Two patients of different age ranges with seizures: Part II

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Ten-year-old patient, male, mixed race (African and Caucasian).

Chief complaint: Seizure.

History of present illness: Previously healthy child who had an episode of seizure-type absence without fever.

1- In the initial evaluation of infants and children during or immediately after an episode of seizure, what should one perform?

A- Serum calcium measurement  
B- Complete blood count  
C- Computed tomography scan  
D- Blood glucose measurement  
E- Electroencephalography

- In the initial evaluation of children and infants during or immediately after an episode of seizure, it is necessary to ensure that airways are patent, to evaluate ventilation and heart function, and to measure the temperature and blood glucose.
- Lumbar puncture is mandatory in patients with an altered mental state or other signs of meningitis even if there is no fever. If the diagnostic hypothesis of meningitis has a low likelihood in the postictal period, the patient should be observed for a 2–3-h period. If the patient returns to normal, a lumbar puncture is not required.
- There is no definite position regarding the need for neuroimaging in children who present to an emergency unit after a first seizure. Imaging tests must be performed if there are new or recent focal deficits, permanent mental alterations, recent traumas, persistent headaches, or partial seizures.
- Electroencephalography is the most important test for evaluating a patient with an unprovoked seizure, but it rarely needs to be performed in acute crises, except if status epilepticus is suspected. It helps to determine the type of crisis, the specific epileptic syndrome, and the risk of recurrence.

The patient was evaluated in an emergency unit, where hypoglycemia (29 mg/dL) was detected and reverted with a glucose flush.

Since then, recurrent episodes of hypoglycemia have occurred, associated with mental confusion, sweating, tremors, sleepiness, and behavioral changes. His pediatrician recommended a scheme of feeding every 3 h, but there was no improvement in the symptoms.

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In the following month, the patient had another episode of generalized tonic-clonic seizure, without sphincter release. He was then evaluated by a neurologist, who asked for the patient to be hospitalized to investigate the condition.

**Pregnancy history:** The mother had five pregnancies, four deliveries, and one miscarriage. She had eight prenatal consultations, starting at the second month. Maternal TORCH serology was negative for all the investigated conditions (SIC). The mother reported systemic arterial hypertension in the third trimester. She denied smoking and alcohol ingestion during pregnancy. The patient was born by cesarean section, weighing 3,140 g and measuring 50 cm. The phenylketonuria test was negative.

**Medical history:** Hospital admission for 6 days at 2 months of age due to dengue fever, with no complications reported. No allergies or surgery.

**Developmental history:** Normal development. The patient attends the 5th grade of elementary school, with good performance.

**Vaccine history:** Completed vaccination card.

**Family history:** The patient’s mother and maternal grandmother have hypertension. The father has asthma. The paternal grandparents are diabetic. Some uncles and cousins, both maternal and paternal, have epilepsy.

**Social history:** The patient lives with his parents and three siblings in their own house, with running water and proper sanitation. They have two dogs. Good family relationship. The mother is 29-year old and is a confectioner. The father, a bricklayer, is 42-year old. Both have completed high-school studies.

**Complementary examinations:**

<table>
<thead>
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<th>Red blood cells</th>
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<tbody>
<tr>
<td>Hemoglobin</td>
<td>13.6 g/dL</td>
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<tr>
<td>Hematocrit</td>
<td>39.8%</td>
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<tr>
<td>MCV</td>
<td>82.2 µm³</td>
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<tr>
<td>MCH</td>
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<tr>
<td>MCHC</td>
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<tr>
<td>RDW</td>
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<td>Platelets</td>
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<tr>
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<td>Myelocytes</td>
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<td>Metamyelocytes</td>
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<tr>
<td>Lymphocytes</td>
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<tr>
<td>Monocytes</td>
<td>7%</td>
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</table>

**Glucose**

- 31 mg/dL

**Other tests**

- Computed tomography of the head: no changes
- Electroencephalography: no changes

**Computed tomography of the upper abdomen:**

- Pancreas with homogeneous density, presenting an anterior contour bulge of the body and a slight hypodense area in that topography.

**Ultrasound**

**Hypoechoic lesion** at the same location, homogeneous, with flows, measuring 1.8 × 1.4 cm.

**Upper abdomen NMR**

Pancreas presenting a small hypointense nodular lesion in T1 and with an intermediate signal in T2, enhanced after contrast and diffusion restriction, measuring approximately 1.5 × 1.2 cm, located in the middle third of the pancreatic body, which could correspond to an expansive lesion originating from the pancreatic islets.
Conduct

- Surgical resection of the lesion was indicated and the specimen was sent for histopathological analysis. Final report: intermediate-stage neuroendocrine tumor, compatible with insulinoma, according to the symptoms (hypoglycemia).
- The patient was discharged without symptoms.

2 - What is the chief cause of persistent hypoglycemia in children and adolescents?

A- hyperinsulinism
B- use of oral hypoglycemic agents
C- tumors
D- malabsorptive syndromes
E- glycogenosis

- Hyperinsulinemia is the most common cause of persistent hypoglycemia in both children and adults.
- In adults, it is more frequently an acquired condition due to insulin-secreting tumors, whereas in infants and children, it is usually due to congenital hyperinsulinism.
- Cortisol and/or growth hormone deficiencies as well as defects in glucose, glycogen, and fatty acid metabolism can also cause persistent hypoglycemia in pediatric patients.

3- In a patient with hypoglycemia, which piece of information from the physical examination may indicate a possible etiology?

A- Telangiectasia
B- Splenomegaly
C- Micropenis
D- Bifid uvula
E- Albinism

- In patients with hypoglycemia, a thorough clinical history should include the moment when the episode occurred and its relationship with meals, weight at birth, gestational age, and family history.
- The physical examination should look for evidence of hypopituitarism (micropenis, cleft lip/palate, and short stature), glycogenosis (hepatomegaly),
adrenal insufficiency (recurrent abdominal pain, hyperpigmentation, anorexia, and weight loss), and Beckwith-Wiedemann syndrome (defects of the anterior abdominal wall, hemihyperplasia, and macroglossia).

4- According to the recommendations from the Pediatric Endocrine Society, which patients should be evaluated for hypoglycemia?

A- Infants and young children who are incapable of reporting their symptoms and who present with a blood glucose level < 50 mg/dL.
B- Children who can report their symptoms reliably and in whom Whipple’s triad is confirmed.
C- All newborns at high risk for hypoglycemia after 24 h of life.
D- Children of all age ranges with a blood glucose level < 60 mg/dL.
E- None of the above.

- The Pediatric Endocrine Society recommends the following:
  - In cooperative children who are capable of reporting their symptoms correctly, evaluation and management should only be conducted in those with documented Whipple’s triad.
  - In infants and young children who are incapable of reporting their symptoms, evaluation and management are indicated in those whose blood glucose, measured by a reliable laboratory, is below the normal threshold of neurogenic responses (< 60 mg/dL).
  - In newborns suspected to be at high risk of persistent hyperglycemia, an evaluation is indicated at or after 48 h of life, once past the period of transitional glucose regulation so that the hypothesis of persistent hypoglycemia can be eliminated before hospital discharge.

5- Which of the following does Whipple’s triad include?

A- Symptoms compatible with hypoglycemia that quickly disappear after glucose is administered and glycemia is corrected.
B- Symptoms compatible with hypoglycemia and ketonemia.
C- Hyperinsulinemia and hypoglycemia.
D- Hyperinsulinism and symptoms compatible with hypoglycemia.
E- Symptoms compatible with hypoglycemia and increased levels of free fatty acids.

- Hypoglycemia may be asymptomatic or may cause symptoms that reflect the response from the nervous system (NS) to brain glucose deprivation.
- Symptoms are usually classified into autonomic or neurogenic and neuroglycopenic.
- Autonomic symptoms result from physiological NS changes triggered by hypoglycemia. The symptoms include both adrenergic responses, such as tremors, palpitations, and anxiety, and cholinergic responses, such as sweating, hunger, and paresthesia.
- Neuroglycopenic signs and symptoms, such as mental confusion, coma, and seizures, result from a brain dysfunction caused by insufficient glucose levels to supply the brain’s energetic metabolism.
- The guidelines highly value Whipple’s triad for diagnosing hypoglycemia in adults, but it has limited importance in children.
- Whipple’s triad includes:
  - Signs and symptoms compatible with hypoglycemia
  - Documented low plasma glucose levels
  - Reversion of signs and symptoms after glycemia is normalized.

6- What can be said about insulinomas?

A- They frequently cause hypoglycemia in adolescents.
B- They generally reach large dimensions with a mass effect.
C- Approximately 50% of them have malignant features.
D- They are frequently located in the head of the pancreas.
E- The most frequent location of ectopic insulinomas is the duodenal mucosa.

- Insulinomas are neuroendocrine pancreatic tumors that have a greater prevalence in adults (41-50 years). They are rare, with an incidence of 1 to 3 persons/1,000,000 persons/year. They should be considered in cases of childhood or adolescence hyperinsulinemic hypoglycemia.
- They are generally small tumors, less than 2 cm long, but giant insulinomas have been described in children. They are equally distributed in the head, body, and tail of the pancreas.
- They tend to be single tumors. Multiple insulinomas are frequently associated with hereditary syndromes.
- Only 3% of insulinomas are ectopic, and the most frequent location of ectopic cases is the duodenal mucosa.
7- Which hereditary syndrome is most frequently associated with insulinoma?

A- MEN-1
B- Fanconi syndrome
C- Kabuki syndrome
D- Sotos syndrome
E- DICER1

- Multiple endocrine neoplasia type 1 (MEN-1), also known as Wermer syndrome, is a dominant autosomal disorder caused by germinal mutations in the 11q13.1 region.
- MEN-1 is a gene that encodes the menin protein, which is related to tumor suppression.
- It is characterized by the presence of multiple endocrine tumors in the parathyroids, anterior pituitary, and pancreatic islets. Tumors have also been described in the adrenal cortex, bronchi, and thymus as well as in the digestive tract.
- The syndrome is associated with several skin tumors, such as facial angiofibromas, collagenomas, and lipomas.

8- Which is the most common alteration in the MEN-1 syndrome in pediatric patients?

A- Hypoglycemia
B- Hyperglycemia
C- Adrenal insufficiency
D- Primary hyperparathyroidism
E- Zollinger–Ellison syndrome

- The Groupe d’étude des tumeurs endocrines (a Franco-Belgian study group on endocrine tumors) studied a cohort of 160 MEN-1 patients aged less than 21 years. The most common manifestation was primary hyperparathyroidism, which occurred in 75% of cases (122/160), most frequently before 10 years of age. It was the syndrome’s initial manifestation in 90 of the patients and was only detected by biological screening in most cases.
- The second and third most frequent manifestations were pituitary adenomas (34%) and neuroendocrine pancreatic tumors (23%).
- In 16 patients (10%) of that cohort the onset of the clinical condition manifested with insulinoma, which in one patient occurred before 5 years of age. The most common hypoglycemic symptoms were loss of consciousness or coma, and weakness associated with seizures in 3 cases.

REFERENCES

1. Mikati MA, Hani AJ. Seizures in Childhood. 2823-2857-e.1