Turk J Phys Med Rehab 2023;69(2):252-256
DOI: 10.5606/tftrd.2023.8815
Available online at www.turkishjournalpmr.com

Case Report

Fibrous dysplasia and McCune-Albright syndrome: A case report with review of literature on the rehabilitation approach

Sefa Gümrük Aslan[1], Kutay Tezel[1], N. Kutay Ordu-Gökkaya[2]

[1]Department of Physical Medicine and Rehabilitation, University of Health Sciences Gülhane School of Medicine, Gaziler Physical Medicine and Rehabilitation Health Application and Research Center, Ankara, Türkiye
[2]Department of Physical Medicine and Rehabilitation, Ankara City Hospital, Ankara, Türkiye

Received: April 19, 2021 **Accepted:** November 02, 2021 **Published online:** June 09, 2022

ABSTRACT

McCune-Albright syndrome is classically defined by the clinical triad of fibrous dysplasia (FD) of the bone, café-au-lait macules, and endocrinopathies. We report the case of a 15-year-old male with a diagnosed with McCune Albright syndrome. McCune-Albright syndrome remains a diagnostic challenge, and delayed diagnosis may have significant consequences. Routine musculoskeletal screening along with other endocrinopathies should be kept in mind. The rehabilitation programs that provides significant improvement in their quality of life. The treatment of McCune-Albright syndrome is directed toward the specific symptoms that are apparent in each individual.

Keywords: Fibrous dysplasia, McCune-Albright syndrome, rehabilitation, scoliosis.

Fibrous dysplasia (FD) is a genetic disease of the mesenchymal origin of the bone and a developmental anomaly of an unidentified cause, provoked by a somatic activating pathogenic variant in GNAS, which encodes the cyclic adenosine monophosphate (cAMP) pathway-associated G-protein, Gsα.[7] Fibrous dysplasia is characterized by the replacement of fibrous tissue with standard or underdeveloped bone tissue or by irregular osteoid formation.[1]

Three clinical forms of fibrous dysplasia have been identified: monostotic form (70-80%), which affects a single bone; polyostotic form (20-30%), which involves multiple bones; and finally, if the polyostotic form is accompanied by cutaneous and endocrine findings, it is called McCune-Albright syndrome.[2]

Although precocious puberty is the most prevalent, excessive release of growth hormone is observed in 21% of the affected cases.[1] Furthermore, multiple endocrine abnormalities, including hyperthyroidism, hypercortisolemia, acromegaly, and hyperprolactinemia, can occur. Hyperthyroidism and acromegaly are the most common endocrine abnormalities in adults.

Fibrous dysplasia can impact any part of the bones of the craniofacial, axial, or appendicular skeleton or combinations thereof, with a mosaic pattern as in the skin. The skull base and proximal femurs are the most frequently involved foci.[3]

Fibrous dysplasia lesions cause bone pain, fracture, deformity, loss of vision, or hearing and cranial nerve compression. In addition to all these, patients with FD should be monitored at routine intervals in terms of progressive and severe scoliosis development.[4] In this report, we present a pediatric patient with

Corresponding author: Sefa Gümrük Aslan, MD. SBÜ Ankara Gaziler Fizik Tedavi ve Rehabilitasyon Eğitim ve Araştırma Hastanesi, 06800 Bilkent, Ankara, Türkiye.
E-mail: sefagumrukk@gmail.com

Cite this article as:
Aslan SG, Tezel K, Ordu Gökkaya NK. Fibrous dysplasia and McCune-Albright syndrome: A case report with review of literature on the rehabilitation approach. Turk J Phys Med Rehab 2023;69(2):252-256. doi: 10.5606/tftrd.2023.8815.

McCune-Albright syndrome whose diagnosis was delayed and discuss the rehabilitation of this patient.

CASE REPORT

A 15-year-old male patient presented with left proximal femoral fracture that occured during a low-energy trauma. It was debriefed from the patient's history that he had undergone numerous low-energy left femur fractures and tibial shaft fractures on both sides. After the patient's fracture treatment was completed, he was referred to the pediatrics and physical therapy department. The patient's existing bone and joint pains were thought of as growth pain prior to diagnosis. Based on the patient's medical history of frequent fractures, the orthopedic surgeon recommended a wheelchair. At the time of admission to the rehabilitation center, the patient was using a wheelchair for mobilization with strict recommendations and had kinesiophobia, which had emerged due to the history of multiple fractures.

The patient was dependent on their family in many activities, including wheelchair transfers. The patient, who had previously not taken an active physical therapy program, was consulted to our rehabilitation center from the pediatric endocrinology outpatient clinic to reevaluate joint pain, muscle atrophies, and mobilization limitations. Bone mineral densitometry was planned considering the patient's endocrinopathies and long-term immobilization. The L1-4 vertebra were evaluated by dual-energy X-ray absorptiometry, resulting in a T-score of -2.5 and a Z-score of -0.3, and the femoral neck T- and Z-scores were -2 and -1.2, respectively. The patient was using pamidronate 90 mg, calcium 1200 mg, and vitamin D 1000 IU daily. After evaluating the direct radiographs of the patient, it was determined to perform whole-body three-phase bone scintigraphy, which revealed multiple increased activity involvements in the craniofacial bones, bilateral upper extremities, hemithorax, bilateral ribs, pelvic bones, bilateral femur, and tibia in accordance with the polyostotic fibrous dysplasia foci. Skeletal lesions were limited to the craniofacial area (Figure 1). The hearing was evaluated and was within standard limits. The Tampa Scale for Kinesiophobia, designed to evaluate the patient's current level of kinesiophobia, scored 52 out of 68.

TABLE 1
Laboratory results of the patient

	Median
Alkaline phosphatase (IU/ L)	**700** ↑ (38-126)
Ca (mg/dL)	9.2 (8.9-10.3)
Phosphore (mg/dL)	3.7 (2.4-4.7)
Growth hormone (mIU/mL)	**1875** ↑ (0-20)
FSH (µIU/mL)	**29.43** ↑ (3.5-12.5)
TSH (µIU/mL)	2.14 (0.35-5.33)
Free T3 (pg/mL)	3.14 (1.71-3.71)
Free T4 (ng/dL)	0.7 (0.70-1.48)
PTH (pg/mL)	21.4 (12-88)
25-OH-D3 (ng/mL)	32.26
Cortisol (µg/dL)	8.82 (6.2-19.4)
Luteinizing hormone (µIU/mL)	6.13 (1.27-19.26)
Estradiol (pg/mL)	33.13 (12.5-166)
Prolactin (µIU/mL)	10.56 (2.64-13.13)
Spot urine Ca (ng/mL)	15.9 (20-50)

Ca: Calsium; FSH: Follicle-stimulating hormone; TSH: Thyroid stimulating hormone; PTH: Parathyroid hormone.

On inspection, irregular edged café-au-lait macules, which are components of the syndrome, were observed on the left side of the patient's back and neck. The patient had a mild bilateral genu valgum deformity and, according to the Simon classification, had Grade 1 gynecomastia. On physical examination, the bilateral proximal upper extremity muscle strengths were 5/5, distally 3/5, the lower extremity muscle strength bilateral ankle dorsiflexions were 3/5, which was induced due to disuse, and other muscles strengths were 4/5 based on the Global Oxford Scale. There was no spasticity. The deep tendon reflexes of the upper and lower extremities were normal, and no pathological reflexes were revealed. Sensory examinations were normal. The plain radiographs of the spine revealed thoracic and lumbar scoliosis with a Cobb angle of 12° and 17°, respectively.

The range of motion of the elbow, hip, and knee was minimally restricted. The decision on whether existing osteoporosis and multiple bone FD will cause a potential fracture was reevaluated with pediatric endocrinology and orthopedic specialists, and an active rehabilitation program was initiated.

During the first two weeks, a comprehensive rehabilitation program was initiated for the patient, including lower and upper extremity paraspinal muscle strengthening without standing up, range of motion stretching exercises, functional electrical stimulation for bilateral ankle dorsiflexors, and aquatic exercises in the pool. At the end of the second week, the patient was reevaluated, and standing, balance/coordination, and proprioception exercises

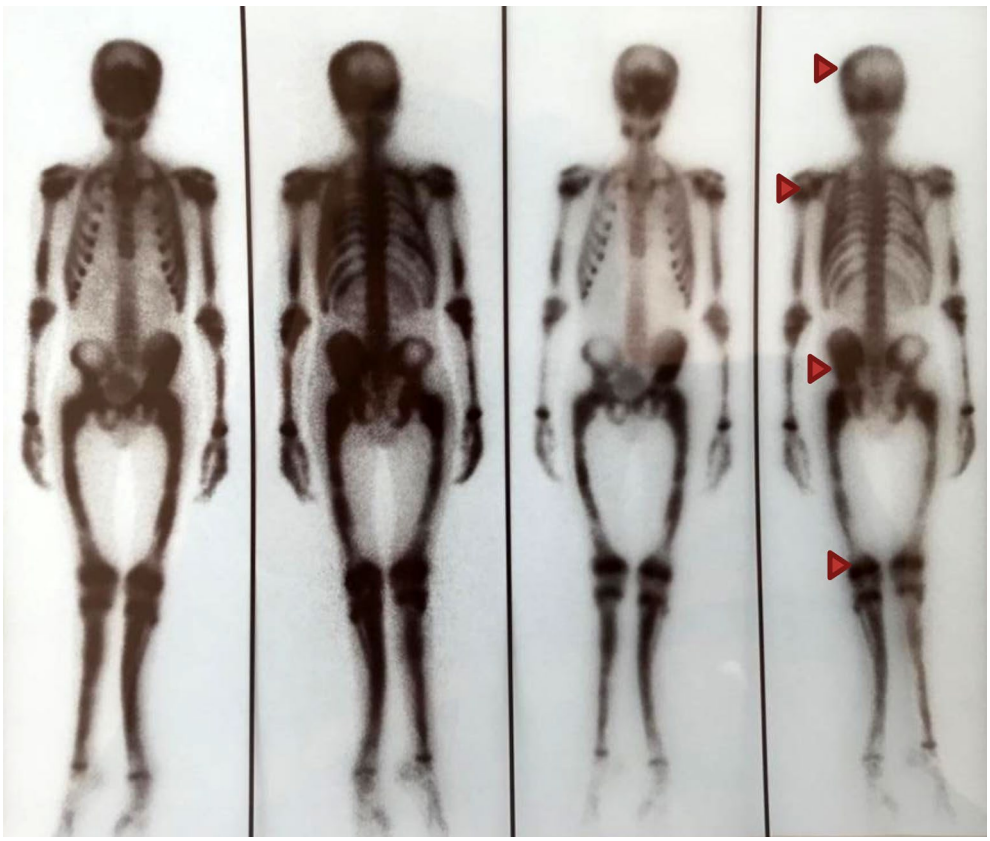

Figure 1. Scintigraphy scan in the areas of fibrous dysplasia. Technetium-99 scintigraphy scan showing increased tracer uptake in areas of fibrous dysplasia, including the craniofacial bones, bilateral upper extremities, bilateral femur, and tibia (red arrowheads).

were added while gradually increasing body weight bearing on the bodyweight elimination treadmill, considering the mobilization goal. At the end of the rehabilitation process, which lasted for eight weeks, five days a week, the patient could stand without support and was discharged after observing the level of independence in daily activities and significant improvement in school and social life with the provision of middle-distance ambulation with personal supervision. The patient's anxiety about moving and falling was significantly reduced. The kinesiophobia assessment score decreased to 20 at the end of the rehabilitation program.

DISCUSSION

McCune-Albright syndrome is characterized by the triad of FD of the bone, café-au-lait spots, and early puberty. It was first described in 1936 by Dr. Donovan McCune and Dr. Fuller Albright.[5,6] It is a rare syndrome with an estimated prevalence between 1/100,000 and 1/1,000,000.[5,6]

Fibrous dysplasia patients have no or few symptoms early in life. The first symptoms often occur in childhood, more specifically, in 80% before the age of 15.[7] Bone pain or fractures can also be seen in the third to fifth decade of life. Fractures can be observed in all effected bones.[8]

Scoliosis is widespread in FD and should not be disdained as it can cause deformities and rarely even death if left untreated.[8] Scoliosis can be detected in most FD patients only by physical examination.[9] If an increasing deformity is detected in the physical examination during the patient's follow-up, the patient should also be scanned with radiographs.

In the literature, there is no study recommending bracing in the treatment and follow-up of patients with FD. It is thought that the use of a corset may be ineffective since most patients with FD have bone involvement that can cause progressive scoliosis.[10] Surgical fixation should be considered if the Cobb angle is above 30° depending on the rate of progression, and

curves of greater magnitude cause loss of pulmonary function.[11]

There is no available medical treatment that can alter the course of the disease in FD; hence, the focus is more on optimizing existing function and minimizing the morbidity associated with fractures and deformity. For instance, although analgesic drugs can be used in mild bone pain and narcotic analgesics in severe bone pain, these drugs do not manage the course of the disease. Bisphosphonates are effectual antiresorptive agents used in controlling the disease.[12] Denosumab has been shown to significantly reduce pain, bone turnover markers and tumor growth rate in FD cases.[13]

Paul et al.[14] revealed that the hip is the most affected lower extremity joint in terms of both strength and mobility in patients with polyostotic FD. In these patients, it was found that the limitation of joint motion in the hip and weakness in the hip belt caused a decrease in ambulation and functionality of the individuals in correlation with the severity of the disease. Therefore, it is assumed that targeting and developing neuro-rehabilitation programs to be applied in patients with McCune-Albright syndrome can lead to increased strength and range of motion. Rehabilitation programs can help patients to increase functionality and reduce morbidity and dependency.[14]

A child with FD should be clinically evaluated twice a year to reduce radiation exposure if there is no history of asymptomatic or new fracture.[15] In the examination, attention should be paid to a possible limitation in joint motion, an angular deformity that may develop in the spine, and the possibility of length difference between the lower extremities. Since the presence of limb length discrepancy might be an early sign for a progressive deformity, it is recommended to evaluate it with a standing long-leg X-ray. Surgical intervention can be applied if a neurological deficit or a deformity due to fracture is observed during the follow-up visits.[15]

As FD patients are prone to fragility due to metabolic problems and decreased activity, methods that prevent weight transfer should be avoided as much as possible during fracture healing. It is assumed that leaving the patient immobile for a long time will only increase the preexisting bone fragility.[16]

In addition to the follow-up and control of the disease, it should be considered that patients might need a comprehensive rehabilitation program that provides significant improvement in their quality of life. The essential goal of rehabilitation programs, as in the case we have presented, should be to ambulate these patients and increase their range of motion and muscle strength.

In conclusion, McCune-Albright syndrome remains a diagnostic challenge, and delayed diagnosis may have significant consequences. Routine musculoskeletal screening along with other endocrinopathies should be kept in mind. In case of scoliosis, skeletal deformities, joint contractures, and muscle weakness, a detailed physical examination must be performed, and a tailored rehabilitation program should be initiated to increase functionality and quality of life.

Patient Consent for Publication: A written informed consent was obtained from the patient and/or parent of the patient.

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

Author Contributions: A written informed consent was obtained from the patient parents of the patient.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Chapurlat RD, Orcel P. Fibrous dysplasia of bone and McCune-Albright syndrome. Best Pract Res Clin Rheumatol 2008;22:55-69.
2. Dahlin DC, Unni KK. Bone tumors: General aspects and data on 8,547 cases 4th ed. United States: Charles C Thomas Pub.; 1986.
3. Kelly MH, Brillante B, Collins MT. Pain in fibrous dysplasia of bone: Age-related changes and the anatomical distribution of skeletal lesions. Osteoporos Int 2008;19:57-63.
4. Leet AI, Chebli C, Kushner H, Chen CC, Kelly MH, Brillante BA, et al. Fracture incidence in polyostotic fibrous dysplasia and the McCune-Albright syndrome. J Bone Miner Res 2004;19:571-7.
5. Albright F, Butler AM, Hampton AO, Smith P. Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction, with precocious puberty in females - Report of five cases. N Engl J Med 1937;216:727-46.
6. McCune D. Osteitis fibrosa cystica: The case of a nine-year-old girl who also exhibits precocious puberty, multiple pigmentation of the skin and hyperthyroidism. American Journal of Diseases of Children 1936;52:743-4.
7. Hart ES, Kelly MH, Brillante B, Chen CC, Ziran N, Lee JS, et al. Onset, progression, and plateau of skeletal lesions in fibrous dysplasia and the relationship to functional outcome. J Bone Miner Res 2007;22:1468-74.

8. Boyce AM, Florenzano P, de Castro LF, Collins MT. Fibrous Dysplasia/McCune-Albright Syndrome. 2015 Feb 26 [Updated 2019 Jun 27]. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, et al. editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK274564/
9. Leet AI, Magur E, Lee JS, Wientroub S, Robey PG, Collins MT. Fibrous dysplasia in the spine: Prevalence of lesions and association with scoliosis. J Bone Joint Surg [Am] 2004;86:531-7.
10. Mancini F, Corsi A, De Maio F, Riminucci M, Ippolito E. Scoliosis and spine involvement in fibrous dysplasia of bone. Eur Spine J 2009;18:196-202.
11. Berglund JA, Tella SH, Tuthill KF, Kim L, Guthrie LC, Paul SM, et al. Scoliosis in fibrous dysplasia/McCune-Albright syndrome: Factors associated with curve progression and effects of bisphosphonates. J Bone Miner Res 2018;33:1641-8.
12. DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. J Bone Joint Surg [Am] 2005;87:1848-64.
13. Boyce AM, Chong WH, Yao J, Gafni RI, Kelly MH, Chamberlain CE, et al. Denosumab treatment for fibrous dysplasia. J Bone Miner Res 2012;27:1462-70.
14. Paul SM, Gabor LR, Rudzinski S, Giovanni D, Boyce AM, Kelly MR, et al. Disease severity and functional factors associated with walking performance in polyostotic fibrous dysplasia. Bone 2014;60:41-7.
15. Stanton RP, Ippolito E, Springfield D, Lindaman L, Wientroub S, Leet A. The surgical management of fibrous dysplasia of bone. Orphanet J Rare Dis 2012;7 Suppl 1:S1.
16. Fang X, Liu H, Lang Y, Xiong Y, Duan H. Fibrous dysplasia of bone: Surgical management options and outcomes of 22 cases. Mol Clin Oncol 2018;9:98-103.