

Case Report

## Closed Pathological Femoral Fracture in a Patient with Thalassemia: A Rare Case Report

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### Abstract

*Thalassemia is a hereditary hematologic disorder that impairs hemoglobin synthesis, often leading to chronic anemia with skeletal complications such as bone marrow expansion and osteoporosis. These changes predispose patients to pathological fractures, although distal femur involvement remains rare and challenging to treat. A 23-year-old male with a known history of thalassemia presented to the orthopedic outpatient clinic of Soeharso Orthopedic Hospital with left thigh pain following a minor fall from bed. The patient was diagnosed with thalassemia at six years old and has received regular blood transfusions twice monthly. He underwent splenectomy in May 2023 and is currently taking folic acid and deferasirox 250 mg (four tablets daily). Thalassemia-associated bone fragility arises from multiple factors including hormonal imbalance (hypogonadism, growth hormone deficiency), iron overload with endocrine dysfunction and disrupted calcium metabolism, as well as decreased physical activity contributing to disuse osteoporosis. The distal femur is particularly difficult to manage due to poor bone quality and high mechanical load, complicating fixation and healing. This case highlights that even minor trauma can result in pathological fractures in thalassemia due to combined effects of hormonal disturbance, iron overload, and reduced activity leading to severe bone fragility.*

**Keywords:** closed pathological fracture, one-third distal femur, thalassemia, a rare case report.

## Fraktur Patologis Tertutup Femur pada Pasien dengan Thalassemia: Sebuah Laporan Kasus Langka

### Abstrak

*Thalassemia merupakan kelainan hematologi herediter yang mengganggu sintesis hemoglobin, sering menyebabkan anemia kronis dengan komplikasi skeletal berupa ekspansi sumsum tulang dan osteoporosis. Perubahan ini meningkatkan risiko fraktur patologis, meskipun keterlibatan femur distal tetap jarang terjadi dan sulit ditangani. Seorang laki-laki berusia 23 tahun dengan riwayat thalassemia datang ke klinik rawat jalan ortopedi Rumah Sakit Ortopedi Soeharso dengan keluhan nyeri pada paha kiri setelah terjatuh ringan dari tempat tidur. Pasien didiagnosis thalassemia pada usia enam tahun dan mendapatkan transfusi darah rutin dua kali per bulan. Ia menjalani splenektomi pada Mei 2023 dan saat ini mengonsumsi asam folat serta deferasirox 250 mg (empat tablet per hari). Kerapuhan tulang akibat thalassemia disebabkan oleh berbagai faktor, termasuk ketidakseimbangan hormonal (hipogonadisme, defisiensi hormon pertumbuhan), kelebihan besi dengan disfungsi endokrin dan gangguan metabolisme kalsium, serta penurunan aktivitas fisik yang berkontribusi pada osteoporosis disuse. Femur distal sangat sulit ditangani karena kualitas tulang yang buruk dan beban mekanik yang tinggi, sehingga menyulitkan fiksasi dan penyembuhan. Kasus ini menyoroti bahwa trauma ringan sekalipun dapat mengakibatkan fraktur patologis pada thalassemia akibat kombinasi gangguan hormonal, kelebihan besi, dan penurunan aktivitas yang menyebabkan kerapuhan tulang berat.*

**Kata kunci:** fraktur patologis tertutup, sepertiga distal femur, thalassemia, laporan kasus langka.

## Introduction

Pathological fractures occur when structurally weakened bones succumb to mechanical stress that normal bone can withstand, often due to underlying systemic or local pathology.<sup>1</sup> Among the hematological disorders known to predispose to skeletal fragility, thalassemia stands out as a significant contributor to compromised bone health. In individuals with thalassemia, factors such as ineffective erythropoiesis, chronic anemia, iron overload, hypogonadism, and endocrine abnormalities collectively impair peak bone mass and elevate fracture risk.<sup>2,3</sup>

Epidemiological studies have demonstrated that fractures are highly prevalent among patients with thalassemia, with estimated lifetime fracture rates ranging from 36% to more than 50%, particularly in transfusion-dependent individuals. Meta-analyses have reported a pooled fracture prevalence of approximately 16%, with rates reaching 18% among patients with beta-thalassemia and transfusion-dependent thalassemia.<sup>4</sup>

While long bones commonly bear the brunt of pathological fractures in thalassemia, occurrences in the distal femur—especially in the one-third region—are exceedingly rare and scarcely documented. To our knowledge, few documented instances have explored this specific anatomical site in the context of thalassemia-related bone pathology, and no case reports have focused on closed pathological one-third distal femur fractures in this patient population.

In this report, we present a rare case of a closed pathological fracture of the distal one-third of the femur in a patient with thalassemia. This case provides insight into an unusual manifestation of skeletal fragility, highlights the complex interplay between disease-related and treatment-related factors affecting bone health, and discusses the diagnostic and therapeutic implications of this uncommon fracture pattern.

## Case Report

A 23 years old male patient presented at the orthopedic outpatient clinic of Soeharso Orthopedic Hospital Surakarta with chief complaints of pain in the left thigh. The pain was felt after the patient slipped and fell off the bed. The pain was persistent until the patient arrived at the orthopedic outpatient clinic, pain scale of 4. The pain subsided when the patient rested or slept, but worsened during daily activities. After the accident, the patient was brought to RSUD Metro, where a cast was applied. Later he was referred to the orthopedic outpatient clinic Soeharso Orthopedic Hospital and prescribed curcuma force tab 3x1, forneuro tab 1x1 and ristonat tab 1x35mg.

The patient has a history of thalassemia, diagnosed at the age of six and had undergone blood transfusion therapy twice a month. He regularly takes folic acid and deferasirox 250 mg, 4 tablets once daily, and underwent a splenectomy in May 2023. No family history of illness was reported.

From physical examination general condition appeared composmentis (Glassgow Coma Scale E4V5M6). Cardiac examination revealed heart sounds S1 and S2 with normal intensity and regular rhythm, and a murmur was audible. Pulmonary examination revealed vesicular breath sounds in both lung fields without any additional sounds. Abdominal examination showed active bowel sounds, supple abdomen, and no tenderness. Examination of the one third distally left femur region showed oedema, tenderness with restricted and painful knee range of motion (Figure 1).

The patient underwent additional tests including a bone survey, femur radiograph (2 views), and adult bone mineral density (BMD) at 3 sites. The bone survey revealed osteolytic lesions in the left femur and proximal part of the left radius, along with a fracture in the distal third of the left femur.



**Figure 1. Clinical Appearance of the Left Distal Femur Region**



**Figure 2. Plain X-Ray of the Full Leg Anteroposterior View**

The femur radiograph (Figure 2) showed a lytic lesion in the one-third distal of the left femur accompanied by a complete fracture in the same region, with displacement and bowing- shortening deformity.

The BMD performed at lumbar two - four, left neck femur, and left distal radius (Figure 3) showed the following results: Lumbar two-four: average T-score of -6.8 and Zscore of -6.0,

indicating osteoporosis, left femoral neck: average T-score of -4.4 and Z-score of -3.4, also indicating osteoporosis. Then from laboratory results included anemia (Hemoglobin 8.4 g/dL), neutropenia (neutrophils 31%), monocytosis (monocytes 55%), direct and indirect hyperbilirubinemia (total bilirubin 1.45 mg/dL, direct bilirubin 0.54 mg/dL) and elevated liver enzymes (SGOT 217 U/L, SGPT 157 U/L).

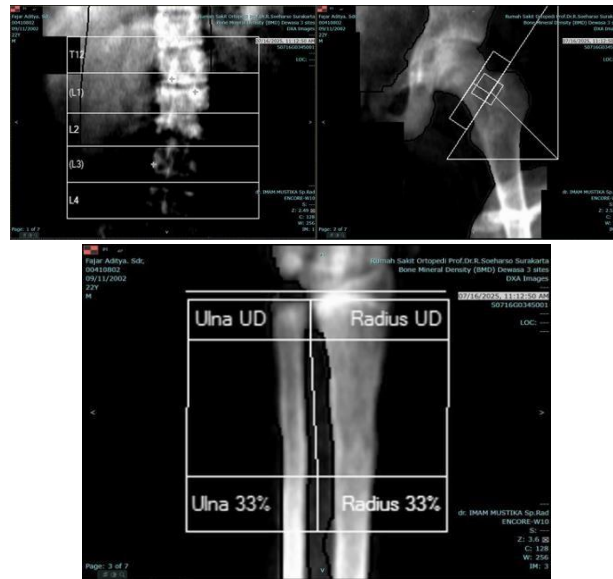


**Figure 3. Bone Mineral Density (BMD) 3 Sites**

The patient underwent Open Reduction Internal Fixation (ORIF) surgery for one-third distal femur with bone graft, biopsy and histopathology sampling. A lateral approach to the femur was used (Figure 4). Intraoperatively, a fracture of the distal third of the femur (os femur pars tertia distalis) was identified. The fracture site was freshened, and a histopathology sample was collected. Reduction was achieved and fixation was performed using a distal femoral locking plate

placed on the lateral aspect of the distal third of the femur, followed by bovine bone graft implantation. Histopathological examination of the biopsy specimen confirmed reactive bone changes consistent with thalassemia-associated bone disease, with no evidence of malignancy or primary bone tumor. Prophylactic antibiotics (cefazolin 2 grams) were administered one hour before incision, followed by cefazolin 1 gram three times daily for two days.



**Figure 4. The Fracture Was Exposed During the Surgery**

The patient was then transferred to the ward for postoperative care and follow-up. One day after surgery, the patient complained of pain around the surgical area. Physical examination by look assessment of the left femoral region

revealed that the wound was covered with dressing, no leakage, swelling, and a drain in place. Approximately 300 cc of blood was collected from the drain. The hip and knee range of motion was limited due to pain.

The ROM exercises immediately included active movements such as coordination training; agility; power; endurance, postural control and stabilization, developmental activities training, motor training, movement pattern training, neuromuscular relearning; relaxation techniques; balance training; vestibular; back and neck exercises; stability; locomotion, functional motor recovery; sensory reintegration; body mechanics and joint ROM training (with and without orthoses; assistive devices; adaptive equipment; prosthetics).

From the internist the patient received desferal 1000 mg once daily, folic acid once daily, iron supplement (TTD) twice daily, 2 units of PRC transfusion (1 unit/day for 2 days).

The patient was given zoledronic acid 4 mg intravenously on the first day postoperative. Oral administration of calcium and calcitriol is given 2x500mg and 2x0.25Ug.

A two-views femur radiograph was performed (Figure 5), which showed fracture discontinuity in the distal one-third of the left femur, internal fixation with plate and screw in place.

At three-month follow-up, the patient reported decreased pain and improved mobility. Clinical examination showed no signs of wound infection and progressive range of motion improvement at the knee. Repeat radiographs at three months demonstrated callus formation at the fracture site, with the locking plate and screws remaining in proper position. At six-month follow-up, the patient was able to perform partial weight-bearing with assistive devices. Radiographic assessment confirmed progressive fracture healing with bridging callus formation. No implant loosening, hardware failure, or secondary complications were observed during the follow-up period.



**Figure 5. Radiograph Post Surgery Open Reduction Internal Fixation with Plate and Screw**

## Discussion

This case presents a rare occurrence of a closed pathological fracture involving the distal one-third of the femur in a patient with thalassemia. Pathological fractures, by definition, happen when structurally weakened bones collapse under forces that healthy bone would withstand.<sup>1</sup> In this patient, the convergence of severe osteoporosis (lumbar T-score -6.8, femoral neck T-score -4.4), post-splenectomy status, transfusion dependency, and hepatic iron overload (SGOT 217 U/L, SGPT 157 U/L) collectively created a bone microenvironment profoundly susceptible to fracture—even from a minor fall. This constellation of risk factors is consistent with published literature identifying splenectomy, iron overload, and endocrinopathy as major determinants of skeletal fragility in thalassemia.<sup>5</sup>

Fractures are relatively prevalent in thalassemic populations, occurring in 35.3% of patients with thalassemia syndromes, especially in transfusion-dependent and beta thalassemia. Compared to patients with alpha thalassemia (16%), those with beta thalassemia (44.1%) had a greater rate of fracture. The most common causes of fractures were falls and auto accidents. Low body mass index, male gender, beta thalassemia, splenectomy, and transfusion were among the fracture risk factors among thalassemia patients.<sup>4,6</sup>

Other large studies have reported fracture histories in roughly 36% of patients, alongside low bone mineral density (BMD) rates exceeding 46% in the spine, 25% in the femur,<sup>7</sup> and multiple fractures were discovered in 28% of the patients.<sup>6</sup>

Bone disease in thalassemia arises from multiple converging factors. First, ineffective erythropoiesis leads to marked bone marrow expansion—up to 30-fold—which erodes trabecular structures and thins the cortex, significantly weakening bone integrity.<sup>8</sup> Second, chronic iron overload—common in transfusion-dependent patients—disrupts endocrine function and directly impairs bone metabolism, increasing osteoclastic activity and suppressing bone formation.<sup>3</sup> Third, associated endocrinopathies—particularly hypogonadism and dysfunction of the

GH-IGF-1 axis—further undermine bone health by reducing peak bone mass and impairing remodeling.<sup>3,5,9</sup>

Furthermore, toxicity from chelation therapy (notably deferoxamine) has been implicated in skeletal dysplasia, including alteration of the distal femur and patellar regions, which is particularly relevant in this patient who received deferasirox as chelation therapy. Although deferasirox has a different mechanism than deferoxamine, iron overload per se—present in this patient as evidenced by elevated liver enzymes (SGOT 217 U/L, SGPT 157 U/L)—remains a key contributor to bone pathology through disrupted endocrine function and impaired osteoblast activity.<sup>10,11,12</sup>

A study involving 70 patients with beta-thalassemia intermedia found that those who had undergone splenectomy exhibited significantly lower bone mineral density (BMD) across multipleskeletal sites. Their trabecular bone score (TBS)—which reflects bone microarchitecture—was also markedly reduced compared to non splenectomized patients.<sup>13</sup> In children and adolescents with beta-thalassemia, history of splenectomy was associated with lower spinal and total-body BMD, and a higher incidence of fractures.<sup>14</sup> In broader thalassemia populations, splenectomy and endocrinopathies emerged as significant risk factors associated with osteoporosis and fractures. A recent large cross-sectional study found that a history of splenectomy was significantly correlated with low BMD, especially in transfusion-dependent thalassemia (TDT) patients.<sup>15</sup>

One third distal femoral fracture in Thalassemia is uncommon but important. While most thalassemia-related fractures occur in vertebrae or proximal femur, this case involving the distal femur adds to the spectrum of skeletal manifestations. It emphasizes how systemic bone fragility can manifest in less typical, yet high-impact sites—particularly relevant for prevention and management strategies.<sup>16,17</sup>

Magnetic resonance imaging studies have noted bone dysplasia in the distal femoral region associated with deferoxamine treatment in thalassemia major, including physeal widening and metaphyseal lesions.<sup>10</sup>

Surgical management of pathologic fractures depends on the fracture configuration. In well-transfused thalassemia patients with non-displaced or minimally displaced fractures, most cases can be managed with standard casting or immobilization techniques; however, careful nutritional support—including vitamin C administration—is important to avoid delayed healing. For long-bone fractures such as those involving the distal third of the femur, surgical fixation is typically required. Intramedullary nails provide strong stabilization with minimal soft tissue dissection and preservation of blood supply. Alternatively, locking plates allow minimally invasive insertion, preserving soft tissue, periosteal blood supply, and overall vascular integrity—factors vital for fracture healing and infection prevention. In this patient, given the distal location of the fracture and the poor bone quality, a distal femoral locking plate was chosen and supplemented with bovine bone graft to enhance stability and promote healing. Bisphosphonates effectively reduce bone turnover and significantly boost BMD in the lumbar spine, hip, and femoral neck in thalassemia-associated osteoporosis. Zoledronic acid and neridronate additionally alleviate bone and back pain.<sup>18,19</sup> Typically given alongside calcium and vitamin D for up to 24–36 months. Regular checks—especially 24-hour urinary calcium—are advised to prevent hypercalciuria and kidney stones. Generally well tolerated, however, rare complications like atypical femoral fractures have been reported.<sup>3,20</sup>

Vitamin D & Calcium are essential for strong bones in thalassemia—especially if their levels are low. Keeping vitamin D (25-OH) above 30 ng/mL is very important, and meet dietary calcium needs. Supplements are needed only when the intake is inadequate, and it is important to monitor for urinary calcium to avoid kidney problems.<sup>21,22</sup>

Hormone Replacement Therapy (HRT) is indicated for thalassemia patients with hypogonadism, a condition that significantly impairs bone strength. Although standard HRT may not fully restore bone mass, it can offer meaningful benefits in slowing bone loss and improving overall bone health in this population. In

this patient, endocrine evaluation and targeted hormonal management should be considered as part of long-term follow-up to optimize bone recovery and prevent future fractures.<sup>23,24,25</sup>

Several clinical implications emerge from this case. First, routine screening of bone mineral density (BMD) should be considered for all patients with thalassemia, particularly those with additional risk factors such as splenectomy, hypogonadism, or prolonged chelation therapy. Second, even minor trauma in a thalassemia patient should prompt evaluation for underlying pathological fracture, given the high prevalence of severe osteoporosis in this population—as demonstrated by this patient's lumbar T-score of –6.8. Third, a multidisciplinary approach involving orthopedic surgery, hematology, endocrinology, and rehabilitation is essential for optimal management of thalassemia-related fractures. Fourth, early initiation of pharmacological bone protection—including bisphosphonates, calcium, and vitamin D supplementation—should be integrated into the standard care of transfusion-dependent thalassemia patients to reduce the risk of both vertebral and long-bone fractures.

## Conclusion

This is a rare case of a pathological one third distal femoral fracture in a patient with thalassemia, reflects the pervasive and multisystemic nature of thalassemia-related bone disease. This case underscores the multifaceted nature of bone disease in thalassemia, where factors like ineffective erythropoiesis, iron overload, endocrine dysfunction, and marrow expansion weaken bone integrity—predisposing patients even to uncommon fractures such as those of the one third distal femur. Multifactorial in origin, these fractures call for comprehensive preventive strategies encompassing regular surveillance, endocrine management, optimal transfusion and chelation protocols, and appropriate pharmacotherapy.

## Conflict of Interest

No authors of this article disclosed conflicts of interest.

## Consent Form

Patient granted written informed consent for case report publication. The journal's editor-in- chief can review written consent upon request.

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## Authors' Contributions

Each author contributed in designing the study concept, write the article, edit it critically for important intellectual content, provide study materials or patients' administrative, technical, or logistical support, acquire and compile data, and approve the final manuscript.

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