F, Mayatepek E, Zoubaa S. Fulminant progression of hyperammonaemic encephalopathy after treatment with valproate in a patient with ureterosigmoidostomy. J Neurol Neurosurg Psychiatry. 2002;73:90–1.
7. Aguilar Reina J. Encefalopatía hepática. Medicine. 2012;11:652–9.
8. Mercadé Cerdá JM, Sancho Rieger J, Mauri Llerda JA, López González FJ, Salas Puig X. Guías diagnósticas y terapéuticas de la Sociedad Española de Neurología 2012. 1. Guía oficial de práctica clínica en epilepsia. [Internet]. Madrid: Sociedad Española de Neurología; 2012. p. 236. Available from: http://www.sen.es/

profesional/guias-y-protocolos/9-sin-categoria/1200 [cited 21.02.16].
9. Choi DE, Lee KW, Shin YT, Na KR. Hyperammonemia in a patient with late-onset ornithine carbamoyltransferase deficiency. J Korean Med Sci. 2012;27:556–9.

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Autoimmune limbic encephalopathy in a girl with type 1 diabetes. Clinical features and outcomes☆

Encefalitis límbica autoinmune en una niña con diabetes tipo 1. Hallazgos clínicos y evolución

Type 1 diabetes mellitus is associated with other autoimmune diseases, most commonly with lymphocytic thyroiditis or celiac disease. Some cases of limbic encephalitis associated with type 1 diabetes, thyroiditis or other autoimmune conditions have been reported in the past decade, even in children.[1–5] Limbic encephalitis is an autoimmune inflammatory process involving the hippocampus and amygdala which until a few years ago was considered to be of paraneoplastic origin. Patients have in blood and/or CSF antibodies (Ab) against the neuronal surface or intracellular antigens, such as anti-GAD Ab. GAD, selectively expressed in neurons and pancreatic cells, is the enzyme that limits the synthesis rate of GABA (aminobutyric acid), the main inhibitory neurotransmitter that modulates and synchronizes neuronal activity in CNS. These Ab inhibit GAD activity, possibly mediated by cytotoxic T cells, and reduce GABA synthesis or exocytosis. They cause neuropsychiatric changes such as hallucinations, refractory temporal epilepsy, memory dysfunction and cognitive impairment, which may be reversed with immunomodulatory treatment.[4–6]

A patient has ''limbic syndrome'' if he/she meets more than one of the following criteria: recent memory impairment, temporal lobe crisis, or psychiatric abnormalities, and also one of the following: neuropathology (chronic medial temporal encephalitis); a tumor diagnosed within five years of the appearance of neurological symptoms and signs; onconeuronal antibodies or VGKC, NMDAR, GAD Ab; the finding in brain MRI of an unexplained increase in the FLAIR/T2 medial temporal signal.[6–9]

The case of a girl with the onset of type 1 diabetes mellitus at four years of age and who experienced cognitive impairment and behavioral disorder at seven years of age is reported below. She had no family or personal history of interest. Psychomotor development had been normal until 7 years of age, but progressive behavioral disorders (aggressiveness, disobedience), memory loss, poor school performance, irrational fear, anxiety, auditory hallucinations, sleep disturbance, and absence seizures, subsequently occurred. The latter increased in severity and frequency, showing signs of complex partial seizures. At 10 years of age, the patient had multiple daily episodes consisting of facial clonus, ocular version, hypertonia, and generalized tonic–clonic seizures. Cognitive impairment and school performance simultaneously worsened, particularly as regards executive dysfunction and memory loss. She also showed poor emotional and impulse control, severe behavioral disorders and aggressiveness (she hit her classmates, took off her clothes in class), and required a special education school.

Despite intensive treatment of diabetes with insulin detemir and lispro following a basal bolus regimen and diet, control was poor because of the multiple daily crises causing hyperglycemia and hypoglycemia; HbA1c 7.8%, TSH 3.00, FT4 0.79, negative microalbuminuria, negative thyroid Ab. Negative transglutaminase IgA Ab. The patient also had early puberty, for which she was treated with triptorelin.

Because of the refractoriness of her epileptic seizures, the patient was referred at the age of 12 to a tertiary hospital where potential surgical treatment for epilepsy was assessed.

- 3T MRI performed there showed atrophy of both hippocampi, with increased T2 and FLAIR signal, suggesting bilateral medial temporal sclerosis. There was a greater decrease in left hippocampal head volume, and more severe signal changes in the right side (Fig. 1).
- PET/CT: bilateral temporal hypometabolism, more marked and extensive in the right temporal lobe, affecting the mesial region, temporal pole, and neocortex.
- Video EEG: intercritical abnormalities: right and left temporal epileptiform abnormalities: 26 right temporal crises and 4 generalized tonic–clonic seizures.
- Neuropsychological assessment revealed cognitive/evolutionary impairment in all domains, an intelligence quotient previously 69, currently 51, impaired memory, especially verbal, as well as executive dysfunction, difficulties in emotional and impulse control, severe behavioral disorder, dissocial behavior.

She was diagnosed with refractory epilepsy with bilateral medial temporal sclerosis, mainly on the right side, refractory to drug treatment. A right temporal lobectomy with right amygdalohippocampectomy was therefore performed.

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