

Genetically Confirmed Hyperphosphatemic Tumoral Calcinosis: A Case Report

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Abstract

Familial hyperphosphatemic tumoral calcinosis is a rare autosomal recessive disorder characterized by periarticular deposition of calcium-phosphate material in soft tissues. We describe the case of a 15-year-old Gabonese patient presenting with multifocal involvement of the left hip, elbow, and shoulder, evolving for four years. The condition was initially misdiagnosed as a giant cell tumor of soft tissues, and a definitive diagnosis was established by histological examination after excision of the elbow mass. Biological workup revealed isolated hyperphosphatemia at 66.0 mg/L and 25-hydroxyvitamin D deficiency at 16.7 ng/mL, with an otherwise unremarkable laboratory profile. Genetic testing identified a homozygous pathogenic variant in the *GALNT3* gene (NM_004482.4:c.484C>T, p.Arg162Ter), confirming familial hyperphosphatemic tumoral calcinosis type 1. MRI of the left shoulder demonstrated multiple calcified nodules within the subcoracoid bursa extending into the surrounding musculature. After histological and genetic confirmation of the diagnosis, management consisted of surgical excision, combined with phosphate-lowering therapy and cautious vitamin D supplementation under biochemical monitoring. This case is particularly noteworthy for its multifocal nature, young age of onset, and initial diagnostic delay.

Categories: Radiology, Rheumatology, Orthopedics

Keywords: hyperphosphatemia, multiple localizations, periarticular calcification, soft tissue calcification, tumoral calcinosis

Introduction

Tumoral calcinosis (TC), also known as lipocalcinogranulomatosis of Teutschlaender, is a rare clinical and histological entity identified by deposition of calcium-phosphate material in periarticular soft tissues [1]. It was initially described by Giard in 1898 [2] and subsequently named “tumoral calcinosis” by Inclan in 1943 [3].

TC primarily affects adolescents and young adults, with a marked predominance in patients of African origin [4]. It may be primary, including familial hyperphosphatemic forms, or secondary to chronic kidney disease with hyperparathyroidism [5]. Familial forms are linked to mutations in *GALNT3*, *FGF23*, and *KL* genes involved in phosphocalcium metabolism [6,7]. The hip, shoulder, elbow, and knee are the most frequent sites [8]. The diagnosis is based on clinical, biological (normocalcemia and hyperphosphatemia), radiological, and histological criteria. Treatment is mainly surgical with a significant risk of recurrence [1].

We report the case of a genetically confirmed multifocal familial hyperphosphatemic TC type 1 in a Gabonese adolescent caused by a homozygous pathogenic variant in *GALNT3*, with an initial diagnostic delay.

Case Presentation

A 15-year-old Gabonese male patient, fourth of six siblings, presented with a progressive enlargement of the left shoulder mass causing limitation of joint mobility. There was no notable medical history and no similar cases in the family.

Symptoms began four years ago with a progressive mass in the left thigh and hip region. Imaging showed a heterogeneous, cystic, calcified soft-tissue mass in the muscle compartments, initially suggesting an old calcified hematoma. Two and a half years later, the first surgical excision was performed. Three months after this surgery, a second surgical excision was required for local recurrence. The histopathological examination concluded a giant cell tumor of soft tissues without signs of malignancy. Eight months after the second surgery, a new mass appeared at the left elbow. A PET-CT scan showed extra-articular soft-tissue hypermetabolism involving the left hip, left elbow, and left shoulder (Figure 1).

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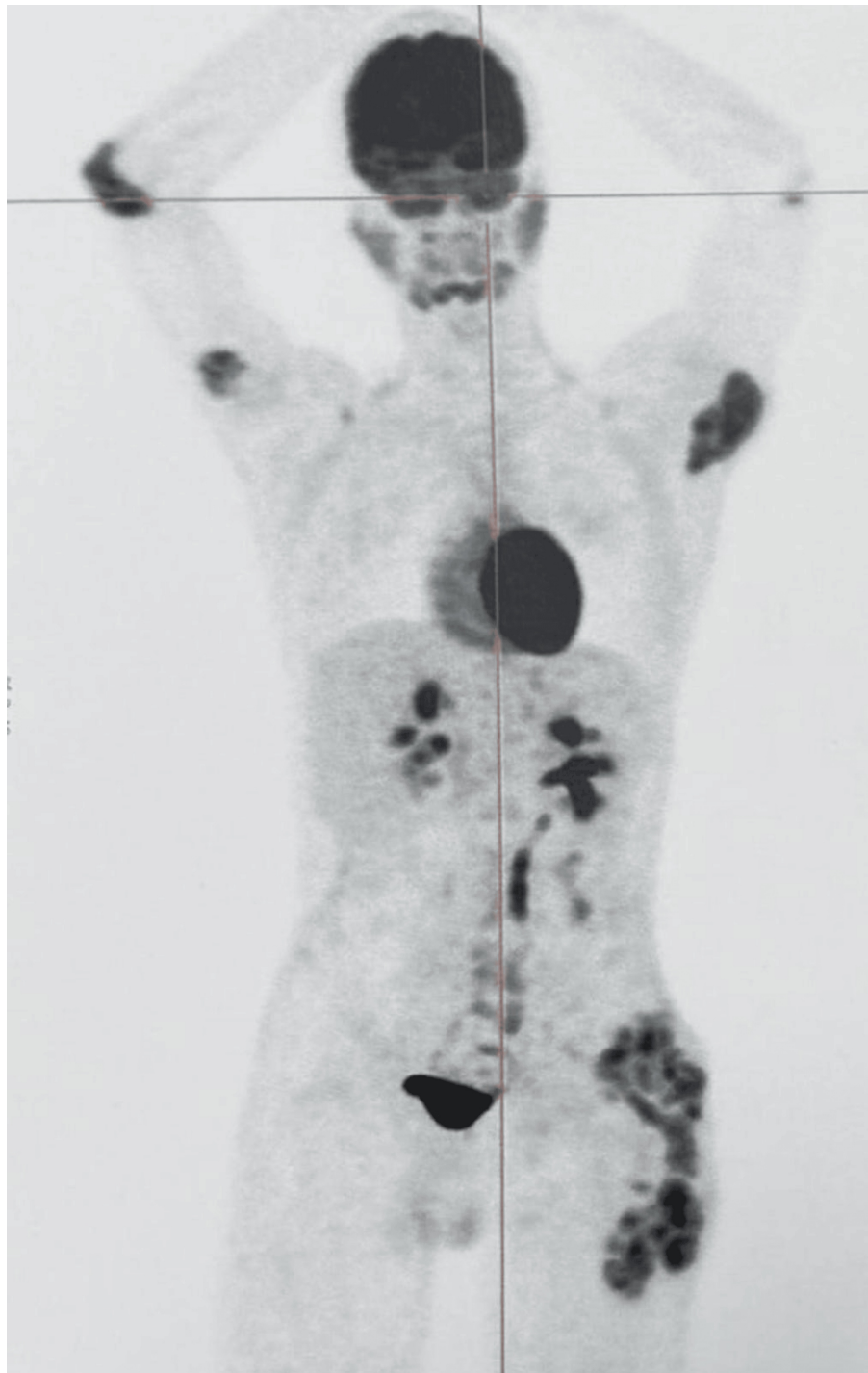


FIGURE 1: Whole-body PET-CT maximum intensity projection image demonstrating multiple areas of increased radiotracer uptake corresponding to peri-articular calcified masses.

Approximately one month after the third surgery, the left elbow mass was excised. Histological examination showed an acellular lesion composed of amorphous calcified material, without cytological atypia or malignancy, consistent with tumoral calcinosis, which corrected the initial diagnosis.

In the present presentation, clinical examination revealed residual scars at the left hip and elbow. The left shoulder showed a posterior swelling, not painful, of firm consistency, limiting joint mobility with no overlying skin changes. Ultrasound examination of the left shoulder demonstrated a heterogeneous, poorly defined soft-tissue mass arising from posterior soft tissues, containing hyperechoic foci with posterior acoustic shadowing, consistent with calcifications. Plain radiography revealed calcifications overlying the

left glenohumeral joint and within the surrounding soft tissues (Figures 2, 3).

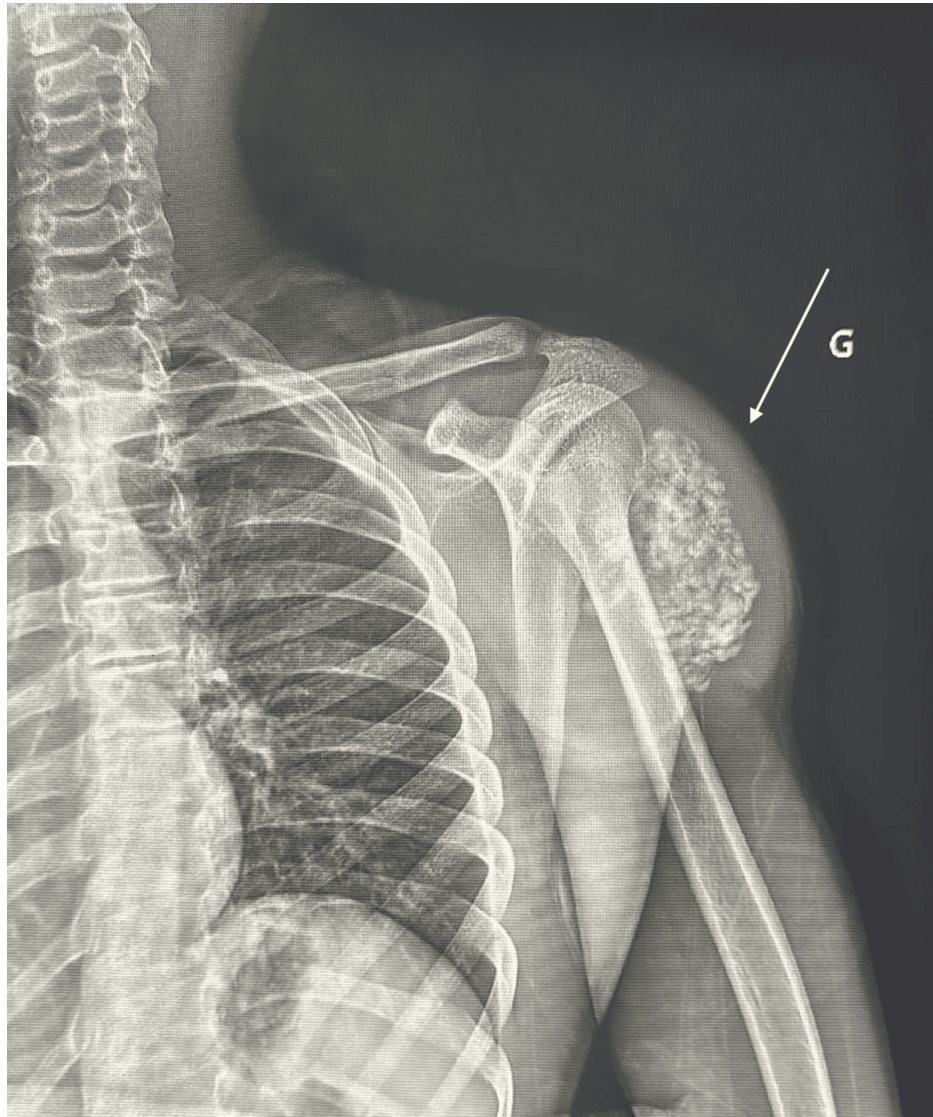


FIGURE 2: Plain radiograph of the left shoulder (lateral view) confirming multilobulated extra-osseous calcifications in the periarticular soft tissues.

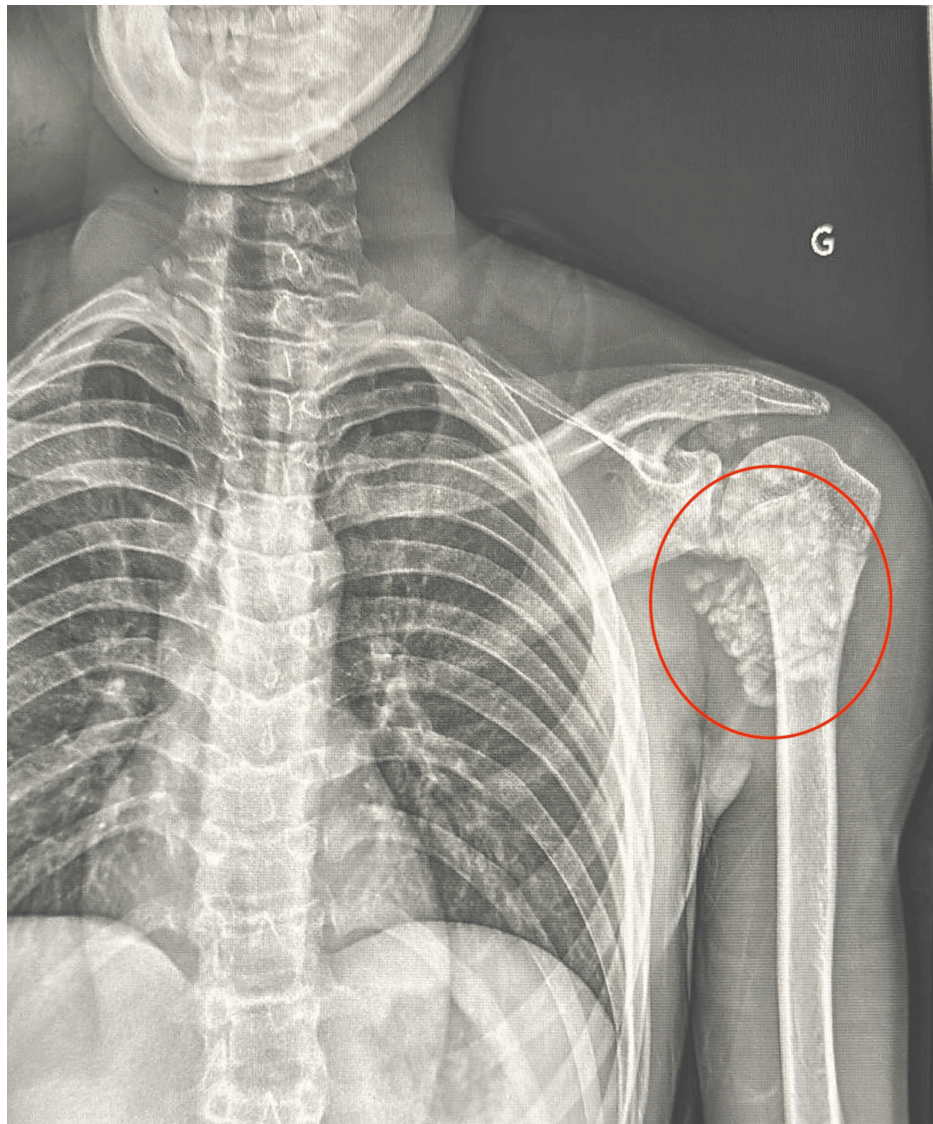


FIGURE 3: Plain radiograph of the left shoulder (anteroposterior view) confirming multilobulated extra-osseous calcifications in the periarticular soft tissues.

MRI of the left shoulder revealed multiple calcified nodules with low signal on T1- and T2-weighted sequences within the subcoracoid bursa, communicating with the glenohumeral joint, infiltrating between the infraspinatus, teres minor, and teres major muscles, with extension to the posterior compartment of the upper third of the arm. MRI also showed synovial thickening with intense enhancement following gadolinium injection (Figures 4, 5).

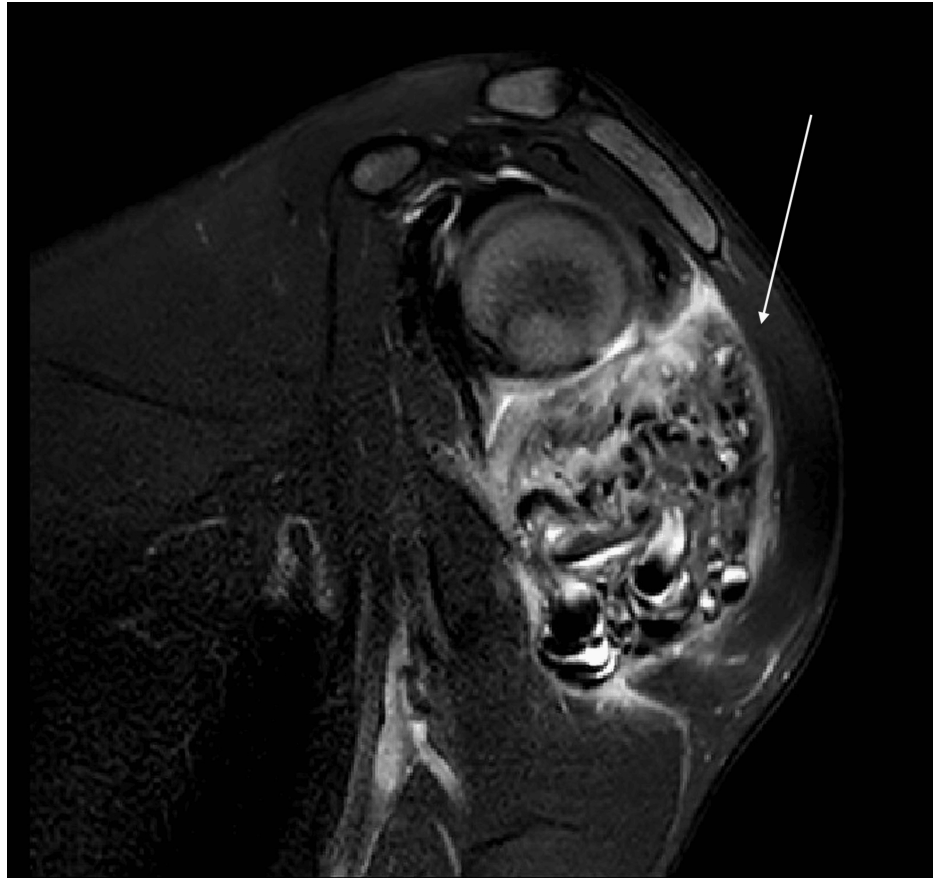


FIGURE 4: Oblique coronal T2-weighted MRI of the left shoulder demonstrating multiple multilobulated periarticular masses with heterogeneous signal intensity and internal fluid-fluid levels.

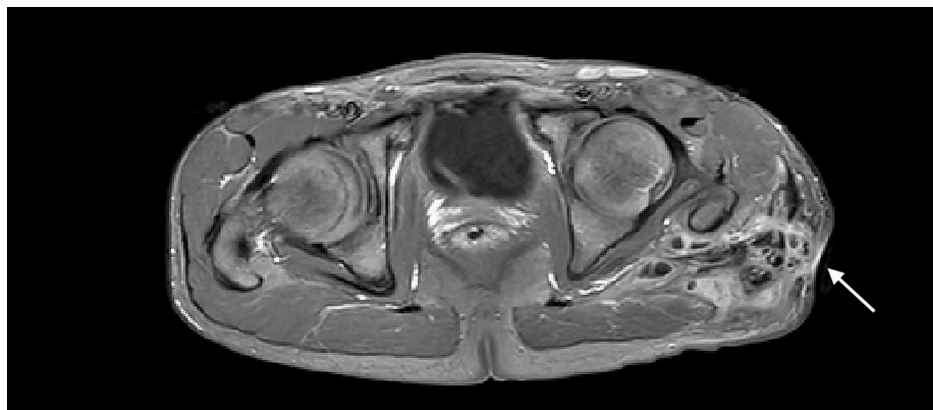


FIGURE 5: Axial MRI of the left shoulder revealing multiple well-defined lobulated periarticular masses with homogeneous low signal intensity on T1- and T2- weighted images reflecting dense calcific content.

Laboratory tests showed normocalcemia at 99.0 mg/L, hyperphosphatemia at 66.0 mg/L, normal renal function, and 25-hydroxyvitamin D deficiency at 16.7 ng/mL (Table [1](#)).

Test	Patient value	Reference range
Calcemia	99.0 mg/L	84 – 102 mg/L
Phosphatemia	66.0 mg/L	23 – 47 mg/L
25-hydroxyvitamin D	16.7 ng/mL	Insufficiency: 20 – 30 ng/mL / Deficiency: < 20 ng/mL

TABLE 1: Biological assessment

Blood test results showing normocalcemia, hyperphosphatemia, normal renal function, and vitamin D deficiency. Vitamin D deficiency is defined as <20 ng/mL and insufficiency as 20-30 ng/mL.

Genetic testing was performed because of the patient's young age, multifocal involvement, and isolated hyperphosphatemia. It identified a homozygous pathogenic variant in the *GALNT3* gene (NM_004482.4:c.484C>T, p.Arg162Ter), resulting in a premature stop codon. This result confirmed the diagnosis of familial hyperphosphatemic TC type 1.

After the definitive diagnosis and genetic confirmation, the family history was reassessed. No similar periarticular masses were reported among first-degree relatives. Given the autosomal recessive inheritance of *GALNT3*-related familial hyperphosphatemic tumoral calcinosis, genetic counseling was recommended, and parental segregation testing was proposed to confirm carrier status.

The patient subsequently underwent surgical excision of the left shoulder mass because of progressive enlargement and limitation of mobility. Phosphate binders were initiated after the definitive diagnosis to control hyperphosphatemia, and cautious vitamin D supplementation was prescribed because of documented deficiency. The surgical objective was complete removal of the calcified mass (Figure 6) while preserving adjacent neurovascular and joint structures. Macroscopically, the excised lesion was multilobulated and firm, consistent with TC.

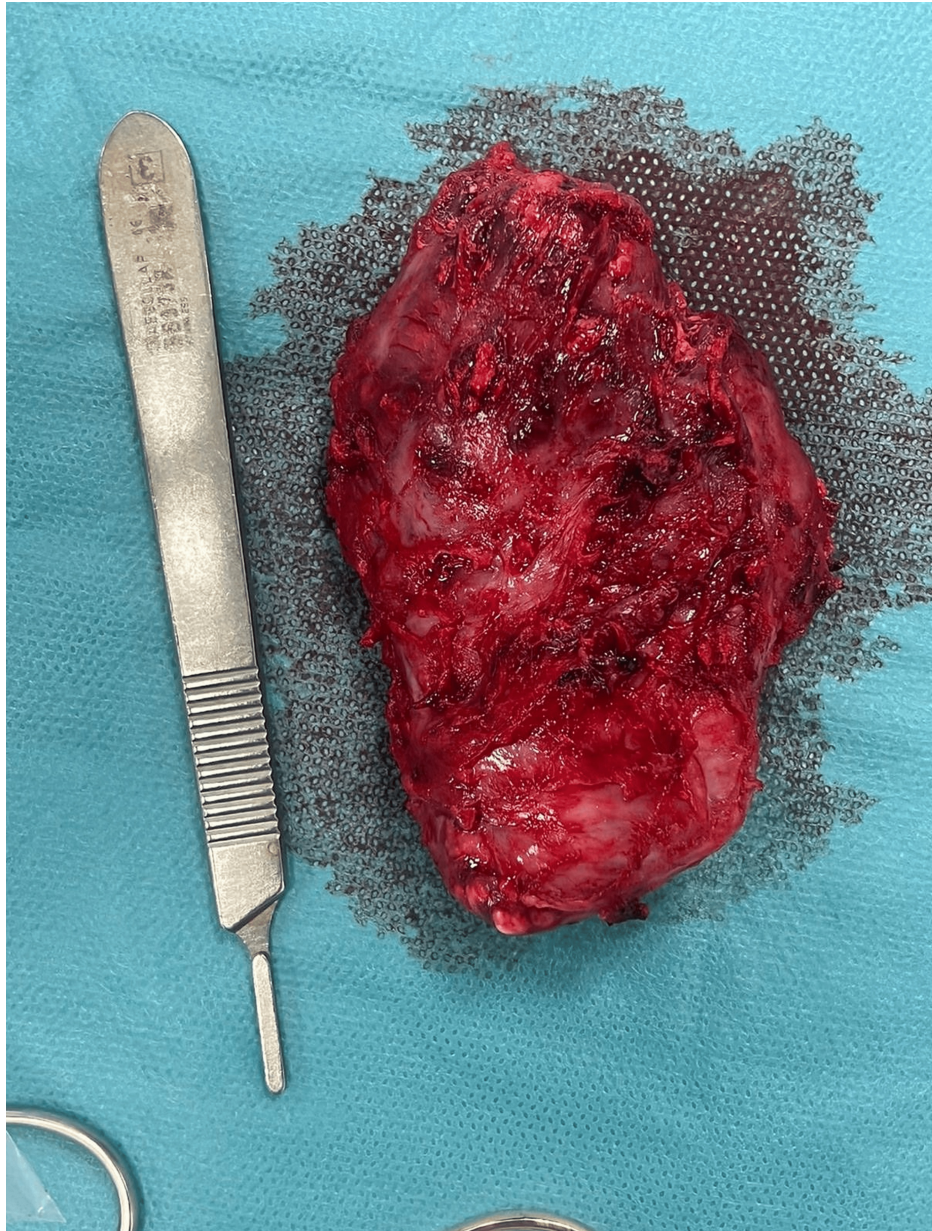


FIGURE 6: Surgical specimen after excision

Appearance of the excised multilobulated periarticular mass from the left shoulder after surgical removal.

Discussion

This case illustrates a genetically confirmed multifocal familial hyperphosphatemic TC type 1 in a Gabonese adolescent with the following distinctive features: the multifocal nature (left hip, elbow and shoulder), young age at onset, isolated hyperphosphatemia with normocalcemia, a homozygous pathogenic *GALNT3* variant, and initial diagnostic delay with an initial histological orientation toward a giant cell tumor of soft tissues.

The diagnostic delay in our case can be explained by several factors. First, the initial lesion was interpreted radiologically as an old calcified hematoma because of its heterogeneous cystic and calcified appearance. Second, the histological presence of giant cells may have contributed to the initial diagnosis of giant cell tumor of soft tissues. Third, the multifocal distribution and the metabolic profile, particularly isolated hyperphosphatemia with normocalcemia and normal renal function, were not initially integrated into the diagnostic reasoning. This case therefore underlines the importance of systematic serum phosphate assessment and careful radiological-pathological correlation in young patients presenting with calcified periarticular soft-tissue masses.

TC is a rare entity reported in the literature in approximately 300 cases [1], with a predominance described among individuals of African origin in 90% of cases according to some series [4]. This ethnic predisposition suggests a genetic involvement. Our patient, of Gabonese origin, fits this epidemiological profile, and genetic testing confirmed *GALNT3*-related familial hyperphosphatemic TC.

Familial hyperphosphatemic TC results from impaired phosphate homeostasis. Fibroblast growth factor 23 (FGF23) plays a central role in this regulation by promoting renal phosphate excretion and reducing 1,25-dihydroxyvitamin D synthesis [9]. Pathogenic variants in *GALNT3*, which encodes a protein involved in O-linked glycosylation, impair FGF23 processing and activity, resulting in increased renal tubular phosphate reabsorption and persistent hyperphosphatemia [6,9]. In our patient, the association of isolated hyperphosphatemia, normocalcemia, and normal renal function was consistent with this mechanism. Genetic testing identified a homozygous pathogenic *GALNT3* variant (NM_004482.4:c.484C>T, p.Arg162Ter), confirming familial hyperphosphatemic TC type 1. Serum intact FGF23 levels were not measured, which remains a limitation of this report.

The identified variant is a nonsense variant predicted to result in premature termination of the *GALNT3* protein. This molecular finding supports the hyperphosphatemic phenotype and justifies genetic counseling and familial assessment [9].

Since *GALNT3*-related familial hyperphosphatemic TC follows an autosomal recessive inheritance pattern, parental segregation testing was proposed to confirm carrier status [9]. Hyperphosphatemic TC has been associated with elevated 1,25-dihydroxyvitamin D concentrations in some reports [10,11]. In our patient, however, 25-hydroxyvitamin D deficiency was documented. Supplementation was therefore prescribed cautiously, with planned monitoring of serum calcium, phosphate, and the calcium-phosphate product.

Clinically, TC manifests as periarticular masses of firm consistency that evolve progressively, are painless in most cases, mobile relative to the skin but adherent to deep structures [8]. Their size ranges from 1 to 30 cm. They are preferentially located at the hip (40-50%), shoulder, elbow, and knee [12]. The multifocal nature is found in 50-70% of cases [1].

On imaging, standard radiography shows rounded or ovoid juxta-articular opacities separated by radiolucent zones creating a “honeycomb” appearance [12]. The presence of fluid-fluid levels or a sedimentation sign may be observed in active lesions [13,14]. Two important negative signs are the absence of osteoporosis and the integrity of the adjacent joint. MRI shows multiloculated masses with low T1 signal and heterogeneous T2 signal with central low-signal areas corresponding to calcifications [15]. In our patient, enhancement of the synovial thickening reflects the associated inflammatory reaction.

Diagnostic confirmation is histological. Macroscopically, the lesion presents as a mass containing multiple compartments filled with chalky material, creating a “sponge-like” appearance [1]. Microscopically, a central deposit of amorphous calcified material is observed, surrounded by a proliferation of macrophages, multinucleated giant cells, and inflammatory elements [16]. A histological classification into three stages based on the degree of cellularity and calcification was proposed by Slavín et al. [17].

The main differential diagnoses were considered in this case. Giant cell tumor of soft tissues was initially suggested because multinucleated giant cells may be present in both entities [18]. However, the multifocal periarticular distribution, the presence of bulky lobulated calcified masses, isolated hyperphosphatemia, and the final histological finding of amorphous calcified deposits without malignancy favored TC.

Myositis ossificans usually follows trauma and shows a characteristic zonal pattern of ossification with peripheral mature bone, which was absent in our patient. Calcific tendinitis is generally tendon-centered, smaller, and more localized, unlike the large multifocal periarticular masses observed here [19]. Synovial sarcoma and extraskeletal osteosarcoma may contain calcifications, but they usually show aggressive soft-tissue features, cellular atypia, malignant spindle-cell proliferation, or malignant osteoid formation, none of which were found histologically. Secondary metastatic calcifications were also unlikely because renal function and serum calcium were normal, and there was no clinical context of chronic kidney disease, hyperparathyroidism, or systemic metastatic calcification [1,8,14].

Regarding management, complete surgical excision remains the main treatment for symptomatic, large, recurrent, or functionally limiting lesions. Incomplete excision carries a risk of local recurrence, as observed in our patient at the hip. Recurrence may occur, particularly after incomplete excision, which supports the need for complete resection when technically feasible [1,9]. Adjuvant medical treatment is based on phosphate-lowering measures, including phosphate binders and dietary phosphorus restriction [20,9]. Acetazolamide, through its phosphaturic effect, has shown some efficacy [21,22]. Medical treatment may be used as an adjunct to surgery to reduce hyperphosphatemia and limit recurrence risk [9]. In our patient, medical treatment was introduced only after histological and genetic confirmation of familial hyperphosphatemic TC type 1. Phosphate binders were prescribed to reduce intestinal phosphate absorption and help control hyperphosphatemia. Vitamin D supplementation was given cautiously because of documented 25-hydroxyvitamin D deficiency, with planned monitoring of serum calcium, phosphate, and

the calcium-phosphate product to avoid worsening of mineral imbalance.

Despite the recurrent and multifocal nature, the long-term prognosis of familial hyperphosphatemic TC is generally favorable, and no malignant degeneration has been reported [9].

Conclusions

Familial hyperphosphatemic TC type 1 is a rare autosomal recessive disorder characterized by normocalcemia associated with isolated hyperphosphatemia and caused by pathogenic variants in *GALNT3*. It primarily affects young individuals of African origin. Diagnosis is based on a combination of clinical, biological, radiological, and histological criteria.

This case highlights the importance of considering TC in any young patient presenting with calcified periarticular masses, particularly when associated with isolated hyperphosphatemia, and underlines the value of genetic testing for diagnostic confirmation and family counseling. Treatment combines surgical excision of symptomatic lesions with phosphate-lowering therapy to control hyperphosphatemia and reduce recurrence risk. The prognosis remains generally favorable despite the often multifocal and recurrent nature of the condition.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Afaf Achchak, Sara Bahloul, Jihad Moulay Berkchi, Lahsen Achemlal

Drafting of the manuscript: Afaf Achchak

Critical review of the manuscript for important intellectual content: Afaf Achchak, Sara Bahloul, Jihad Moulay Berkchi, Lahsen Achemlal

Supervision: Afaf Achchak, Sara Bahloul, Jihad Moulay Berkchi, Lahsen Achemlal

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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References

1. Olsen KM, Chew FS: Tumoral calcinosis: pearls, polemics, and alternative possibilities. *Radiographics*. 2006, 26:871-85. [10.1148/rg.263055099](https://doi.org/10.1148/rg.263055099)
2. Giard A: On hibernial calcification (Article in French). *C R Soc Biol*. 1898, 10:1013-5.
3. Inclan A, Leon P, Camejo MG: Tumoral calcinosis. *JAMA*. 1943, 121:490-5. [10.1001/jama.1943.02840070018005](https://doi.org/10.1001/jama.1943.02840070018005)
4. Smack D, Norton SA, Fitzpatrick JE: Proposal for a pathogenesis-based classification of tumoral calcinosis. *Int J Dermatol*. 1996, 35:265-71. [10.1111/j.1365-4362.1996.tb02999.x](https://doi.org/10.1111/j.1365-4362.1996.tb02999.x)
5. McGregor DH, Mowry M, Cherian R, et al.: Nonfamilial tumoral calcinosis associated with chronic renal failure and secondary hyperparathyroidism: report of two cases. *Hum Pathol*. 1995, 26:607-13. [10.1016/0046-8177\(95\)90165-5](https://doi.org/10.1016/0046-8177(95)90165-5)
6. Topaz O, Shurman DL, Bergman R, et al.: Mutations in *GALNT3*, encoding a protein involved in O-linked glycosylation, cause familial tumoral calcinosis. *Nat Genet*. 2004, 36:579-81. [10.1038/ng1358](https://doi.org/10.1038/ng1358)

7. Ichikawa S, Imel EA, Kreiter ML, et al.: A homozygous missense mutation in human KLOTHO causes severe tumoral calcinosis. *J Clin Invest*. 2007, 117:2684-91. [10.1172/JCI31330](#)
8. Goldblum JR, Folpe AL, Weiss SW: *Enzinger and Weiss's Soft Tissue Tumors*. 6th ed. . Elsevier Saunders, Philadelphia, PA; 2013.
9. Ramnitz MS, Gafni RI: Hyperphosphatemic familial tumoral calcinosis . *GeneReviews* [Internet]. Adam MP, Ardinger HH, Pagon RA, et al. (ed): University of Washington, Seattle, WA; 2018.
10. Prince MJ, Schaeffer PC, Goldsmith RS, Chausmer AB: Hyperphosphatemic tumoral calcinosis: association with elevation of serum 1,25-dihydroxycholecalciferol concentrations. *Ann Intern Med*. 1982, 96:586-91. [10.7326/0003-4819-96-5-586](#)
11. Lyles KW, Halsey DL, Friedman NE, Lobaugh B: Correlations of serum concentrations of 1,25-dihydroxyvitamin D, phosphorus, and parathyroid hormone in tumoral calcinosis. *J Clin Endocrinol Metab*. 1988, 67:88-92. [10.1210/jcem-67-1-88](#)
12. Martinez S, Vogler JB 3rd, Harrelson JM, et al.: Imaging of tumoral calcinosis: new observations. *Radiology*. 1990, 174:215-22. [10.1148/radiology.174.1.2104680](#)
13. Hug I, Gunçaga J: Tumoral calcinosis with sedimentation sign . *Br J Radiol*. 1974, 47:734-6. [10.1259/0007-1285-47-562-734](#)
14. Martinez S: Tumoral calcinosis: 12 years later . *Semin Musculoskelet Radiol*. 2002, 6:331-39. [10.1055/s-2002-36732](#)
15. Senol U, Karaali K, Cevikol C, Dincer A: MR imaging findings of recurrent tumoral calcinosis . *Clin Imaging*. 2000, 24:154-6. [10.1016/s0899-7071\(00\)00190-x](#)
16. Bukholm G, Bjørnland K, Ellekjaer H, Berdal BP, Degré M: Vesicular stomatitis virus infection enhances invasiveness of *Salmonella typhimurium*. *J Pathol Microbiol Immunol*. 1988, 96:400-6. [10.1111/j.1699-0463.1988.tb05322.x](#)
17. Slavin RE, Wen J, Kumar D, et al.: Familial tumoral calcinosis. A clinical, histopathologic, and ultrastructural study with an analysis of its calcifying process and pathogenesis. *Am J Surg Pathol*. 1993, 17:788-802. [10.1097/0000478-199308000-00004](#)
18. Folpe AL, Morris RJ, Weiss SW: Soft tissue giant cell tumor of low malignant potential: a proposal for the reclassification of malignant giant cell tumor of soft parts. *Mod Pathol*. 1999, 12:894-902.
19. Hwang ZA, Suh KJ, Chen D, Chan WP, Wu JS: Imaging features of soft-tissue calcifications and related diseases: a systematic approach. *Korean J Radiol*. 2018, 19:1147-60. [10.3348/kjr.2018.19.6.1147](#)
20. Mozaffarian G, Lafferty FW, Pearson OH: Treatment of tumoral calcinosis with phosphorus deprivation . *Ann Intern Med*. 1972, 77:741-5. [10.7326/0003-4819-77-5-741](#)
21. Yamaguchi T, Sugimoto T, Imai Y, et al.: Successful treatment of hyperphosphatemic tumoral calcinosis with long-term acetazolamide. *Bone*. 1995, 16:247-50.
22. Puschett JB, Egel J, Pfanstiel J: Brush border vesicle transport effects of 1,25-dihydroxy vitamin D3 . *Adv Exp Med Biol*. 1984, 178:133-4. [10.1007/978-1-4684-4808-5_19](#)