PEARL
Anorexia and emaciation result from various conditions, including digestive diseases, metabolic disorders, chronic inflammation, chronic infections, malignancies, and psychiatric problems. Intracranial tumors can also cause a reduction in food intake, thus mimicking anorexia nervosa, through various mechanisms. Fourth ventricular tumors, particularly hemangioblastomas, can cause prolonged appetite loss and extreme body weight loss, without any apparent focal neurologic deficits.

OY-STER
Screening for brain tumors is imperative in cases of anorexia and emaciation because a serious delay in the diagnosis of brain tumors may lead to poor outcomes.

INTRODUCTION
Intracranial tumors may cause anorexia and subsequent extreme body weight loss. In patients with anorexia and emaciation, examinations usually start with exploration to identify gastroenterological problems because these are much more common than brain tumors. This tendency is even more pronounced if the primary symptoms are anorexia and extreme body weight loss, without any focal neurologic deficits. However, this approach can result in serious delay in the treatment of brain tumors and lead to worse outcomes.

We describe 2 cases of patients presenting with appetite loss and emaciation in whom the lack of focal neurologic deficits delayed the diagnosis of cerebellar hemangioblastoma as the underlying disease process. One of these 2 patients suddenly collapsed and eventually died, despite an emergency surgery. A retrospective analysis identified 5 additional cases of cerebellar tumor cerebellar tumor that presented with prolonged anorexia and emaciation as the sole complaint. We shed light on the high incidence of prolonged appetite loss among patients with cerebellar hemangioblastomas, and propose that screening for cerebellar tumors should be considered in patients with otherwise unexplained anorexia and emaciation, to prevent delay in treatment.

CASE REPORTS
Case 1. A 75-year-old woman had an 8-month history of progressive anorexia and marked weight loss. She visited a gastroenterologist with a complaint of food aversion and underwent thorough workups repetitively over months, including upper and lower endoscopic examinations and serologic studies for anorexia. All studies failed to show any abnormal findings. She had no history of psychological problems. She had lost more than 15 kg over 6 months, had become less active, and was eventually unable to ambulate. When she was admitted to our hospital for pneumococcal pneumonia and lethargy, her body weight was 32 kg and her body mass index was 15.2. Although she was slightly drowsy, detailed neurologic examinations failed to detect any focal deficits, such as lower cranial nerve dysfunctions or dysphagia. She presented no sign or symptom of hydrocephalus, such as headache, vomiting, or papilledema. MRI revealed a 5-cm cystic tumor (figure, A). The mass had a mural nodule in the posterior wall of the cyst and compressed the brainstem posterolaterally. She had a suboccipital craniotomy and total resection of the mural nodule. Postoperatively, she regained her appetite immediately and returned to a normal lifestyle after rehabilitation. No sign of recurrence was noted at the 15-month follow-up after surgery.

Case 2. A 21-year-old woman had a 6-month history of nonspecific appetite loss. Although she consulted a gastroenterologist and underwent multiple examinations for anorexia, all results were negative. She gradually lost 13 kg over 6 months, as her anorexia aggravated. She had to quit her job because of general weakness. She also visited an otolaryngologist for her occasional feeling of dizziness, but the symptom was mild and was deemed attributable to the rapid body weight loss. She had no headache, ataxia, or precedent symptoms suggestive of hydrocephalus. Subsequently, it was recommended that she consult a psychiatrist, and she was started on antidepressant medications. Six months after the onset of her anorexia, she suddenly collapsed at home and had a respiratory arrest. She was taken to the emergency room of our hospital. She...
was unconscious and her pupils were bilaterally dilated. A head CT scan performed on admission revealed a large cystic mass in the fourth ventricle that caused obstructive hydrocephalus (figure, B). Emergency craniotomy and tumor resection with ventricular drainage were performed, but she did not respond to the treatment and died 1 week after admission. The pathologic diagnosis was hemangioblastoma.

DISCUSSION Anorexia and emaciation can be caused by various conditions, including digestive diseases, metabolic disorders, chronic inflammation, chronic infections, malignancies, CNS disorders, and psychiatric problems. Intracranial tumors can also cause a reduction in food intake, thus mimicking anorexia nervosa, through various mechanisms. For example, large brain tumors can increase intracranial pressure and induce chronic headache or nausea, resulting in food aversion. Meningiomas and schwannomas located around the lower cranial nerves often cause dysphagia, resulting in reduction of food intake. In addition, hypothalamic tumors can trigger anorexia, which is specifically known as diencephalic syndrome in pediatric patients. Diencephalic syndrome is characterized as profound emaciation with normal caloric intake, absence of cutaneous adipose tissue, locomotor hyperactivity, euphoria, and alertness.

In addition to these conditions of secondary reduction of food intake, recent studies also revealed that brain tumors can directly cause a dysfunction of the center of appetite. The right frontal and temporal lobes have also been reported as being involved in the development of anorexia. These hemispheric lesions are frequently accompanied by locoregional symptoms, such as epilepsy and obsessive-compulsive disorder.

As observed in our cases, however, when the patient exhibits anorexia alone, a serious delay in diagnosis can occur. We reviewed the medical records pertaining to tumors located in the posterior fossa, as well as their clinical progression. Between October 1996 and August 2013, 159 patients with tumors in the posterior fossa, including 77 schwannomas, 22 hemangioblastomas, 21 meningiomas, 21 metastatic tumors, 12 gliomas, and 6 tumors of other types, underwent surgical resection at our institution. Among these 159 patients, 5 patients (4 cases of hemangioblastoma and 1 case of ependymoma) had prolonged anorexia and emaciation as their chief complaint before surgery, which represents a high incidence of prolonged anorexia in patients with cerebellar hemangioblastoma. We carefully excluded the patients with hydrocephalus-related symptoms. We also reviewed the English literature and found 7 cases of brain tumors of the posterior fossa with symptoms that mimicked anorexia nervosa (table e-1 on the Neurology® Web site at www.neurology.org). Four of the 7 cases were hemangioblastomas, and 6 of the 7 tumors were located in the fourth ventricle, suggesting a strong correlation between tumor location and the etiology of anorexia. The recent literature reports accumulating evidence that satiety is controlled by the brainstem. The information regarding satiety converges in the nucleus tractus solitarius, which integrates sensory information from the gastrointestinal tract and abdominal viscera. The nucleus tractus solitarius is located in the dorsal part of the medulla oblongata, close to the floor of the fourth ventricle, which may account for the observation that tumors located in the fourth ventricle can theoretically cause dysfunction of the nucleus.

Based on our data and the previous literature, hemangioblastomas appear to have an increased tendency to cause anorexia compared with other types of tumor. A study of 44 patients with von Hippel–Lindau disease with hemangioblastomas reported that 2 patients (3.9%) presented with anorexia before surgery. A plausible explanation for the higher incidence of anorexia in hemangioblastomas would be that these tumors frequently arise in the dorsal region of the brainstem and lead to direct compression of the floor of the fourth ventricle. In addition, the slow growth of hemangioblastomas based on their benign biological nature may account for their characteristic insidious progression with minimal neurologic deficits, which may also lead to a diagnostic delay. Table e-1 demonstrates that the average period for the establishment of a proper diagnosis of cerebellar tumors is 4.6 years. A critical delay based on the misdiagnosis of cerebellar tumors can result in a life-threatening situation, similar to that described in case 2. Slow-growing lesions close to the fourth ventricle resulting in a significant compression of the floor of the fourth ventricle, such as...
hemangioblastomas, can lead to the development of anorexia and emaciation.

AUTHOR CONTRIBUTIONS
Dr. Oya: conception and design, acquisition of data, analysis and interpretation of data, drafting of the article, revising the submitted version of the manuscript. Dr. Nejo: acquisition of data, critically revising the article, revising the submitted version of the manuscript. Dr. Indo: critically revising the article, revising the submitted version of the manuscript. Dr. Matsui: critically revising the article, revising the submitted version of the manuscript, administrative/technical/material support.

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