Antipituitary Antibodies in a Postpartum Woman With Partial Pituitary Deficiency and a Normal Pituitary MRI Scan

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ABSTRACT: We highlight the diagnostic consideration of lymphocytic adenohypophysitis (LAH) in the postpartum patient with unexplained partial pituitary insufficiency. Further, we emphasize that in patients with a normal magnetic resonance imaging scan, the measurement of antipituitary antibodies (APA) may provide an alternative means of confirming the diagnosis. Finally, although assays of APA are nonstandardized, intensive study and development of a reliable APA assay could promote our understanding of the autoimmune process, eventually facilitating the diagnosis of LAH and eliminating the need for biopsy.

LYMPHOCYTIC ADENOHYPOPHYSITIS (LAH) is being recognized with greater frequency as a cause of pituitary insufficiency. The majority of patients diagnosed with this entity have been women in the postpartum period with signs of sellar mass or hormonal deficiencies. Historically, the diagnosis of LAH was only recognized at pituitary surgery or autopsy. However, it has now become evident that the syndrome of LAH may manifest without a sellar mass on radiographic imaging, making pituitary surgery unnecessary. We describe the case of a patient having the classic presentation of LAH with positive antipituitary antibodies (APA) but with a normal pituitary magnetic resonance imaging (MRI) scan.

CASE REPORT

A 34-year-old woman (gravida 2, para 2) came to us 7 weeks after delivery of a preterm infant with complaints of fatigue, lethargy, hair loss, and abnormal results on thyroid function tests. Her pregnancy had been complicated by flu-like symptoms, dehydration, and preterm labor, but there was no hypotension, shock, or hemorrhage during parturition. A previous pregnancy in 1985 was uncomplicated. Her family history was significant for a sister in whom postpartum thyroiditis developed. Laboratory evaluation at her postpartum visit included the following values: thyroxine, < 2.5 μg/dL (normal, 4.5 to 11.5); triiodothyronine resin uptake, 26.3% (normal, 25 to 35); thyroid-stimulating hormone (TSH), 7.10 mU/L (normal, 0.3 to 5.1); triiodothyronine, 26 ng/dL (normal, 70 to 185). Testing for antithyroglobulin antibodies yielded negative results. A diagnosis of postpartum thyroiditis was made, and levothyroxine, 0.125 mg daily, was prescribed.

The patient returned 3 months after her initial visit, reporting only minimal improvement of previous symptoms and the development of orthostatic dizziness, muscle cramps, profound weakness, amenorrhea, and lack of lactation. Physical examination revealed orthostatic hypotension with supine blood pressure 90/60 mm Hg, supine pulse rate 85/min, standing blood pressure 60/40 mm Hg, and standing pulse rate 110/min. There was sparse pubic and axillary hair and poor muscle tone. A short cosynotropin (Cortrosyn) stimulation test, using 250 μg cosynotropin intravenously (IV), revealed a cortisol level of < 2 μg/dL at baseline; at 30 minutes, the cortisol level was 3.10 μg/dL. The levotiroxine was discontinued, and a diagnosis of hypocortisolism was made. A combined multiple stimulation of the pituitary was done using synthetic gonadotropin-releasing hormone, 100 μg IV, ovine corticotropin-releasing hormone (o-CRH), 100 μg IV, and protirelin (TRH), 500 μg IV, given consecutively. Results are shown in the Table.

Stimulated responses of luteinizing hormone and follicle-stimulating hormone were normal. The corticotropin (ACTH) response to o-CRH stimulation was flat and was consistent with central hypocortisolism. Initial prolactin levels were mildly elevated and could be attributed to the underlying adrenal insufficiency. After TRH stimulation, the prolactin response was abnormally blunted but was nondiagnostic. While the patient was not taking thyroid medication, the TRH stimulation test showed a flat TSH response consistent with central hypothyroidism. In short, the combined test was indicative of central hypocortisolism and hypothyroidism.

An MRI scan of the pituitary gland was normal (Figure). The patient’s serum was negative for antiadrenalin, antithyroglobulin, and antimicrosomal antibodies. The serum was then screened for the presence of pituitary autoreactive antibodies, using an indirect immunofluorescence technique that has been described previously. Briefly, frozen sections of surgically resected normal human pituitary tissue were used. The patient’s serum and normal control serum were prepared in phosphate buffered saline (PBS), then applied to the pituitary sections and incubated for 30 minutes. After they were rinsed and washed with PBS, the sections of pituitary tissue were incubated with either a 1/40 dilution of fluorescein isothiocyanate-labeled rabbit antihuman IgM or a 1/50 dilution of rabbit antihuman IgG for another 30-minute period.

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Finally, the sections were washed in a PBS bath, mounted in 10% glycerol-PBS, and examined under a Nikon fluorescence microscope using epi-illumination and interference excitation at 495 nm. Examination of our patient’s serum on prepared pituitary sections revealed the presence of IgM antibodies at a titer of 1/50 but no IgG antibodies. Identification of the specific pituitary cell types was not done. Control serum resulted in no immunofluorescent staining of pituitary sections. All samples were done in duplicate.

A diagnosis of LAH with corticotropin and thyrotropin deficiency was suggested by the clinical presentation and was confirmed by positive testing for APA. Therapy was begun with prednisone, 5 mg every morning and 2.5 mg every evening, and levothyroxine, 0.125 mg daily. With therapy, the patient had complete resolution of her symptoms, including resumption of menses. A repeat MRI scan done 11 months later was normal with no change from the previous scan.

**DISCUSSION**

The clinical presentation of LAH has previously been well described as occurring primarily in women, with the onset of symptoms usually late in pregnancy or in the postpartum period. Symptoms in most patients suggest aellar mass (ie, headaches, visual disturbances) or a hormonal deficiency (ie, fatigue, weakness, amenorrhea, galactactia). However, should the pituitary MRI scan reveal a normal pituitary gland, the diagnosis of LAH should not be excluded. Indeed, pathologic data on pituitaries with lymphocytic hypophysitis have revealed that the pituitary gland may be enlarged, small, or normal in size. The endocrine evaluation may also reveal a wide range of results, from completely normal function to panhypopituitarism. However, what appears to be distinctive about LAH is its ability to produce isolated ACTH deficiency or combined ACTH/TSH deficiencies while maintaining normal gonadotropin function. This characteristic suggests that a pituitary lesion may be due to LAH rather than a nonfunctioning mass lesion causing compression of normal pituitary tissue, which typically produces loss of gonadotropins first. Indeed, our patient had the typical characteristics of hypothyroidism, and postpartum thyroiditis was erroneously diagnosed. However, when her condition did not improve with thyroid replacement therapy, subsequent evaluation confirmed the deficiencies of both ACTH and TSH. Other possible causes, such as Sheehan’s syndrome or pituitary infarct, that might also explain the partial hypopituitarism, are unlikely in this case. There was no peripartum history of hypotension, hemorrhage, or vascular compromise to suggest Sheehan’s syndrome. Our patient did not have diabetes, which might predispose a patient to pituitary infarction, and she had no prior history of visual disturbances or headache to suggest a pituitary mass or infarct. In fact, the normal MRI scan without evidence of hemorrhage, calcification, an enlarged sella, or an empty sella is further evidence to support our clinical impression and negate apoplexy.

The definitive diagnosis of LAH requires histopathologic evidence of lymphocytic infiltration of the anterior pituitary. Unfortunately, when the MRI scan of the pituitary gland is normal,
biopsy of the pituitary is not recommended. The suspected diagnosis of LAH can be confirmed by measuring APA in the patient’s serum. Although assays of APA are still evolving and are nonstandardized, they may still be clinically helpful in identifying the exact cause of the pituitary insufficiency. Refinement of an APA assay, as well as its clinical significance in pituitary disease, is ongoing, but its utility in select cases should be recognized.

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References

Esophageal Perforation Caused by Coin Ingestion

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ABSTRACT: Esophageal perforation and acquired tracheoesophageal fistulae (ATEF) are rare sequela of foreign body ingestion in the pediatric population. Here we discuss the cases of two patients with esophageal perforation caused by prolonged impaction of a coin; in one case, a tracheoesophageal fistula developed. The presence of aerodigestive symptoms and signs in infants and small children should prompt physicians to consider foreign body ingestion and the presence of an ATEF. Clinical presentation, diagnostic modalities, and technical considerations for surgical management are outlined.

Surgeons are commonly involved in the treatment of congenital tracheoesophageal fistulae. Acquired tracheoesophageal fistulae (ATEF), from a variety of causes, are more common in the adult population. Treatment options depend on the foreign object ingested, the condition of the esophagus and trachea, and the physiologic status of the patient.

CASE REPORTS

Case 1. A 3-year-old boy was brought to the emergency department with a 2-day history of fever to 38.8°C and productive cough with associated nausea, vomiting, and anorexia. The mother reported no recent history of foreign body ingestion, but a coin had been recovered from the child’s esophagus through an endoscope 6 months earlier. In the interim, he had had frequent bouts of asthma, for which he had been treated with albuterol sulfate syrup and inhalers. Examination revealed bilateral basilar rhonchi with coarse rales over the right anterior chest. The white blood cell count was 38,300/mm³ with a left shift. A chest film showed a discoid foreign body in the midportion of the esophagus opposite the carina and posterior to the trachea, and bilateral pulmonary infiltrates. Treatment with intravenous antibiotics was instituted. Rigid esophagoscopy revealed marked edema of the anterior wall of the midesophagus with mucosal erosion distal to the thoracic inlet. The coin, a penny, was visualized broadside, but the edge could not be engaged with grasping forceps due to resistance of adjacent tissues. It had eroded through the anterior esophageal wall and was situated between the trachea and the esophagus. A barium swallow (Fig 1) showed the esophageal lumen posterior to the coin with a sinus tract extending from the esophagus to the posterior aspect of the coin. After several days of antibiotic therapy, the pneumonia improved, and the patient was returned to the operating room. Rigid bronchoscopy revealed a large tracheal perforation 1 cm proximal to the carina; the coin could be seen through this defect. A right posterior thoracotomy exposed the coin, which was embedded in thick, fibrous tissue, forming a tracheoesophageal fistula (Fig 2). The fistula was divided at its midpoint, and the coin was removed. The esophagus was closed with a single layer of interrupted silk sutures.

The trachea was repaired with a single layer of interrupted nylon suture incorporating the fibrous capsule in the closure, and a pleural pedicle flap was sutured between the trachea and the esophagus. Insertion of a chest tube and a tube gastrostomy completed the procedure. The postoperative course was complicated by a transhiatal esophageal leak on the 7th postoperative day. A barium swallow on the 10th postopera-