Association of Slipped Capital Femoral Epiphysis With Panhypopituitarism Due to Pituitary Macroadenoma: A Case Report

James B. Harris1*, Bhuvana Sunil, MD1*, Michael K. Ryan, MD2, and Giovanna Beauchamp, MD1

Abstract
Slipped capital femoral epiphysis (SCFE) commonly occurs in overweight or obese adolescents, but can also be associated with endocrine disorders including hypothyroidism, pituitary tumors, and growth hormone deficiency. In this article, we present a case of panhypopituitarism that initially presented with SCFE. A 16-year-old male presented with right SCFE. After a right hip open reduction and percutaneous pinning procedure, findings of skeletal maturity that lagged behind his chronologic age and a delayed Tanner stage resulted in a referral to an endocrine specialist. Endocrine laboratory evaluation identified elevated prolactin levels (1493 ng/mL), hypogonadotropic hypogonadism, and central adrenal insufficiency as evidenced by low morning cortisol level of 1.0 µg/dL. Magnetic resonance imaging revealed a large pituitary T2 isointense mass measuring 1.8 × 2.7 × 2.3 cm. The patient was diagnosed with panhypopituitarism due to a pituitary macroadenoma. Multidisciplinary collaboration for treatment of this patient consisted of oral cabergoline, oral levothyroxine, oral hydrocortisone therapy, intramuscular testosterone therapy, and a prophylactic closed reduction percutaneous pinning of the left hip due to high risk of also developing SCFE of the left hip. Panhypopituitarism should be considered as a diagnosis after atypical presentations of SCFE. In our case, an astute clinical assessment resulted in prompt endocrine referral and management of panhypopituitarism. Our report highlights the importance of multidisciplinary collaborations to guarantee early detection of endocrinopathies in patients with SCFE undergoing surgical interventions in order to avoid potential complications, such as adrenal crisis during surgery.

Keywords
SCFE, prolactinoma, endocrine disorders, pituitary tumor

Introduction
Slipped capital femoral epiphysis (SCFE) is defined as the posteroinferior displacement of the femoral epiphysis (head) from the metaphysis (femoral neck) through the epiphyseal plate (physise).1,2 The condition commonly occurs in adolescents, and the average age at onset is 12.7 years (13.5 in males and 12.0 in females).2 SCFE frequently presents in overweight or obese adolescents with groin/hip pain or knee pain that can be acute or chronic.2 Increased shear forces on the physis and weakness in the hypertrophic zone of the physis predispose individuals to SCFE.2,3 Reports have associated obesity and rapid growth of the physis during puberty as likely causes of SCFE in adolescents.4 Endocrine disorders, including hypothyroidism, pituitary tumors, and growth hormone deficiency, have also been associated with SCFE.3,5,6 To our knowledge, our patient is the youngest reported case to present with a combination of panhypopituitarism secondary to a functioning pituitary macroadenoma and SCFE. Our case illustrates the importance of considering

1University of Alabama at Birmingham, AL, USA
2Andrews Sports Medicine & Orthopaedic Center, Birmingham, AL, USA
4Joint first authorship.

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Corresponding Authors:
Giovanna Beauchamp, MD, University of Alabama at Birmingham, 1600 4th Avenue South, CPP 230, Birmingham, AL 35233, USA.
Email: gbeauchamp@peds.uab.edu

Michael K. Ryan, MD, Andrews Sports Medicine & Orthopaedic Center, Birmingham, AL 805 St Vincents Dr #100, Birmingham, AL 35205, USA.
Email: mkryanmd@gmail.com
secondary causes of SCFE prior to surgery, for an overall optimized management of these concomitant issues. It also emphasizes the importance of collaboration between orthopedics and endocrinology for early recognition and treatment of SCFE-related endocrinopathies.

Case Report

A 16-year-old male presented to an orthopedic clinic with a 1-week history of right knee pain that radiated to the right thigh, weakness of the right lower extremity, and a significant limp. There was no history of trauma. The patient reported constant, sharp pain that became worse with prolonged standing and walking. The patient was 165.1 cm tall (16th percentile, Z score = −1.01), weighed 81.6 kg (89th percentile, Z score = 1.23) with a body mass index of 29.9 kg/m² (96th percentile, Z score = 1.73). The physical examination determined a right hip flexion strength of 2+/5. Knee and lumbar spine radiographs were normal and demonstrated open physes. Notably, an anteroposterior (AP) X-ray of the lumbar spine revealed loss of disk height at vertebrae L1-2, and the right leg pain was thought to be secondary to lumbar radiculopathy. A plan was developed to start physical therapy, nonsteroidal anti-inflammatory drugs, and use of an assistive device for ambulation.

Two weeks later, the patient returned to the orthopedic clinic with persistent symptoms. Magnetic resonance imaging (MRI) of his lumbar spine was ordered and found to be unremarkable. Despite this, the patient remained reliant on a walker for ambulation and he reported continued pain that was worse with weight bearing, which had only mildly improved with conservative treatment. New hip radiographs revealed a severe SCFE with near-complete physeal dislocation (see Figure 1A). In the frog lateral pelvis radiograph, the right hip SCFE was determined to be severe due to a Southwick slip angle of 70° (angles >50° are considered severe with this classification). The duration of the pain suggested an acute or acute-on-chronic classification of SCFE. The patient was asked to come to the emergency department, where he was admitted and taken to the operating room for urgent fixation of a severe right hip SCFE with a physeal dislocation. The patient underwent a right hip open reduction and percutaneous pinning. The patient was admitted to the hospital and had a normal recovery. The patient was discharged 1 day after the procedure. The patient presented at 2-week, 6-week, and 3-month follow-up visits and was released to full weight bearing and started a return to golf and running protocol at the 3-month follow-up. Preoperatively, there was a concern for delayed puberty prompting endocrine referral.

From an endocrine standpoint, his initial physical examination was remarkable for undervirilization (Tanner 2 pubic hair, lack of facial and axillary hair, and scant

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Figure 1. (A) Anteroposterior radiograph of severe slipped capital femoral epiphysis with near-complete physeal dislocation. Note the posteroinferior displacement of the femoral epiphysis from the metaphysis through the physis (growth plate). (B) Anteroposterior radiograph after an open reduction and percutaneous pinning of the right hip and prophylactic closed reduction percutaneous pinning of the left hip. Cannulated screws are highlighted through the femoral metaphysis, physis, and epiphysis to correct the deformity and prevent further slippage.
body hair) relative to testicular volume (18 mL using the Prader Orchidometer). The patient denied presence of headache, vision changes, or galactorrhea. As shown in Table 1, evaluation of pituitary function was significant for (a) central hypothyroidism with a low free thyroxine level by dialysis (0.23 ng/dL) with an insufficient thyroid stimulating hormone response (5.7 mIU/mL), (b) hypogonadotropic hypogonadism with an undetectably low testosterone level with inappropriately low-normal gonadotropins (luteinizing hormone 0.3 mIU/mL and follicle-stimulating hormone 1.0 mIU/mL), and (c) central adrenal insufficiency as evidenced by low morning cortisol level of 1.0 µg/dL with poor peak response to high-dose cosyntropin stimulation test (4.8 µg/dL). The insulin-like growth factor 1 (IGF-1 or somatomedin C) level was low at 81 ng/dL. Bone age radiograph was significantly delayed (162 months) for his chronological age (201 months), which is >3 SD below the mean for age. These central (pituitary) defects were thought to be secondary to the mass effect caused by a prolactinoma, as the initial prolactin level was elevated at 1493 ng/mL. An MRI of the brain with and without contrast showed a large pituitary T2 isointense mass measuring 1.8 × 2.7 × 2.3 cm that infiltrated through the floor of the sella into the clivus posteriorly (Figure 2A). Suprasellar extension with superior displacement and mass effect on the optic chiasm and prechiasmatic optic nerves was noted, confirming the diagnosis of a pituitary macroadenoma.

Treatment was initiated with 0.25 mg twice weekly oral cabergoline, a long-acting dopamine receptor agonist with a high affinity for D2 receptors for the treatment of hyperprolactinemia. This is the gold-standard therapy for hyperprolactinemia, as prolactin secretion is normally inhibited by dopamine, released by hypothalamic tuberoinfundibular neurons. To treat the pituitary insufficiencies, oral levothyroxine 75 µg, 8 mg/m² oral hydrocortisone therapy, intramuscular testosterone therapy 100 mg monthly were also initiated. Within 8 weeks of starting therapy, his prolactin levels decreased to 272 ng/mL, and doses of cabergoline were titrated up to achieve further suppression of prolactin levels (see details in Figure 3).

The patient was at an increased risk of developing SCFE in the left hip due to his panhypopituitarism. The patient underwent a prophylactic closed reduction percutaneous pinning (CRPP) of the left hip, for which he received stress-dose steroids. A Synthes 7.3 mm fully threaded, cannulated screw was inserted through fascia and drilled into the left femoral neck into a center-center position. The patient was released with weight bearing as tolerated on the left hip. The patient presented to our clinic to follow-up for both his right and left hip. Imaging revealed that the physis was fused in the right hip due to his panhypopituitarism. The patient continues on cabergoline; he remains clinically well, but dependent on hormonal supplementation with levothyroxine and testosterone. His hypothalamic-pituitary-adrenal axis recovered, and he is no longer dependent on steroid therapy.

**Table 1.** Significant Laboratory Values and Interpretation.

| Laboratory parameter | Value   | Reference range | Endocrine interpretation |
|----------------------|---------|-----------------|--------------------------|
| Hemoglobin           | 11.6 g/dL | 12.1-14.5 g/dL  | A pubertal teenage boy should have higher hemoglobin and hematocrit levels secondary to testosterone mediated erythropoiesis |
| Hematocrit           | 33%     | 35-44%          |                          |
| Prolactin            | 1493 ng/dL | 2-18 ng/mL     | This degree of prolactin elevation is suggestive of a prolactin-producing pituitary adenoma |
| IGF-I                | 101 ng/mL | 153-542 ng/mL  | Stable downstream effect mediator of growth hormone whose levels vary throughout the day depending on diet and activity levels |
| Free thyroxine by dialysis | 0.23 ng/dL | 0.7-1.22 ng/dL | The low free thyroxine level should have prompted a higher elevation in the TSH levels; hence, this mildly elevated value is inappropriate |
| TSH                   | 5.7 mIU/mL | 0.5-4.8 mIU/mL |                          |
| AM cortisol          | 1.0 µg/dL | 6.2-19.4 µg/dL  | The low morning cortisol level should have prompted an elevation in the ACTH levels; hence, this normal value is inappropriate |
| ACTH                  | 13.0 pg/mL | 2.2-13.3 pg/mL |                          |
| LH                    | 0.3 mIU/mL | 0.79-4.76 mIU/mL | The low morning testosterone level should have prompted an elevation in the namely, FSH and LH; hence, these low values are inappropriate |
| FSH                   | 1.0 mIU/mL | 0.78-5.10 mIU/mL |                          |
| Testosterone          | < 3 ng/dL  | 188-882 ng/dL   |                          |

Abbreviations: IGF-I, insulin-like growth factor; TSH, thyroid stimulating hormone; ACTH, adrenocorticotrophic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

Discussion

The overall pathophysiology of SCFE is poorly understood. Our patient had several risk factors that predisposed him to the development of SCFE, including age, obesity, and panhypopituitarism. Adolescence is the time of peak growth velocity, and susceptibility to SCFE during this time is hypothesized to be secondary to several dynamics, including...
In our case, SCFE developed after a subjective growth spurt as typically described in the literature, but sexual hormones and IGF-1 levels were low secondary to panhypopituitarism. Smaller clinical reports have suggested that children with SCFE may have lower than expected values of gonadotropins, testosterone, thyroid and growth hormones in comparison with controls in the absence of obvious endocrine issues. Smaller clinical reports have suggested that children with SCFE may have lower than expected values of gonadotropins, testosterone, thyroid and growth hormones in comparison with controls in the absence of obvious endocrine issues. Our patient was obese, and the current understanding is that insulin resistance with hyperinsulinism may have an IGF-1 mimic effect on the IGF-1 receptor, increasing the susceptibility to SCFE. Obesity also results in elevated leptin levels and there has been an association with increased width of the proliferative zone with SCFE. Hypothyroidism has been the most frequently associated endocrine abnormality with SCFE. It has been proposed that hypothyroidism results in a heightened risk of SCFE through the proteins that might be involved in the regulation of pubertal growth because a reduced expression of Indian hedgehog–parathyroid hormone-related hormone causing altered regulation of chondrocyte differentiation and osteocyte maturation.
An astute clinical assessment resulted in the prompt endocrine referral and management of panhypopituitarism. Fortunately, this patient remained hemodynamically stable during his first surgery despite his adrenal insufficiency. Undiagnosed adrenal insufficiency can precipitate an adrenal crisis if not treated adequately prior to surgery. Therefore, multidisciplinary collaborations are crucial to guarantee early detection of endocrinopathies in patients with SCFE undergoing surgical interventions.

Prompt surgical treatment is the standard treatment for acute SCFE, and in the case of severe SCFE with epiphyseal displacement, emergent treatment is warranted due to risk of vascular compromise and eventual avascular necrosis (AVN) of the epiphysis. The optimal approach for this patient with severe, acute SCFE was open capsulotomy, joint hematoma evacuation, epiphyseal reduction, and percutaneous pinning. A previous study indicated that an open reduction and use of K-wires for fixation in an emergent setting is a safe and reliable treatment option. Good clinical outcomes from this technique are attributed to low rates of developing AVN and a reduced rate of secondary procedures to manage residual deformities. Approaching the case as an emergency reduces the time for AVN to develop due to vascular insufficiency from the femoral head instability. Phillips et al reported a lower risk of developing AVN in patients with SCFE who are treated within 24 hours of the onset of severe symptoms. Open reduction of the affected hip allows for a more accurate realignment of the epiphysis and metaphysis, and it allows for evacuation of the joint effusion, which has been reported to reduce the occurrence of AVN.

For an open reduction, anterior arthrotomy and longitudinal capsulotomy are performed to expose the proximal femur and hip joint. The effusion within the joint is evacuated before addressing the dislocation. A central K-wire is inserted through the greater trochanter to the metaphyseal border to assist with proper open reduction. The fingertip of the surgeon inside the capsule then guides the femoral neck as the affected leg is maneuvered until reduction is achieved. After successful reduction, the K-wire is advanced into the femoral head to stabilize the realigned epiphysis and metaphysis. The affected leg is then placed in the frog position and intraoperative radiographs confirm the reduction and placement of the K-wire. Once imaging confirms satisfactory reduction of the hip and proper alignment of the K-wire, fully threaded, cannulated screws are inserted along the trajectory of the K-wire in the femoral neck to attain stable fixation. The cannulated screws provide stable control for the shear forces applied across the physis during weight bearing.

Obesity contributes to the increase in shear forces on the femoral physis. The irregular hormone levels due to panhypopituitarism previously mentioned can result in a prolonged open physis, decreasing its resistance to the increased shear forces. Collectively, these factors make the patient more susceptible to developing SCFE. In the setting of endocrinopathy, there is an increased risk of developing bilateral SCFE. Some studies have reported the incidence of bilateral SCFE as high as 100% in the presence of endocrinopathy. For our patient, a prophylactic CRPP of the left hip was performed due to his increased risk. A previous study documented that the complication rate of the prophylactic procedure is considerably lower than the risks associated with the development of acute SCFE in the contralateral hip. The timing of the prophylactic pinning is not standardized within the treatment plan for SCFE in the presence of endocrinopathy. Our patient recovered well from the right hip fixation and was released to full weight bearing on the primary affected hip before undergoing the CRPP. In our experience, rehabilitation after the CRPP was more manageable after recovery from the initial procedure on the primary affected hip was completed.

In conclusion, patients with an endocrinopathy are at an increased risk for developing SCFE. Comprehensive attention to all clinical findings in patients with SCFE is warranted, especially in obese patients. In nonemergency situations, preoperative laboratory tests should be considered. Prior to surgery, discussion with the anesthesia team for a potential need of corticosteroid stress dose may be needed. Any concern should result in a referral to pediatric endocrine specialists.

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Our institution does not require ethical approval for reporting anonymized individual cases or case series.

Informed Consent
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ORCID iDs
James B. Harris https://orcid.org/0000-0003-3460-9597
Bhuvana Sunil https://orcid.org/0000-0003-1105-7056

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