

but may possibly be due in this case to severe cranial sclerosis obliterating the cribriform cartilage of the ethmoid bone, thus damaging the olfactory fibers. While this patient had high prolactin levels, these were not so high as to explain hypogonadism. It is therefore likely that the cause could be related to gonadotroph cell damage due to fibrous dysplasia of the sella turcica.

Fibrous dysplasia results from GNAS gene mutation and causes abnormal proliferation and differentiation of osteoblasts together with increased osteoclastic activity. This mutation is also associated with increased expression of fibroblast growth factor 23, which increases renal phosphate excretion, causing hypophosphatemia and aggravating the bone mineralization defect.^{2,8} It should be noted that this patient had mild hypophosphatemia upon admission. Based on pathophysiological understanding of the disease, bisphosphonates have been increasingly used in recent years. Pamidronate and zoledronic acid are the most commonly used bisphosphonates.^{9,10} The prognosis of polyostotic disease is usually good, but tends to be worse in patients with MAS having excess GH.² Monitoring is based on bone turnover markers such as alkaline phosphatase, which are elevated in active disease and tend to decrease in response to antiresorptive treatment.²

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Factitious hypoglycemia[☆]

Hipoglucemia facticia

Hypoglycemia is defined as plasma glucose levels less than 50 mg/dL.¹ However, the definition of hypoglycemia may vary depending on whether glucose is measured in venous or capillary blood. The cut-off point of the glucose level that triggers a physiological response to hypoglycemia and the resultant symptoms may also vary. The diagnosis of hyperglycemia is based on Whipple's triad: low blood glucose level, symptoms of hypoglycemia, and symptom improvement once blood glucose returns to normal. Hypoglycemia causes adrenergic symptoms such as tachycardia, palpitations, tremor, sweating, pallor and anxiety, and non-adrenergic or neuroglycopenic symptoms including hunger, headache, weakness, visual disturbances, confusion, lethargy, seizures, and even coma.¹ The most common cause in our environment is glucose lowering treatment

(oral hypoglycemic drugs and insulin). Other potential causes include end-stage renal failure, sepsis, hormone deficiencies, big mesenchymal tumors, insulinoma, congenital metabolic diseases, etc. Plasma glucose levels in the hypoglycemic range not associated with clinical signs are sometimes detected. Such cases may be due to the inadequate perception of hypoglycemic symptoms or to "factitious hypoglycemia". The case of a patient with an uncommon cause of hypoglycemia is reported below.

The patient was an 83-year-old male with a history of high blood pressure treated with spironolactone 25 mg daily and furosemide 20 mg daily, hypercholesterolemia treated with atorvastatin 40 mg daily, chronic renal failure secondary to nephroangiosclerosis, paroxysmal atrial fibrillation, cognitive impairment, vascular parkinsonism, and depressive syndrome. He had also been seen by different specialists due to frequent presyncopal episodes and based on laboratory tests reporting a WBC count of 22,400/ μ L, a RBC count of 6.3×10^6 / μ L, hemoglobin 17.1 g/dL, hematocrit 53%, and a platelet count of 441,000/ μ L, he had been diagnosed with moderate pancytopenia. Tests for myeloproliferative syndrome were negative. The patient was

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Table 1 Fasting test results.

| Hours of fasting | Capillary glucose, mg/dL | Venous glucose, mg/dL | Insulin (<27 μ U/mL) | C-reactive peptide (0.7–4 ng/mL) |
|------------------|--------------------------|-----------------------|--------------------------|----------------------------------|
| 0 | 96 | 79 | 16 | 6.79 |
| 6 | 82 | 67 | 11.7 | 6 |
| 12 | 72 | 56 | 5.6 | 3.6 |
| 18 | 70 | 53 | 7.6 | 3.90 |
| 24 | 75 | 57 | 6.20 | 3.73 |
| 30 | 69 | 50 | 1.70 | 3.47 |
| 36 | 65 | 36 | 0.20 | 3.45 |

referred to endocrinology to rule out hypoglycemia as the cause of syncopal episodes after a venous fasting blood glucose level of 41 mg/dL was found. No history of diabetes or use of hypoglycemic drugs was found. Presyncopal episodes were not related to intake or fasting. The physical examination was normal. Prior laboratory tests found blood glucose levels ranging from 40 to 70 mg/dL. At this first visit, he was given a glucometer to record capillary blood glucose in the event of presyncopal symptoms and instructions to follow a fractionated diet. At subsequent visits, the patient provided capillary blood glucose measurements revealing no hypoglycemia. Laboratory tests results included: creatinine 1.6 mg/dL, glomerular filtration rate 44 mL/min/1.73 m,² lactate dehydrogenase 1440 IU/L (313–618), chromogranin A 769 ng/mL (19–98), C peptide 6.81 ng/mL (0.7–4), and insulin 10.7 μ g IU/mL (<25 μ U/mL), with 41 mg/dL blood glucose. Results of additional tests were: C peptide 3.64 ng/mL and insulin 16.5 μ g IU/mL, with a blood glucose level of 56 mg/dL. C-reactive peptide levels were interpreted taking into account that its clearance was decreased due to the presence of renal failure. Chromogranin A, used as a biochemical marker of neuroendocrine tumors, may be falsely elevated in patients with renal failure and poorly controlled high blood pressure. Abdominal ultrasound revealed no remarkable findings in the pancreatic head and body, and a homogeneous 12.5 cm spleen. Computed tomography (CT) of the abdomen and pelvis, which was performed without contrast due to renal failure, showed a non-specific nodular lesion some millimeters in size in the pancreatic tail, homogeneous splenomegaly, and lytic lesion at the T11 vertebra. Because of the low blood glucose levels found in several measurements, with detectable insulin and C-reactive peptide, together with the occurrence of a pancreatic lesion, admission for hypoglycemia work-up was decided. A fasting test was discontinued at 36 h due to a venous blood glucose level of 36 mg/dL, with no symptoms of hypoglycemia and decreased insulin levels (Table 1).

The main pathophysiological characteristic of endogenous hyperinsulinism is lack of suppression of insulin secretion during hypoglycemia. This causes the occurrence during the fasting test of plasma insulin levels higher than 6 μ U/mL and C-reactive peptide levels higher than 0.6 ng/mL with plasma glucose levels less than 45 mg/dL and symptoms of hypoglycemia. The results of that test therefore ruled out the existence of endogenous hyperinsulinism and demonstrated a marked discrepancy between capillary

and venous blood glucose levels. Such variability depends on factors such as the glucometer used and the adequate performance of the procedure.

Because of the elevated WBC count, lack of hypoglycemic symptoms, and disagreement between glucose levels measured by the glucometer and in venous blood, it was decided to rule out glucose consumption by blood cells. For this, two samples were taken, of which one was centrifuged immediately and the other after 50 min, the estimated usual time for sample arrival at the laboratory. Levels found in these two samples were 61 mg/dL and 46 mg/dL, respectively. These results suggested decreased plasma glucose levels due to glucose consumption by blood cells and ruled out the existence of true hypoglycemia. The patient refused to undergo additional tests to further characterize the pancreatic nodule and lytic lesion found in abdominal CT.

Hypoglycemia due to glucose consumption in blood cells is usually not easy to recognize, unlike as occurs with hypoglycorrhachia in bacterial meningitis.² Glucose circulating in blood is usually consumed by RBCs and WBCs by glycolysis, a process that converts glucose into pyruvate.³ In the presence of a myeloproliferative syndrome, leukemic states, or leukocytosis from other causes, glucose consumption by blood cells increases, and low glucose levels may be found.^{1,4–6,8} *In vitro* decrease in glucose is directly related to sample incubation time and temperature and to WBC count.² At room temperature, glucose levels decrease from 7 to 20 mg/dL/hour, regardless of the initial glucose level.⁷ High temperatures also accelerate the glycolytic process.³ The rate of glycolysis is also higher in blood from patients with leukocytosis. However, this phenomenon is independent of WBC type (lymphocytes or polymorphonuclear), and the “blood glucose/leukocytosis” ratio is specific for each individual.⁷ On the other hand, the glycolytic process was once thought to be faster when leukocytosis was at the expense of immature forms. However, when blood samples from patients with leukemia were compared to blood samples from healthy individuals with similar WBC counts, glucose consumption by leukemic cells was shown to be less than one-fifth of the consumption by non-leukemic cells, except when the WBC count exceeded 60,000/ μ L. Thus, the *in vitro* glucose consumption rate is related to WBC count rather than to cell maturation or differentiation.⁹

There are several ways to prevent glucose consumption *in vitro*.¹⁰ First, high temperatures should be avoided, as

well as delay in sample testing. It is recommended that the sample be kept at a temperature of approximately 4 °C and that transportation time be minimized. Time periods longer than two hours from sampling to testing have been associated with significant drops in blood glucose.¹¹ Second, early centrifugation of the sample is recommended. Finally, to avoid this phenomenon, blood samples should be drawn into tubes containing inhibitors of glycolysis such as sodium fluoride or potassium oxalate. However, as these compounds may interfere with some laboratory methods, their use now tends to be avoided.

Hypoglycemia due to blood cell consumption should be suspected in the event of marked leukocytosis for any reason, venous hypoglycemia with no symptoms of hypoglycemia and no improvement after glucose administration (Whipple's triad), or a potential mistake in sample collection or processing.

Multiple classifications of the causes of hypoglycemia are available, but few of them mention the cause reported in this case. It is advisable to be aware of and to suspect this phenomenon so as to prevent false diagnoses and unnecessary tests.

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Rhinomucormycosis and type 1 diabetes mellitus[☆]

Rinomucormicosis y diabetes mellitus tipo 1

Rhinomucormycosis, an opportunistic infection caused by fungi of the *Phycomycetes* class, usually occurs in diabetic patients with poor metabolic control and in those with organ transplant, cancer, neutropenia, or immunodeficiency.^{1–3} The main pathogens belong to the species *Rhizomucor*, *Rhizopus*, *Absidia*, and *Mucor*. The most common presentation is rhino-orbital-cerebral mucormycosis. We report the case of a patient with oral mucormycosis and type 1 diabetes mellitus (DM).

The patient was a 22-year-old female diagnosed with primary hypothyroidism and type DM since six years of age. She had been admitted to hospital several times for diabetic ketoacidosis (DKA), and her most recent glycosylated hemoglobin value was 14%. Her treatment included insulin glargine 29 IU/day, insulin aspart 6 IU with each meal, and levothyroxine 50 mcg/day. During the previous week she had experienced malaise, headache, and decreased sensitivity

in the left side of the face (territory of the maxillary branch of the 7th cranial nerve). Physical examination revealed hypesthesia in the above region and lysis with sphacelation at palate level (Fig. 1).

No changes were found in the complete blood count, kidney function, thyroid function, venous blood gases, and microalbuminuria. Blood glucose and glycosylated hemoglobin levels were 107 mg/dL and 10.7% respectively. Computed tomography (CT) of the paranasal sinuses revealed partial occupation of the basal and lateral region of the left maxillary sinus without air-fluid levels, with thinning and dehiscence of the alveolar recess and soft tissue occupation (Fig. 1).

The patient underwent nasosinusal endoscopic surgery consisting of uncinectomy, anterior ethmoidectomy, and maxillary antrostomy. Because of the presence of infected tissue and necrosis at the middle septal region, debridement was performed up to the healthy bone area.

A pathological study found fragments of nasosinusal mucosa with mixed inflammatory infiltrate (lymphoplasmacytic proliferation and polymorphonuclear white blood cells) and fibrosis with granulomatous reaction with multinucleated giant cells. PAS and Grocott stains revealed the presence of mitotic figures consistent with *Mucor* (Fig. 1). Based on these results, antibiotic treatment was started with intravenous amphotericin B 50 mg/12 h

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