Case 1 Presentation
A 4-year-old boy has had 6 days of intermittent nausea and vomiting without diarrhea or fever. Two days into the illness, he was given promethazine suppositories for presumed viral gastroenteritis; overnight the vomiting subsided. He now experiences an unsteady gait and needs help to stand still for urination. He says that he sees “two daddies.” There has been no weight loss, headache, mental status changes, upper respiratory tract symptoms, skin lesions, or trauma.

On physical examination, his weight, height, and head circumference are appropriate for age. His vital signs are normal, and he appears comfortable, talkative, and playful, although slightly pale. His abdomen is soft and nontender with normoactive bowel sounds. He has a well-healed scar resulting from pyloromyotomy in the first postnatal month. Despite the acute history of ataxia and diplopia, a thorough neurologic evaluation reveals normal findings, as does the rest of the examination.

An imaging study reveals the cause of his vomiting, ataxia, and diplopia.

Case 2 Presentation
A 15-year-old girl who experienced menarche at age 13 years has had no menstrual periods for 7 months. Her only symptom is an occasional headache occurring at the end of the day. She denies sexual activity, medication use, and substance abuse and has had no recent weight change, heat or cold intolerance, skin or hair problems, difficulties with vision, or fainting. The patient’s family history includes a granduncle who has acromegaly.

On physical examination, she looks well. Her height is in the 50th percentile, weight is in the 75th percentile, blood pressure is 113/62 mm Hg, and pulse is 90 beats/min. Her skin is not flushed or dry, and she has no rashes or abnormalities of hair pattern or hirsutism. Extraocular movements, visual fields by confrontation, and pupils all are normal. Heart, lung, abdominal, and neurologic examinations yield normal findings. Breasts and external genitalia are at sexual maturity rating 4 and normal, with a patent vagina and palpable uterus.

Normal laboratory findings include follicle stimulating hormone, 4.5 mIU/mL (4.5 IU/L); luteinizing hormone, 6.6 mIU/mL (6.6 IU/L); testosterone, 46 ng/dL (1.6 nmol/L); dehydroepiandrosterone sulfate, 122 mcg/dL (3.3 mcmol/L); thyroid-stimulating hormone, 1.28 mIU/mL; thyroxine, 8.9 mcg/dL (114.5 nmol/L); and total cholesterol, 186 mg/dL (4.8 mmol/L). A pregnancy test is negative. Pelvic ultrasonography reveals a normal uterus and no free fluid. Two final studies reveal the origin of the patient’s amenorrhea.

Case 3 Presentation
An 8-year-old girl presents with the acute onset of severe right lower quadrant colicky pain and mild right flank pain associated with nausea and vomiting. She has no fever, dysuria, or diarrhea. Yesterday she had a similar but milder episode that lasted for a few hours and resolved spontaneously. At the age of 2 years, she underwent an uneventful bilateral inguinal hernia repair.

On physical examination, the girl is in severe pain. Her temperature is 97.6°F (36.1°C), pulse is 93 beats/min, blood pressure is 100/62 mm Hg, and respirations are 22 breaths/min. Her abdomen is soft and nondistended. Bowel sounds are normal.
There is mild right lower quadrant tenderness to deep palpation without any peritoneal signs. Neither costovertebral tenderness nor palpable masses are present.

Normal values are found on a complete blood count and measurements of serum electrolytes, glucose, and urea nitrogen. Urinalysis reveals 5 to 10 red blood cells per high-power field.

One additional test helps to determine the cause of her illness.

Case 1 Discussion
Computed tomography (CT) of the brain revealed a 2.5 cm × 3.0 cm posterior fossa mass that occupied the fourth ventricular space and extended into the foramen of Luschka on the left. Subsequent magnetic resonance imaging (MRI) revealed the presence of blood products of various ages in the fourth ventricle and in the posterior fossa region in very close proximity to a venous angioma of the left cerebellar hemisphere. From these findings, an arteriovenous malformation (AVM) with acute and subacute hemorrhage was diagnosed.

Differential Diagnosis
The combination of ataxia and diplopia, as experienced by this child, should alert the physician to the likelihood of a lesion in the posterior fossa.

The differential diagnosis of ataxia includes congenital, infectious, toxic, neoplastic, metabolic, degenerative, and traumatic causes, most of which were not relevant to this child’s situation.

Diplopia occurs from malalignment of the visual axes, which may result from heterophoria, cranial nerve palsy, or proptosis. Other causes of double vision include increased intracranial pressure, pituitary or optic chiasm tumors, orbital tumors, other brain tumors, orbital cellulitis, and myasthenia gravis. General depression of cerebral function, as in alcohol intoxication, can cause dysconjugate gaze and diplopia. Monocular diplopia results from dislocation of the lens or a defect in the media or macula.

Making the Diagnosis
The first step in searching for the cause of this child’s ataxia and diplopia is to take a careful history, which will provide information that allows the clinician to focus on the most likely possible causes. Given his prior good health, normal growth and development, and family history devoid of anyone having ataxia, congenital causes were low on the list of possibilities. There was no history of mental status changes, seizures, headaches, or ingestions. There was no trauma history or any reason to suspect nonaccidental trauma. Infectious causes, such as labyrinthitis and acute cerebellar ataxia, as well as mass lesions, remained most likely. The initial search was for a posterior fossa tumor or mass lesion affecting the cerebellum and compressing cranial nerve IV or VI, leading to diplopia, with increased intracranial pressure causing the vomiting.

Neuroimaging is essential in evaluating any child suspected of having an intracranial tumor or mass lesion. CT reveals acute intracranial trauma, cerebral edema, hemorrhage, and hydrocephalus. MRI is superior to CT for detecting the age of hemorrhages, structural abnormalities in the posterior fossa, and brainstem anomalies. It also is useful in delineating the relationship between vascular malformations and the surrounding neural structures. On MRI, AVMs typically appear as several dilated and tortuous arteries supplying a tangled vascular mass, from which one or more draining veins emerge.

It should be noted that signs and symptoms can vary with any posterior fossa lesion, whether AVM or tumor.

The Condition
AVMs are congenital communications of dilated, thin-walled arteries and veins that characteristically lack connecting capillaries and can occur in many organs. Symptomatic AVMs are detected at a rate of approximately 1 per 100,000 person-years. AVMs may be found in several areas of the brain, including the cerebrum, corpus callosum, cerebellum, basal ganglia, and brainstem.

The most common presenting signs of intracranial AVMs are manifestations of hemorrhage or seizures, although more subtle findings such as headache and focal neurologic deficits also may be presenting signs and symptoms. Fifty percent of intracranial AVMs present with rupture of the fragile abnormal vessels. The risk of hemorrhage is 2% to 4% per year. The average risk of death after an initial rupture of an AVM is 10%. This risk escalates with each subsequent hemorrhage. The incidence of a new neurologic deficit occurring with each hemorrhage is approximately 50%.

The prognosis depends largely on the size and the location of the mass and its accessibility to surgical correction. Persistent neurologic dysfunction is a risk of both AVM hemorrhage and its surgical correction. Younger patients may have a lower degree of risk due to their potential for reorganization of the brain.

Treatment
Microsurgical removal of this patient’s AVM was undertaken, with successful resection of the abnormal vessels. This technique is used most
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commonly to remove AVMs that have hemorrhaged or caused seizures. Other therapeutic techniques include endovascular embolization and radiotherapy. Endovascular embolization is performed by introducing thrombosing agents that block blood flow through the abnormal vessels. This technique can reduce the size of the malformation but rarely accomplishes total obliteration. Embolization often is used in combination with surgery or focused radiation. Radiosurgery can be effective in treating AVMs smaller than 3 cm in diameter. Gamma knife, proton beam, or linear accelerator methods can deliver high-beam radiation directly to the AVM noninvasively, with minimal effects on the surrounding normal tissue.

Lessons for the Clinician
Although the differential diagnosis of ataxia includes almost every organ system, a careful history and physical examination can narrow the choices significantly. The clinician must search for other symptoms and signs of increased intracranial pressure in any child who presents with vomiting and neurologic dysfunction. This search should involve eliciting a history of headaches, examining the eyes for papilledema, testing the gait, and monitoring vital signs. If a brain lesion is suspected, neuroimaging is essential, and the clinician should obtain an MRI quickly, if possible, or CT if MRI is not available. (Therese M. Marren, MD, Edward J. Epstein, MD, University of California Medical Center at San Diego, San Diego, CA)

Case 2 Discussion
The patient’s prolactin level was 120 ng/mL (120 mcg/L) (normal, 1 to 20 ng/mL [1 to 20 mcg/L]). MRI of her head revealed a 1-cm low-signal area in the midline extending eccentrically to the left, consistent with an adenoma within the pituitary fossa. Cabergoline was administered to treat the presumed prolactinoma. The prolactin level normalized, and menses resumed after initiation of therapy.

The Hormone
Prolactin is a hormone that is produced and stored by the anterior pituitary gland. It stimulates milk production after childbirth and the production of progesterone by the corpus luteum. Prolactin is produced intermittently, with peak production occurring during sleep. Secretion is inhibited by dopamine concentrations. As the dopamine level rises, the prolactin level falls. Excessive prolactin secretion may cause galactorrhea.

Hyperprolactinemia occurs in normal states, including during pregnancy and the initial postpartum period, when there is stress, with breast stimulation, after eating, and with exercise. It is seen with the use of drugs such as risperidone, phenothiazines, amitriptyline, cimetidine, and haloperidol. Hypothyroidism, polycystic ovary syndrome, pituitary tumor, hyperplasia of lactotropes, and hypothalamic disease are among the endocrinologic causes of hyperprolactinemia. Chronic renal disease, renal and bronchogenic carcinomas, herpes zoster, atopic dermatitis of the chest, and chest wall trauma are other causes. In some patients, hyperprolactinemia is idiopathic.

The Underlying Cause
Prolactinomas are pituitary tumors that produce prolactin. They are the most common type of pituitary tumor in adolescents but occur frequently in children and are more common in women than men. Males more often have a macroadenoma at presentation. Prolactinomas in females of reproductive age may become symptomatic earlier because of the disruption of normal menses and presentation with amenorrhea.

Clinical Presentation
The functional effects of a prolactinoma result from increased serum concentrations of prolactin and from the mass effect of the tumor on nearby structures and pituitary function. The mass effect of the tumor can suppress gonadotropin secretion as well as locally compress or destroy pituitary tissue. This destruction may create other hormonal effects, including growth changes and delayed or arrested puberty.

Prolactinomas are rare in prepubertal children and may present with headache, visual problems, and growth failure. Pubertal women display amenorrhea, galactorrhea, headache, halted pubertal development, and rarely, visual problems. Pubertal men who have prolactinomas may present with headaches, visual disturbances, gynecomastia, and hypogonadism.

Diagnosis
Clinical evaluation of a patient who has secondary amenorrhea should include discussion of menstrual history, pregnancies, drug use, acne, hirsutism, symptoms of thyroid disease, headaches, and vision difficulties. The physical examination should focus on signs of thyroid disease, hirsutism, visual field defects, breast discharge, funduscopic findings, neurologic signs, evidence of androgen excess, and vaginal estrogenization.

Hyperprolactinemia may indicate a range of problems, including pituitary hyperplasia, tumors, and cysts. A pituitary tumor is suggested by blood prolactin levels greater than 100 ng/mL (100 mcg/L). The level of serum prolactin often corresponds...
to the size of the prolactinoma. A large tumor associated with minimal elevation of prolactin is consistent with a nonprolactin-secreting tumor causing pituitary stalk compression. Insulin-like growth factor-1 concentrations should be measured if acromegaly is present. Other neuroendocrine testing is indicated for macroprolactinomas and preoperatively. Estrogen status should be evaluated because of the risk of low bone density in patients who have hyperprolactinemia and low serum estradiol levels.

Pituitary lesions are visualized best by using MRI, which allows clear views of the pituitary region and depicts anatomy of the region in three dimensions. Prolactinomas are classified based on diameter as either microadenomas (<1.0 cm) or macroadenomas (1.0 cm).

Management
Several different strategies are employed to control growth of prolactinomas, to reverse or halt deleterious hormonal effects, and to restore vision and menses. The modality used is based on the clinical presentation. Important considerations include tumor size, estrogen status, presence or absence of galactorrhea, contraception use, and desire for fertility.

Medical management employing dopamine agonists is the treatment offered most commonly for macroadenomas. A lack of treatment risks an increase in the size of the tumor, pituitary dysfunction, and visual problems. Common dopamine agonists include bromocriptine and cabergoline. These medications decrease tumor volume and prolactin concentrations. They also are effective in treating estrogen deficiency, promoting fertility, and stopping galactorrhea. Although tumor size generally is reduced with these medications, dopamine agonists must be used continuously. The primary disadvantages of bromocriptine are nausea, emesis, headache, fatigue, and postural hypotension. Cabergoline requires administration only once or twice per week and has fewer adverse effects than bromocriptine.

Teenagers who have microadenomas may be estrogen-deficient, which creates a high risk for bone loss. These patients usually are treated with dopamine agonists to restore normal menses. Some patients can discontinue dopamine agonists after 2 to 4 years of therapy. Treatment with cyclic conjugated estrogens and medroxyprogesterone or low-dose oral contraceptives may be an alternative, but close follow-up is required. Patients desiring pregnancy are treated with bromocriptine or cabergoline. Dopamine agonists should be stopped once the patient becomes pregnant. Patients having microadenomas are unlikely to experience adverse effects, but those having macroadenomas may have a more complicated pregnancy course. After delivery, prolactin levels decline and breastfeeding may occur; patients may need to resume dopamine agonist medications.

If a patient cannot tolerate the adverse effects of dopamine agonist medication, if the tumor grows or fails to shrink after a medication trial, if the patient has visual loss and chiasmal compression, or if sudden pituitary failure occurs, clinicians may consider surgery. Transsphenoidal surgery is the favored surgical strategy for prolactinomas. Radiotherapy is used infrequently to treat prolactinomas. When used, it is reserved for large prolactinomas that have failed to respond to medical and surgical therapy.

Lessons for the Clinician
When evaluating a patient who has secondary amenorrhea, it is important to look for hyperprolactinemia. Prolactinomas are diagnosed by serum prolactin testing and radiologic studies and usually are treated with dopamine agonist medication. Long-term follow-up includes monitoring prolactin levels as well as performing serial examinations and MRIs. Treatment may need to be lifelong, but it can afford patients more comfortable lives. (Stacey Maslow, MD, Southboro Medical Group, Framingham, MA)

Case 3 Discussion
CT of the abdomen showed ovarian enlargement, small peripheral follicles, and some intraperitoneal fluid. These findings were consistent with the diagnosis of ovarian torsion. At surgery, the right ovary and fallopian tube were found to be tor sed and infarcted. A large, hemorrhagic follicular cyst occupied the right ovary.

Abdominal pain is the most common chief complaint of patients seen in pediatric emergency departments. The causative condition often is obscure, with an unconfirmed or uncertain diagnosis reported in more than 40% of patients.

Ovarian torsion is a well-known yet poorly recognized clinical entity that can involve the fallopian tube, ovary, and ancillary structures. It is the fifth most common gynecologic emergency, with a reported incidence of 3% in one series of acute gynecologic complaints. However, the diagnosis of ovarian torsion often is missed. The diagnosis is delayed in most affected patients because of failure to consider this condition, which can have nonspecific clinical findings.

Pathophysiology
Adnexal torsion typically is associated with a mass such as a cyst, which is most likely, or a benign or malignant tumor. Functional ovarian cysts

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in children usually develop following hormonal stimulation that occurs during two peak periods: the first year of life and around the time of menarche. Even cysts that occur normally with ovulation may cause ovarian enlargement and predispose to torsion, as can large hemorrhagic cysts. It is believed that the increase in the weight and the size of the ovary may alter the anatomy of the fallopian tube and cause twisting.

Adnexal torsion presents as severe sudden pain due to twisting of the ovary, the fallopian tube, or a para-tubal cyst. The most common form of torsion involves the ovary and the distal aspect of the fallopian tube, wherein the ovary rotates on its pedicle and compromises the blood supply. Torsion of the ovary initially interferes with the venous and lymphatic circulation. If unrelied, torsion of the ovary progresses rapidly to occlusion of the arterial circulation, which may be irreversible and lead to necrosis. Because necrosis can lead to loss of fertility, infection, sepsis, and death, torsion is considered a surgical emergency.

Clinical Features
The symptoms and signs associated with ovarian torsion are variable, often nonspecific, and can be misleading. The classic history in ovarian torsion is the abrupt onset of colicky pain in a lower quadrant, with radiation to the flank or groin that mimics renal colic. The pain associated with torsion is acute, severe, and unilateral. Most patients have nausea, vomiting, and lower quadrant pain, but these findings are associated with many other abdominal causes of pain and are not specific for ovarian torsion. Objective findings also are variable and rarely impressive in patients experiencing ovarian torsion. This paucity of objective findings may suggest the need to consider ovarian torsion. Patients who have ovarian torsion generally present without fever and have a normal white blood cell (WBC) count and differential count, although some may have an elevated WBC count or low-grade temperature. The patient may describe a prior history of similar episodes.

The ability to diagnose adnexal torsion depends on the physician’s consideration of the condition in the differential diagnosis, which is especially important when a patient has an ovarian mass. It is important to remember that even if the patient is pregnant, ovarian torsion still may occur. Ovarian torsion has been reported in patients who underwent untwisting of the ischemic adnexa when they were 6 to 20 weeks pregnant. It also is very important in pregnant patients to differentiate torsion from an ectopic pregnancy, which can present as severe abrupt pain and an adnexal mass.

Differential Diagnosis
The first priority in evaluating a child who has abdominal pain is to determine if he or she requires immediate surgical intervention. Besides ovarian torsion, the differential diagnosis of acute lower abdominal pain in a girl must include acute appendicitis, ectopic pregnancy, intussusception, intestinal obstruction, and ruptured ovarian cyst. Significant pain also can be caused by renal stones, pelvic inflammatory disease, constipation, gastroenteritis, mittelschmerz, and urinary tract infection.

Ovarian torsion should be considered in patients who have moderate-to-severe unilateral adnexal pain and tenderness. In addition, an adnexal mass often is palpable. A history of prior torsion is important. Patients may present with recurrent episodes of pain over several months, which may be caused by incomplete torsions that resolve. It is important to realize that prepubertal girls can experience torsion of the ovary; the clinician should not discount this condition in a young girl who has a compatible clinical picture.

Gastroenteritis is the most common cause of abdominal pain not requiring surgery; appendicitis is the most common cause for which surgery is necessary. Acute appendicitis is the condition misdiagnosed most frequently in patients who have adnexal torsion. In many cases, torsion is indistinguishable from acute appendicitis on clinical grounds. Initially, patients who have appendicitis often report poorly defined, constant pain in the periumbilical region. As the disease progresses, the pain shifts from the periumbilical region to the right lower quadrant. Anorexia, nausea, vomiting, and fever often follow the pain. The differentiation of appendicitis from adnexal torsion often requires imaging studies.

It is difficult to diagnose ectopic pregnancy accurately by history and physical examination alone. Abdominal pain associated with amenorrhea is the most common presenting complaint. Diagnostic accuracy has improved with the combination of serum quantitative beta-human chorionic gonadotropin assays and transvaginal ultrasonography.

Laboratory Testing
General laboratory studies usually are not helpful in diagnosing ovarian torsion, but they may help to diagnose other conditions. A pregnancy test must be performed in the emergency department on all female patients of reproductive age who have abdominal pain, regardless of their sexual or menstrual history, which may be unreliable. In a variety of situations, it is essential that clinicians consider adolescent girls pregnant until they have been tested. Ec-
Pregnancy is a fatal condition without intervention and is the leading cause of death in the first trimester of pregnancy. A pregnant patient having abdominal pain must be considered to have an ectopic pregnancy until proven otherwise.

This patient had microscopic hematuria, which has been noted in several case reports of adnexal torsion. The hematuria may be related to the retroperitoneal inflammation associated with torsion, similar to what occurs in cases of retroperitoneal appendicitis.

Ultrasonography is the primary modality used to diagnose torsion and reveals the affected ovary, usually as a uniformly echogenic mass. Sonographic findings consistent with torsion include a solid, cystic, or complex pelvic mass with or without a fluid collection in the pouch of Douglas. A more specific finding is the demonstration of multiple follicles (8 to 12 mm in size) in the cortical portions of a unilaterally enlarged ovary. This finding is attributed to the transudation of fluid into the follicles as part of the congestion of the ovary that results from circulatory impairment. Sonographic identification of a normal ovary in its normal position may help to exclude the diagnosis of torsion. Because most cases of torsion are due to large ovarian cysts or masses, the finding of a normal-size ovary makes adnexal torsion unlikely.

Doppler ultrasonography commonly is used to evaluate suspected adnexal torsion. When torsion is present, the lack of blood flow on Doppler examination probably indicates that an ovary is beyond salvage.

CT often reveals a complex ovarian mass and can demonstrate or exclude other abdominal and pelvic disease, such as appendicitis. However, the definitive diagnosis and management of torsion require laparotomy.

Management
Prompt diagnosis is important both to establish the diagnosis and to increase the rate of salvage of the ovary. An ovarian salvage rate of less than 10% has been reported. The interval between the onset of symptoms and the necrosis of adnexal structures is not known, but in the case of testicular torsion, irreversible changes may occur after only 4 hours. Early surgical intervention is required in both entities to preserve fertility.

Treatment of ovarian torsion mandates early surgical exploration and may require unilateral salpingo-oophorectomy. When the diagnosis remains unclear, laparoscopy can assist in making the diagnosis. Laparoscopy often is performed when an adnexal mass is not demonstrated on physical examination or on imaging studies and the diagnosis is unclear. Salpingo-oophorectomy may be necessary if there is evidence of necrotic tissue and was the treatment of choice for all torsions in the past; however, multiple studies support the concept of untwisting non-necrotic adnexa if possible. When unilateral torsion is diagnosed, oophoropexy (plication) of the contralateral adnexa may be indicated.

Lessons for the Clinician
Ovarian torsion is a cause of acute abdominal pain that requires prompt surgical intervention and always should be considered in the differential diagnosis of a girl who has acute abdominal pain. Considering torsion is especially relevant when evaluating patients who are being observed for the possibility of appendicitis. Early diagnosis of adnexal torsion is imperative to preserve fertility. Time is critical when ovarian torsion is present. A high level of clinical suspicion and expeditious imaging may decrease the surgical delay and improve the likelihood of ovarian salvage. (Muhammad Waseem, MD, Sandhya Ganti, MD, Joel Gernsheimer, MD, Lincoln Hospital, Bronx, NY)
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