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CASE REPORT

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# Slipped capital femoral epiphysis as primary presentation in an adolescent with primary hyperparathyroidism due to ectopic mediastinal parathyroid adenoma

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**Key Clinical Message**

Ectopic mediastinal parathyroid adenoma causes primary hyperparathyroidism presenting as hypercalcemia. When children with hypercalcemia present with slipped capital femoral epiphysis, a detailed evaluation for hypercalcemia must be done before surgery.

**Abstract**

The association between slipped capital femoral epiphysis (SCFE) and hyperparathyroidism has been reported and is rare. Each is known to affect different age groups. We report a case of a 13-year-old boy with SCFE and primary HPT leading to hypercalcemia and skeletal deformities.

**KEYWORDS**

4D CT, ectopic parathyroid adenoma, hyperparathyroidism, slipped capital femoral epiphysis

## 1 | BACKGROUND

Although obesity is the common risk factor for slipped capital femoral epiphysis, it may be associated with endocrine disorders including hyperparathyroidism, hypothyroidism, and growth hormone deficiency. The association between slipped capital femoral epiphysis and hyperparathyroidism is not commonly reported in the literature. No literature is available on SCFE being the primary presentation of hyperparathyroidism due to ectopic mediastinal parathyroid adenoma which has been exemplified in our case report.

## 2 | CASE PRESENTATION

We report a case of a 13-year-old boy with normal developmental milestones, born to a non-consanguineous couple who presented to the orthopedic department with a painful limp for 1 year. The hip pain was persistent and had worsened over the past 5 months. The patient walked with a limp and had an antalgic gait. There was no history of trauma or injury. The patient denied tremors or muscle cramps.

Physical examination revealed an alert boy with a body mass index (BMI) of 19 $kg/m^2$. Bony tenderness was elicitable in the anterior aspect of the right hip. His height was normal, and his bone age corresponded to the chronological age of 13 years. At presentation, he had normal intelligence and pubertal development. Examination of the hips revealed a restricted range of motion, predominantly involving internal rotation.

A radiograph of the pelvis with both hips showed osteopenia with a coarse trabecular pattern. There was a widening and irregularity of both proximal femoral epiphyseal

plates. There was an inferior displacement of both femoral heads with respect to metaphysis and positive Trethowan's sign (Femoral head below Klein's line) consistent with slipped capital femoral epiphysis (Figures 1 and 2). A skeletal survey for hyperparathyroidism was performed. There was osteoporosis with a coarse trabecular pattern and subperiosteal resorption with cortical thinning seen along the proximal phalanges of the left hand. Dorsolumbar spine radiograph showing osteopenia with prominent vertical trabeculations and relative prominence of end plates (Figure 3).

Lab investigations revealed a hemoglobin of 15 g/dL with elevated serum calcium (11 mg/dL). Further workup for hypercalcemia showed elevated alkaline phosphatase (871 IU/L) and serum parathormone levels: 2081 pg /with thyroid, liver, and renal functions within normal limits. His serum phosphate level was 2.9 mg/dL. The possibility of tertiary hyperparathyroidism was ruled out considering normal renal function tests (BUN: 16 mg/dL Serum Creatinine: 0.6 mg/dL). Vitamin D level was 6.4 ng/mL. DEXA scan of the hip showed a *Z*-score of −4.9.

Due to PTH-dependent severe hypercalcemia, parathyroid imaging in the form of ultrasound of the neck, four-dimensional computed tomography (4D CT) of the neck, and 99 Tc Sestamibi scan were done. Ultrasonography of the neck was normal.

CT neck showed a well-defined arterially enhancing soft tissue density lesion in the pre-vascular space of the anterior mediastinum, not in relation to the normally positioned thyroid gland, suggestive of an ectopic parathyroid adenoma (Figures 4 and 5). Sestamibi scan showed hypermetabolic tissue corresponding to the mass on 4D CT.

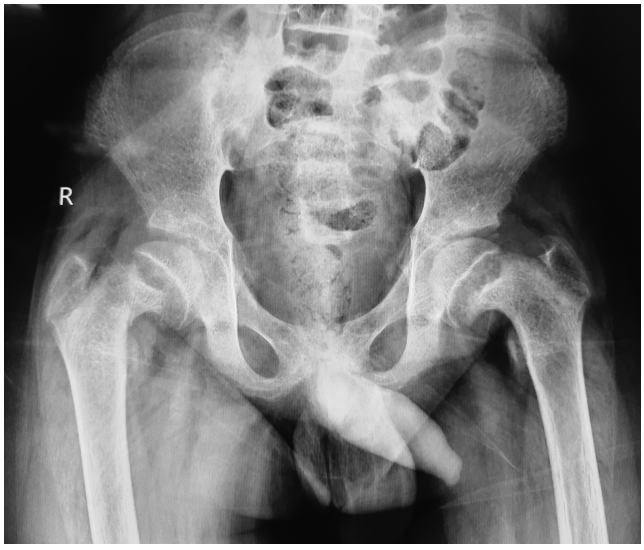


**FIGURE 1** Radiograph of the pelvis with both hips showed osteopenia with a coarse trabecular pattern. Widening and irregularity of both femoral epiphyseal plates were noted. There was an inferior displacement of both femoral heads with respect to the metaphysis.

In view of primary hyperparathyroidism (PHPT) at a young age with arterially enhancing lesion in the anterior mediastinum, multiple endocrine neoplasia (MEN) types 1 and 2 were ruled out after assessing serum prolactin, serum calcitonin, and 24-h urine estimation of metanephrine, normetanephrine, and vanillylmandelic acid, all which were within normal limits.

The patient underwent excision of the mediastinal lesion. Pre-operative PTH was 1150 pg/mL with post-operative PTH being 7 pg/mL. The bolded values show there was a significant fall in serum PTH (>50%) indicating the successful removal of the culprit gland. Pre-operative serum calcium was 11 mg/dL and serum phosphorous was 2.9 mg/dl. Postoperatively, on day eight, serum calcium returned to the normal range (Serum calcium: 9.8 mg/dL), while phosphorous levels increased to 3.6 mg/dL. (Table 1) Histopathology revealed an adenoma of the ectopic parathyroid gland (Figure 6).

The patient developed postoperative symptomatic hypocalcemia with perioral and digital tingling, numbness, and positive Chvostek and Trousseau signs. Hypocalcemia was managed with 540 mg IV calcium gluconate over 18 h along with oral calcium carbonate and Vitamin D. Hypocalcemia resolved, as did hypocalcemic symptoms and signs.

For treating the SCFE per se, the patient was advised to rest and avoid weight bearing on the legs as much as possible using crutches or a wheelchair. After a period of 3 weeks, internal fixation in situ using a single cannulated screw was performed bilaterally. The patient tolerated the surgery well and was discharged with plans for outpatient follow-up. Although the patient did not have symptoms of hypocalcemia then, recognizing his recent orthopedic surgery, calcium, and activated Vitamin D were supplemented for 1 month.

## 3 | DISCUSSION

Most cases of SCFE are reported in adolescence owing to the growth spurt during puberty.[1] Displacement of the femoral head posteroinferiorly with respect to the femoral neck is the central dogma in SCFE and is also termed adolescent coxa vara. Obesity is an important risk factor because it predisposes to an increase in shear forces around the proximal growth plate. Although most cases are idiopathic in origin, they may be associated with endocrine disorders including obesity, hypothyroidism, growth hormone deficiency, or growth hormone treatment. Despite the good association between primary hyperparathyroidism and SCFE, SCFE as the primary presentation in

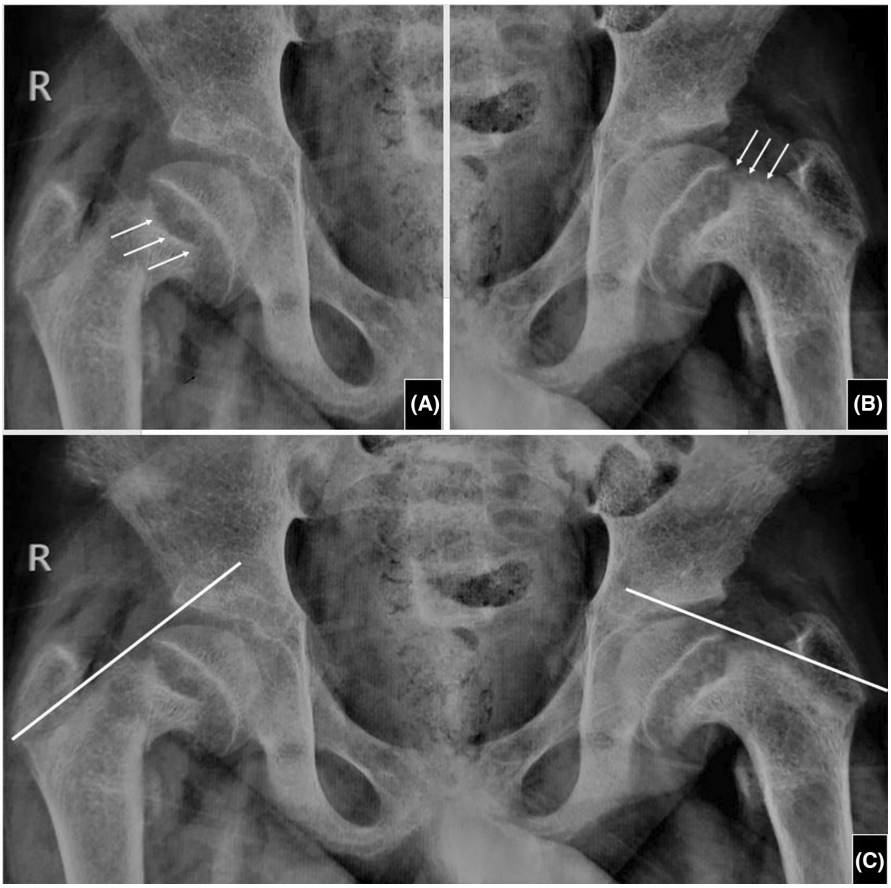


**FIGURE 2** Radiographic signs in SCFE: (A) Physeal widening and irregularity. (B) Loss of normal concavity of femoral head–neck junction. (C) A line drawn parallel to the femoral neck (Klein's line) not intersecting the femoral epiphysis due to displaced epiphysis.

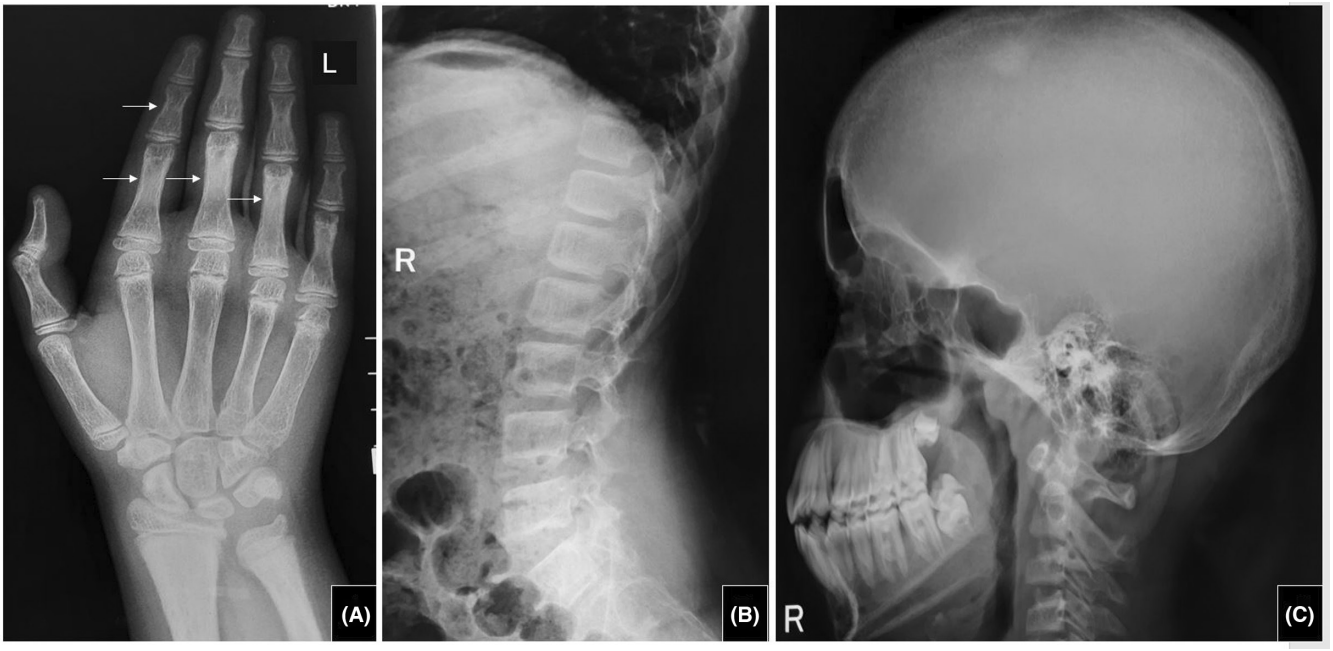


**FIGURE 3** Skeletal survey for hyperparathyroidism: (A) Radiograph of left-hand shows osteoporosis with a coarse trabecular pattern. Subperiosteal resorption with cortical thinning is seen along the proximal phalanges (white arrows). The lateral radiograph of the dorsolumbar spine (B) shows osteopenia with prominent vertical trabeculations and relatively prominent end plates. The lateral radiograph of the skull (C) showed no abnormality.

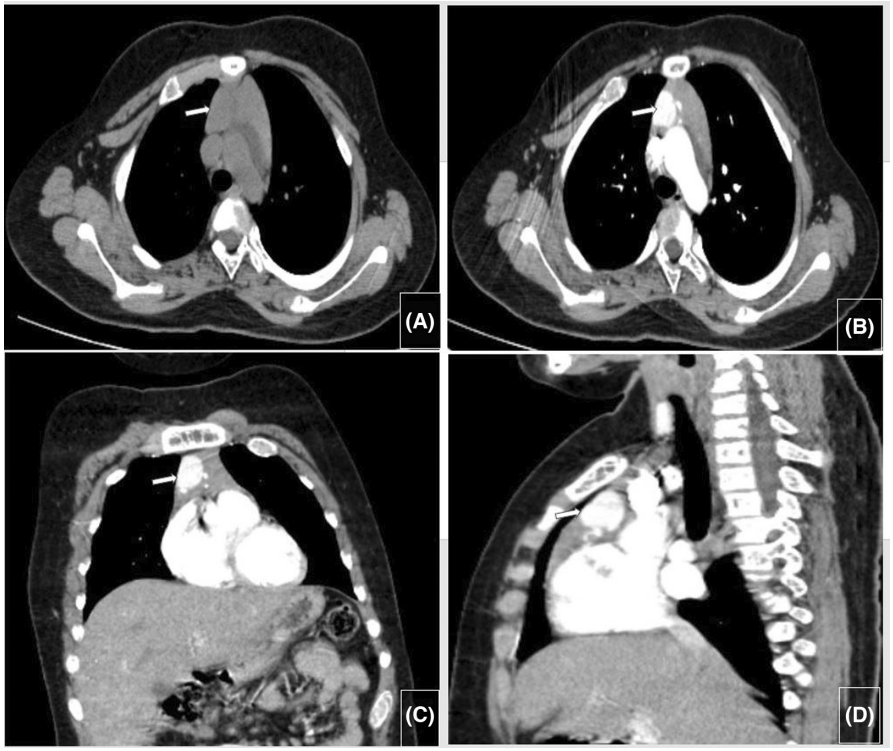


**FIGURE 4** Localization of adenoma on 4D CT: Pre-contrast axial (A) showing an isodense lesion (white arrow) in the pre-vascular compartment. Arterial phase axial image (B) with coronal(C) and sagittal (D) reformations shows a 2.1 × 1.6 cm sized well-defined intensely enhancing lesion in the pre-vascular compartment.

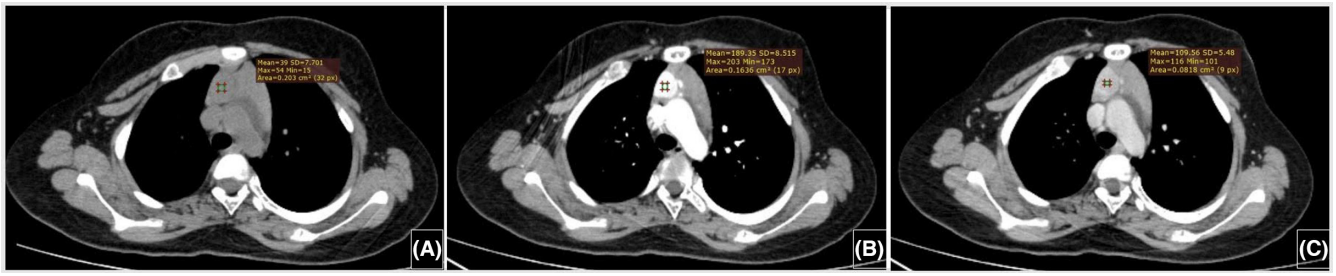


**FIGURE 5** Perfusion pattern of ectopic parathyroid adenoma during 4D CT scan. Pre-contrast CT scan(A) showing an isodense mass lesion in the pre-vascular compartment. The arterial phase axial (B) image shows avid early enhancement of the ectopic parathyroid adenoma. Delayed phase scan(C) shows washout of contrast 85 s after contrast administration.

**TABLE 1** Blood parameters pre- and post-excision of ectopic mediastinal parathyroid adenoma.

| Date | 16/02/21 3 weeks prior to surgery | 04/03/21 On the day of surgery | 05/03/21 Post-op day 1 | 06/03/21 Post-op day 2 | 10/03/21 Post-op day 6 | 12/03/21 Post-op day 8 |
|---|---|---|---|---|---|---|
| Ca/ PO4 (mg/dl) | 11/**2.9** | 9.8 | Morning-8.5<br>Evening-7.6 | 8/**3.5** | 9/4.2 | 9.8/3.6 |
| Creatinine (mg/%) | 0.6 | | 0.8 | | 0.7 | 0.9 |
| Mg (mg/dL) | | | 1.58 | 1.59 | | |
| PTH (pg/ml) | **2081.6** | Pre-op 1150<br>Intra-op 118.4<br>Evening **7.4** | | | | |

patients with hyperparathyroidism is limited. Most of the reported associations between SCFE and PHPT are due to eutopic parathyroid adenoma.

The zone of maturation and hypertrophy within the epiphyseal cartilage is the zone with a dense population of PTH receptors and is also the commonest site for slipping of femoral epiphysis.[2] Few theories have been proposed to explain the association between SCFE and HPTH: a defect in protein synthesis weakening the epiphyseal synchondrosis and an imbalance of growth

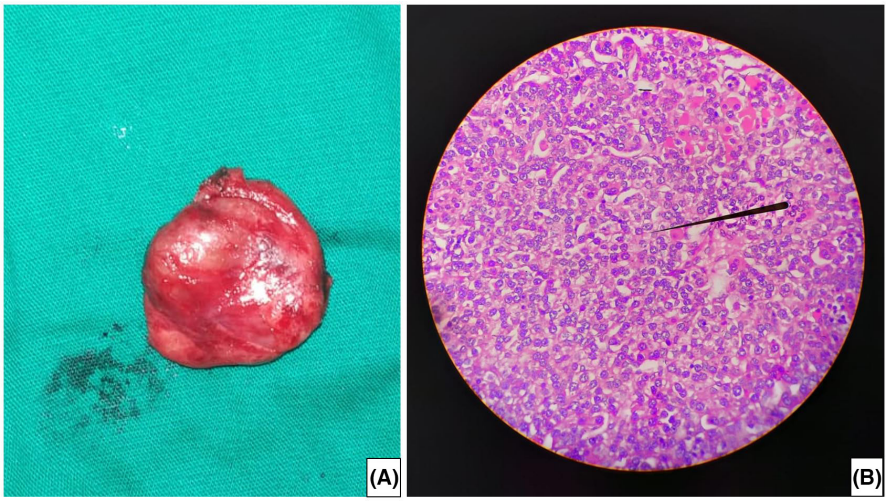


**FIGURE 6** Gross specimen (A) shows a lobulated, well-circumscribed rounded lesion. (B) High-power microscopy shows highly cellular sheets of chief cells showing amphophilic cytoplasm and prominent fat droplets.

**TABLE 2** Review of literature for cases of primary hyperthyroidism in a pediatric population.

| Author | AGE/ SEX | Calcium | PTH | Alkaline phosphate | SCFE | HPR |
|---|---|---|---|---|---|---|
| Yang WE et al.[5] | 13/M | High | High | High | Bilateral | Adenoma |
| Bone et al.[6] | 13/F | 6MEQ/L | 451MICROLEQ/ML | – | Bilateral | Adenoma |
| Alghamdi et al.[7] | 13Y/F | 2.91MMOL/L | 239PMOL/L | 2008 IU/L | Bilateral | Adenoma |
| Gautam Kumar et al.[8] | 15Y/M | 12.3MG/DL (Normal: 8.5–10.5) | 2512PG ()10–65 | 832 IU/ML (Normal: 35–140) | Bilateral | Right inferior adenoma |
| Geena Susan George et al.[9] | 15Y/M | 17.2 mg/dL (Normal: 8.7–10.3 mg/dL) | 1052 pg/mL (Normal: 8–51 pg/mL) | – | Bilateral | Bilateral inferior adenomas |
| Masaki Takao et al.[10] | 8Y/F | 7.2MG/DL (LOW) | 1763 pg/mL | 5269 U/L | Bilateral metaphyseal bone collapse | Renal Osteodystrophy |
| Nicholas J Goel et al.[11] | 12Y/M | LOW | 1113 pg/mL (Normal range 15–65) | Elevated | Bilateral | Pseudohypoparathyroidism type 1b |
| Laila Qadan et al.[12] | 13/F | 2.78MMOL/L (Normal: 2.2–2.6MMOL/L) | 27.9 pmol/L [Normal: 1.3–7.6 pmol/L] | 1780 U/L (Normal: 50-136 U/L) | Bilateral | Left upper pole adenoma |
| J Kinoshita et al.[13] | 16Y/M | 11.5 mg/dL unbound (Normal 8.4–10.5) | 3.4 ng/mL (Normal 0.3–1.0) | 6.9 × 103 IU/1 (Normal: 66.7–241.5) | Bilateral | Right adenoma |
| Madeira et al.[14] | 18/M | 13.6 mg/dL | 1524 pg/mL | 3449 U/L | Bilateral | Right inferior adenoma |
| Bhadada et al.[15] | 12Y/F | 10.4 mg/dL (Normal: 8.5–10.2) | 1523 pg/mL (Normal: 10–69) | 22 KAU (Normal: 3–13) | Bilateral | Left inferior adenoma |
| Monica Serrano-Gonzalez et al.[16] | 14Y/F | 13.4 mg/dL (Reference range: 8.4–10.2 mg/dL) | 1013 pg/mL Reference range, 9–69 pg/mL | – | Right | Parathyroid carcinoma |

hormone and estrogen levels.[3] The alternative accepted theory of action of parathyroid hormone on chondrocytes of growth plate mediated by metalloproteinases resulting in abnormalities associated with cartilage mineralization and delaying epiphyseal fusion.[4] Similar pathogenesis which occurs in renal osteodystrophy may involve SCFE. Prolonged periods of uncalcified cartilage and increasing body weight causing shear stress on the upper femoral epiphysis, are among the main provoking factor for SCFE in adolescents.

Most of the cases of PHTH reported in children are due to adenoma and a rare incidence of carcinoma among children. From our case and the literature reviewed below.[5–16] (Table 2), we found that almost all the cases were reported

in later adolescence with an average age of 13.5 years and there was no difference in incidence among males and females.

Antero-posterior and frog-leg lateral views of the hip joint are the commonest recommended radiographs for the evaluation of SCFE. Epiphysiolysis or growth plate widening is the earliest radiological sign noted. There is a loss of normal concavity of the anterior femoral head–neck junction. The blurring of proximal femoral metaphysis due to overlapping of the posteriorly displaced epiphysis and femoral metaphysis is termed a 'metaphyseal blanch' sign.[17] Klein's line is drawn on the AP view along the superior border of the femoral neck which will not intersect with the femoral head in patients with SCFE.

4D CT is a commonly used CT protocol for the identification of parathyroid adenomas which involves three dimensions of multiplanar CT (Axial acquisition with coronal and sagittal reformations) with the fourth dimension being the enhancement pattern of adenoma over unenhanced, arterial, and venous phases[18] The classic pattern of enhancement of adenoma includes intense arterial phase enhancement followed by washout in the venous phase which helps in distinguishing the thyroid gland and lymph nodes. The reason behind the greater incidence of inferior ectopic adenomas as compared to superior parathyroid adenomas is delayed and variable embryologic descent. These ectopic inferior adenomas are found to be located anywhere from the carotid bifurcation to the aortopulmonary window.

Video-assisted thoracoscopic surgery (VATS) has a low incidence of complications as compared to other techniques according to a literature review conducted by Alesina et al.[19] The common recommendation in patients with SCFE and hyperparathyroidism is to undergo excision of adenoma as a reduction in PTH levels will result in imminent closure of the physeal plate. A similar approach was followed in our patient.

## 4 | CONCLUSIONS

Since the incidence of hypercalcemia is rare in children, it should be properly evaluated with serum levels of alkaline phosphatase and PTH, and metaphyseal bone changes beneath the physis. When children with hypercalcemia present with a displacement of the capital femoral epiphysis, a detailed evaluation of the cause of hypercalcemia must be done before any surgical intervention of skeletal deformities.

### AUTHOR CONTRIBUTIONS

**Padma Vikram Badhe:** Data curation; investigation; validation; visualization; writing – original draft. **Sanika Patil:** Conceptualization; investigation; methodology; writing – review and editing. **Vikram Reddy:** Data curation; formal analysis; investigation; methodology. **Harini Seshadri:** Validation; writing – review and editing. **Sanjay Jain:** Supervision; writing – review and editing. **Tejas Nikumbh:** Writing – review and editing.

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### CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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