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Case Report

Panhypopituitarism diagnosed in adulthood: Imaging findings of bone and other organs ☆

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ABSTRACT

A 38-year-old man who was delivered in a breech position presented with delayed development of secondary sexual characteristics and malaise. He was diagnosed with panhypopituitarism caused by interruption of the pituitary stalk due to perinatal complications. Brain magnetic resonance imaging findings for pituitary stalk interruption syndrome are well-documented; however, reports of the imaging findings of the bones and several organs related to the effects of panhypopituitarism are limited. In this patient with anterior pituitary dysfunction, imaging revealed diverse sequelae, including delayed skeletal maturation, osteopenia, genital atrophy, fatty liver, and adrenal atrophy. Radiologists may find it difficult to discern complex imaging findings unless they are informed of the clinical course of the patient. Therefore, radiologists should coordinate with clinicians to arrive at a diagnosis.

Introduction

Pituitary stalk interruption syndrome is known to cause panhypopituitarism. It is an extremely rare condition that is estimated to occur in only 0.5 per million live births. Pituitary stalk interruption syndrome is reportedly associated with breech presentation and difficult delivery [1]. Later in childhood, patients may experience symptoms such as short stature, reduced growth, seizures, hypotension, intellectual retardation, and delayed puberty [2].

Magnetic resonance imaging (MRI) findings of the brain in pituitary stalk interruption syndrome are well known; however, imaging findings of the bones and other organs in patients with panhypopituitarism are limited. Imaging findings of anterior pituitary dysfunction may reveal diverse sequelae, including delayed skeletal maturation, osteopenia, genital atrophy, fatty liver, and adrenal atrophy. Thus, radiologists may find it difficult to discern the complex imaging findings without prior knowledge of the clinical course. However, once clinical information on hormone depletion becomes available, each imaging finding can be interpreted to represent the

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diverse pathophysiology of anterior pituitary hormone depletion. Herein, we report the case of a 38-year-old man who presented with a chief complaint of delayed development of secondary sexual characteristics and malaise.

Case report

A 38-year-old man presented with delayed development of secondary sexual characteristics and malaise. He was born prematurely, 1 month before the due date, and was delivered in a breech position. He had a history of rubella at age 5. He developed hyperlipidemia at age 20. He experienced angina pectoris at the age of 38 and was on medical treatment. He was described as small and physically weak throughout his childhood. His height was approximately 140 cm in junior high school, 150 cm in high school, 160 cm at 18 years of age, and 168 cm at 20 years of age. However, at age 38, he had grown to be 175 cm tall, and he continued to grow after puberty. His pulse was bradycardic at 58 beats/min, and his blood pressure was low at 87/45 mm Hg. His body weight was 48 kg. Examination at presentation revealed that his voice had not broken and that he had no pubic or axillary hair, and he had nonpalpable testes. In addition, the body was rounded in shape. An endocrinological evaluation revealed central hypoadrenal function, hypothyroidism, hypogonadism, and growth hormone deficiency, leading to the diagnosis of panhypopituitarism. Genetic analysis revealed no abnormalities.

Brain MRI revealed an ectopic posterior pituitary lobe with no continuity of the pituitary stalk (Fig. 1). The patient had a history of pelvic delivery, and interruption of the pituitary stalk was presumed to be the causative lesion of hypopituitarism. A diagnosis of panhypopituitarism was made based on obstetric complications.

Pelvic radiograph reveled the absence of closure of the growth plates of the femoral head or greater tuberosity, and irregularities of the diaphysis and epiphysis. An abnormal elongation of the femoral neck with coxa valga was observed, as well as irregularities of the acetabulum, pubic symphysis, and sacroiliac joints. Apophyses were not visible, and irregularities were observed in the iliac crest. The ischiopubic synchondroses were fused. In addition, pelvic radiograph revealed reduced bone density (Fig. 2).

Due to the patient's financial situation, only corticosteroids, thyroid hormone compensatory therapy, and hyperlipidemic medication were initiated. Bone mineral density analysis was not conducted. Nevertheless, the patient's fatigue improved, blood pressure increased to 128/59 mm Hg, and pulse increased to 101 beats/min.

Four years after treatment, he underwent an abdominal computed tomography (CT) scan due to abdominal pain.

The cause of his discomfort remained unclear; however, ileal edema (not shown) and gas were observed in the portal vein (Fig. 3A, B), which improved with conservative treatment.

The CT scan also revealed several health concerns, including a fatty liver, bilateral adrenal atrophy, and atrophy of the internal genitalia (seminal vesicles, testes, and prostate) and external genitalia (penis) (Fig. 3A-F). In addition, the apophyses were absent, and irregularities were observed in the iliac crest. Irregularities of the acetabulum were also noted (Fig. 3G). The apophysis of the sciatic tuberosity was not fused (Fig. 3H); however, the ischiopubic synchondroses were fused. Furthermore, the spine showed signs of platyspondyly, and irregularity of the upper and lower margins of the vertebral body and neurocentral synchondrosis were apparent (Fig. 3G, I, J). Calcification of the costal cartilage was poor (Fig. 3A). CT scout image revealed a rounded body shape with decreased muscle mass (Fig. 3K).

Discussion

Patients with pituitary stalk interruption typically experience growth retardation in the first decade of life due to a deficiency in growth hormones [3]. This condition presents as an isolated growth hormone deficiency; however, it but may progress to multiple pituitary hormone deficiencies with the eventual development of panhypopituitarism with preservation of posterior pituitary function [2,4]. Pituitary stalk interruption syndrome is also associated with a higher-than-normal frequency of breech presentation and difficult delivery [5]. This patient also presented with short stature, fatigue, and delayed development of secondary sexual characteristics. We determined that the panhypopituitarism was caused by perinatal complications. Although the patient was not examined closely until adulthood, he was ultimately diagnosed with this condition. Imaging findings revealed delayed skeletal maturation, osteopenia, external and internal genital atrophy, fatty liver, and adrenal atrophy.

Delayed skeletal maturation

Damage to the anterior lobe of the pituitary gland during skeletal growth is associated with abnormal osseous development [6], including delayed appearance and growth of ossification centers and a similar delay in their fusion and disappearance. The growth plate may disappear eventually, although osseous fusion can still occur at an advanced age [6]. In the present case, these findings were revealed on a pelvic anteroposterior radiograph (Fig. 2) during the initial evaluation.

Estrogen is involved in the closure of the epiphyseal line in both sexes. In men, estrogen is produced from testosterone by the action of aromatase [7]. In our patient, who had delayed closure of the epiphyseal line, decreased secretion of luteinizing hormone and follicle-stimulating hormone caused a decrease in the levels of testosterone, which, in turn, decreased the levels of estrogen, subsequently delaying the closure of the epiphyseal line. Abnormal elongation of the femoral neck is associated with delayed epiphyseal line closure [8]. Findings of coxa valga and irregularities of the metaphysis, acetabular roofs, pubic symphysis, and sacroiliac joints were also observed, which are common abnormalities of the femur most commonly seen in children [9,10]. Although the patient was short in childhood owing to reduced growth hormone, he

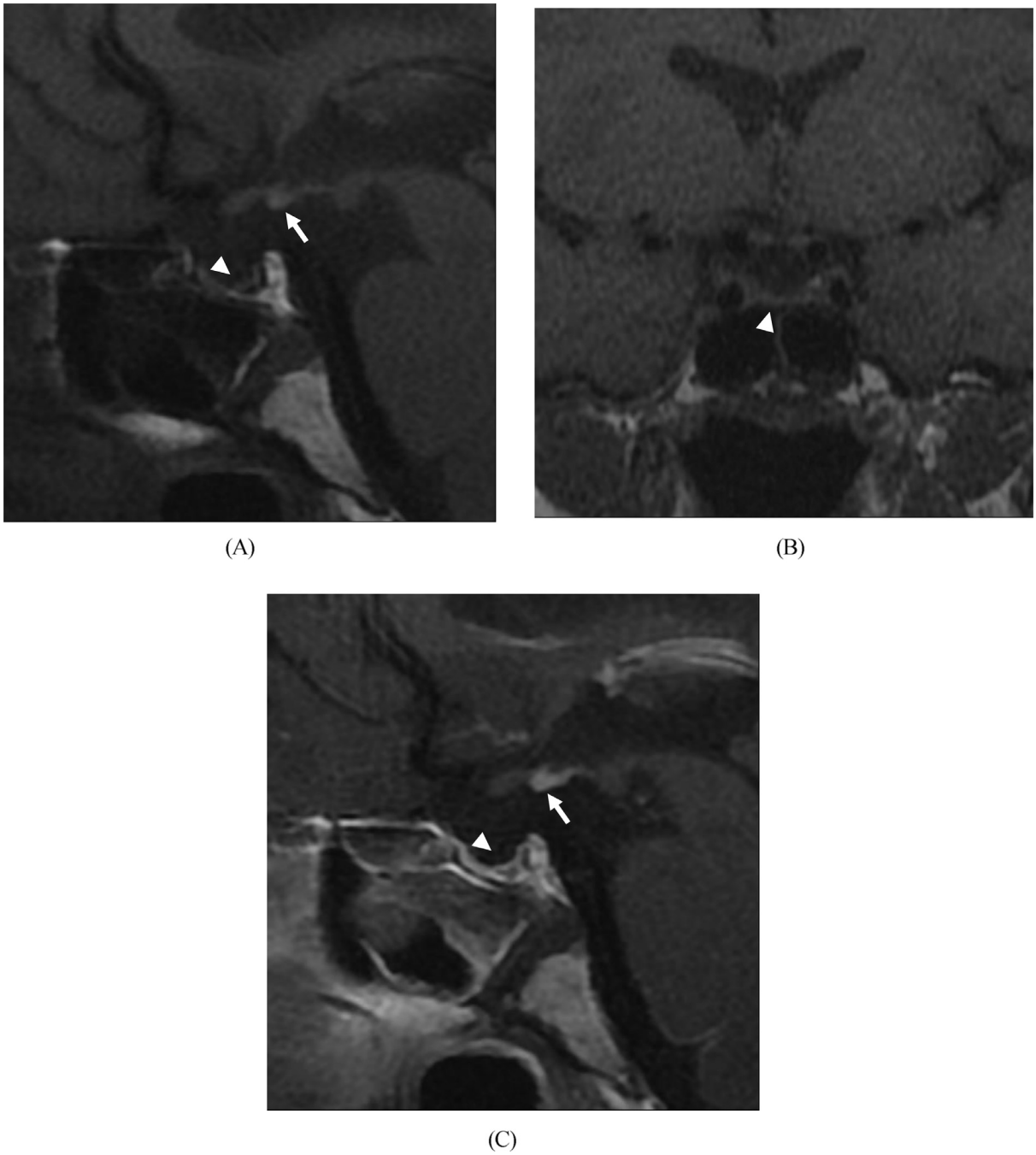


Fig. 1 – Panhypopituitarism in 38-year-old man presenting with delayed secondary sexual characteristics. Sagittal (A) and coronal T1-weighted magnetic resonance (MR) images (B) and contrast-enhanced sagittal T1-weighted MR image (C) at the time of initial evaluation. Sagittal (A) and coronal T1-weighted MR images (B) showing the pituitary stalk was absent and the pituitary gland (arrowhead) was very small and scarred. High signal (arrow) is seen in the median eminence, suggesting an ectopic posterior lobe. Contrast-enhanced T1-weighted images (C) showing ectopic posterior lobes (arrow) and pituitary gland (arrowhead).

continued to grow in stature after puberty and reached a normal height without treatment. Delayed epiphyseal line closure may have contributed to this condition.

Irregularities were observed in the upper and lower margins of the vertebral body in the spine (Fig. 3G, H), and the neurocentral synchondrosis was found to be age-inappropriate (Fig. 3J). These are morphologies commonly observed in the bones of children and findings that indicate delayed bone maturation [11]. Platyspondyly is observed in several diseases, including hormonal abnormalities, such as panhypopituitarism and hypothyroidism, and skeletal dysplasia, such as achondroplasia [12].

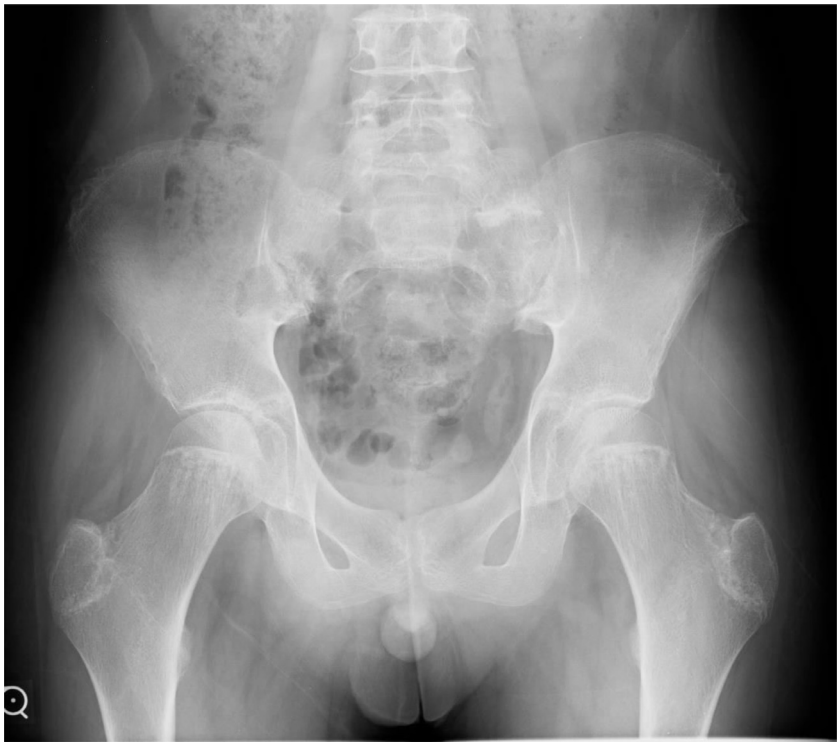


Fig. 2 – Panhypopituitarism in 38-year-old man presenting with delayed secondary sexual characteristics. Pelvic anteroposterior radiograph at the time of initial evaluation shows no closure of the growth plates of the femoral head or greater tuberosity and irregularities of the metaphysis. Abnormal elongation of the femoral neck and coxa valga are observed. Irregularities of the acetabular roofs, pubic symphysis, and sacroiliac joints are seen. In the iliac crest, the apophyses are not seen and irregularities are observed. The ischiopubic synchondroses are fused. In addition, diffuse osteopenia is seen.

Osteopenia

The pelvic radiograph (Fig. 2) revealed reduced bone density, which is a known characteristic of osteoporosis observed in panhypopituitarism [13]. In men, estrogen may play an important role in the regulation of bone remodeling [14]. Decreased secretion of growth hormone may also play a role.

External and internal genital atrophy

Under the control of the pituitary hormones—luteinizing hormone and follicle-stimulating hormone—the Leydig cells located in the testes produce testosterone and germ cells are nurtured by Sertoli cells to divide, differentiate, and mature into sperm. During embryonic development, testosterone and dihydrotestosterone induce the Wolffian duct and virilization of the external genitalia. During puberty, testosterone promotes somatic growth and the development of secondary sexual characteristics. In adults, testosterone is necessary for spermatogenesis, libido, normal sexual function, and maintenance of muscle and bone mass [15]. Testosterone is also converted to dihydrotestosterone, which induces the formation of the prostate and the external male genitalia, including the penis, urethra, and scrotum [15]. The patient had low testosterone levels, which were caused by low levels of luteinizing hormone, resulting in delayed development of secondary sexual characteristics and poor development of both external and internal genitalia.

Fatty liver

The patient did not consume alcohol but was found to have progressive liver dysfunction. An abdominal CT scan revealed a fatty liver, and although a liver biopsy was not performed, nonalcoholic steatohepatitis (NASH) was clinically suspected. The most common factors involved in the development of NASH are obesity, particularly visceral obesity, and associated insulin resistance. Endocrine abnormalities are attracting attention as one of the causes of NASH. Adult patients with hypopituitarism and growth hormone deficiency demonstrate a high prevalence of NASH. The growth hormone-insulin-like growth factor-1 system plays a particularly important role [16]. It is suspected that the patient's fatty liver was caused by a decrease in the levels of growth hormone. He had also experienced hyperlipidemia and angina pectoris, possibly due to the reduced production of growth hormone.

Adrenal atrophy

The patient was found to have central hypoadrenalism during the endocrinological assessment. Central hypoadrenalism is characterized by secondary adrenal insufficiency, which is

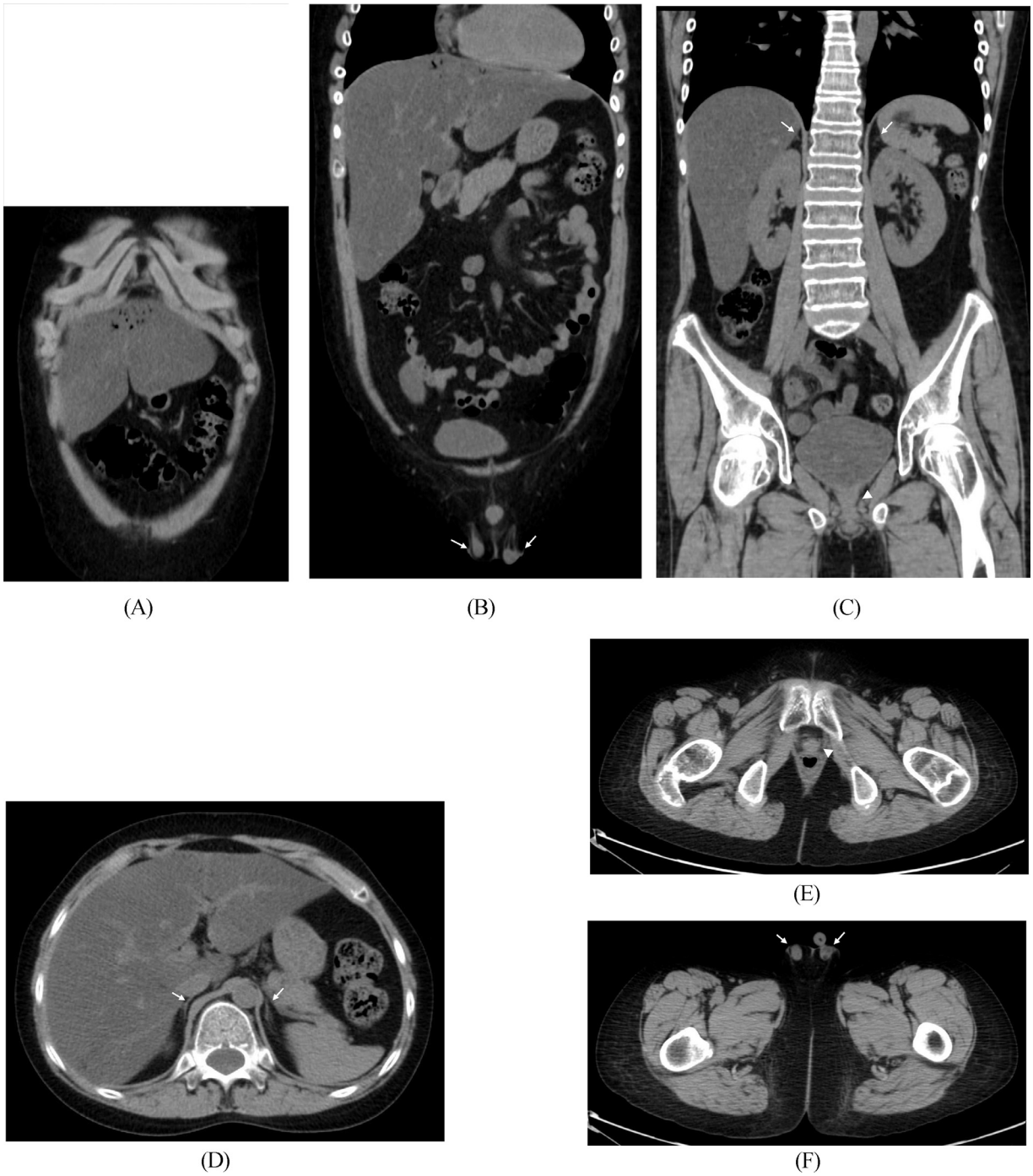
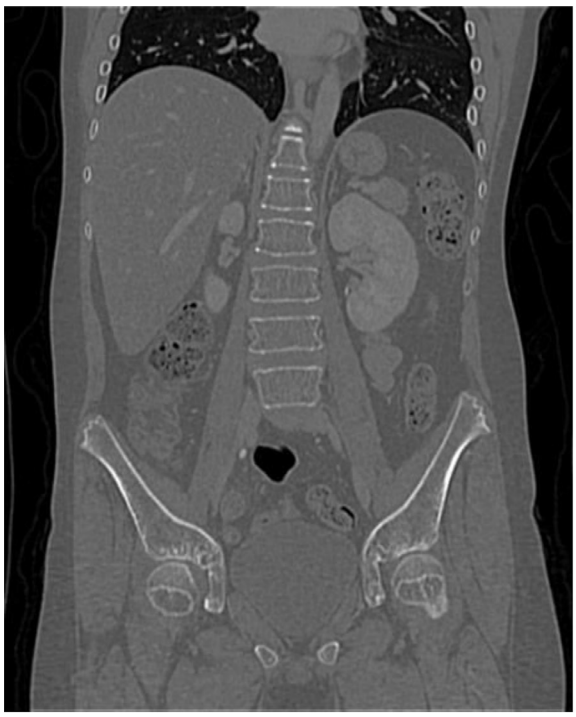
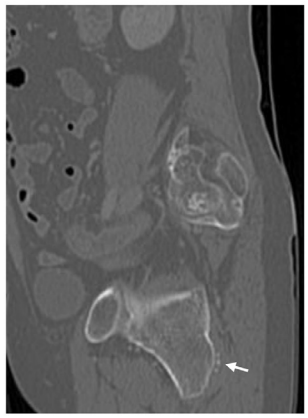


Fig. 3 – Panhypopituitarism in a 42-year-old man who underwent an abdominal CT scan for abdominal pain 4 years after treatment. Abdominal unenhanced (A-F), contrast-enhanced bone window (G-J) CT scans, and CT scout image (K) of the same patient. The cause of the abdominal pain is not clear, but portal venous gas (A, B) can be seen, which improved with conservative follow-up. The calcification of the rib cartilage is scarce for the patient's age (A). The CT scan revealed a fatty liver, bilateral adrenal atrophy (C, D arrow), prostate (C, E arrowhead), atrophy of the testes (F arrow), and penis (F). In the iliac crest, the apophyses are not seen and irregularities are observed (G). Irregularities of the acetabulum are also seen (G). The apophyses of the sciatic tuberosity are not fused (H arrow). In the spine, platyspondyly, irregularities of the vertebral body upper and lower margins (G, I) are observed and neurocentral synchondrosis is apparent for the patient's age (J). CT scout image shows rounded body shape with decreased muscle mass. Both femoral necks are abnormally elongated with coxa valga (K).



(G)



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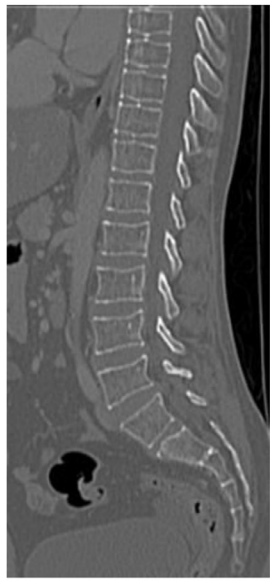
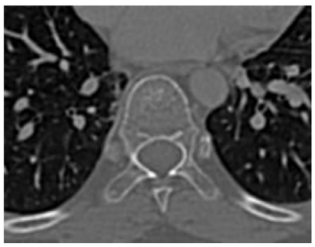
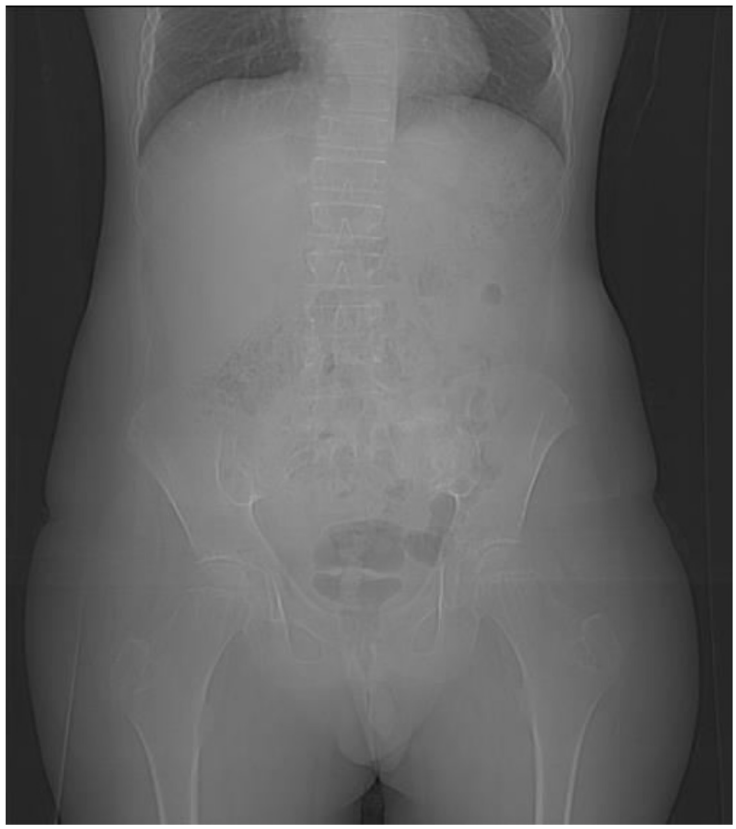


(I)



(J)



(K)

Fig. 3 – Continued

caused by a lack of stimulation of the adrenal gland by the pituitary gland. During the chronic stage, both adrenals appear small and atrophic as observed in this patient (Fig. 3C, D) [17]. This patient also showed bilateral adrenal atrophy on imaging. The patient had been taking corticosteroids for 4 years, which may have contributed to bilateral adrenal atrophy. Furthermore, adrenal insufficiency is also associated with atrophy of the male external and internal genitalia.

This case presented with a variety of imaging findings, which the radiologist initially struggled to interpret. Without prior knowledge of the patient's medical history of panhypopituitarism, the radiologist may have suspected other conditions, such as skeletal dysplasia or other systemic diseases. The imaging findings attributable to anterior pituitary dysfunction are diverse, including delayed skeletal maturation, osteopenia, external and internal genital atrophy, fatty liver, and adrenal atrophy. However, the complex consequences of low levels of anterior pituitary hormones were identified, making the imaging findings noteworthy. In particular, the abnormally elongated femoral neck with coxa valga is a notable imaging finding and was possibly caused by delayed bone maturation and epiphyseal line closure. Thus, radiologists must coordinate with clinicians to make an accurate diagnosis.

Patient consent

Written informed consent for the publication of this case report was obtained from the patient.

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