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Total Hip Arthroplasty in Dyggve-Melchior-Clausen Syndrome: Literature Review and Case Report

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ABSTRACT

Dyggve-Melchior-Clausen (DMC) disease is a rare spondyloepiphyseal autosomal recessive disorder characterized by skeletal dysplasia and intellectual disability. Hip arthritis, often secondary to hip dysplasia, presents at an early age. Current literature suggests that osteotomies do not benefit DMC syndrome-associated hip disease but reports of total hip arthroplasty in these patients are lacking. We present a case of bilateral hip replacement in a 31-year-old patient with DMC syndrome. After planning the operation with the use of computed tomography, we chose to use a small-dimension porous cup along with an appropriately sized version control stem in order to address the unique acetabular and femoral deformities. In conclusion, we consider total hip replacement in DMC syndrome to be safe and effective in addressing a challenging hip pathology.

Introduction

Dyggve-Melchior-Clausen (DMC) disease is a rare spondyloepiphyseal autosomal recessive genetic disorder characterized by skeletal dysplasia and intellectual disability. The disorder is caused by mutations in the DYM gene located on the 18q12-12.1 chromosomal region. It was first described in 1962 as a condition resembling Morquio-Ullrich in a series of 3 patients described by Dyggve et al. [1]. There is typically a good prognosis for general health and survival in the condition [2]. As of 2007, there were over 90 individuals with DMC or the variant Smith-McCort syndrome [3]. There have been at least 16 different dymeclin mutations described in at least 21 unrelated families with founder effects in countries such as Morocco, Lebanon, Egypt, and Guam Island [4,5].

DMC is a rare type of spondyloepiphyseal dysplasia (SED) that is associated with a progressive spondyloepimetaphyseal dysplasia (SEMD). It is further characterized by progressive dwarfism with a short trunk, rhizomelic limb shortening, facial dysmorphism, coarse faces, and other skeletal deformities. Intellectual disability can range from mild to severe. Characteristic radiographic findings of the condition include an iliac crest apophysis with lacy, irregular ossification, double vertebral hump with central constriction, odontoid hypoplasia with atlantoaxial instability, and hip dysplasia. Hip pathology is characterized by hypoplastic acetabula, subluxated femoral heads, and notable hip arthritis [6,7].

What differentiates DMC from SEMD and mucopolysaccharidosis is its features of facial dysmorphism, body habitus, and pathognomonic radiological signs. DMC syndrome has the absence of corneal clouding, deafness, and cardiac abnormalities that can be seen in mucopolysaccharidosis. In SEMDs, the double vertebral hump with central constriction is absent. Rather, the vertebrae demonstrate more anterior pointing and narrowed disk spaces, sclerotic end plates, and without odontoid hypoplasia. A distinct form of SEMD can present with microcephaly and intellectual disability but without the radiographic lacy appearance of the iliac wings as seen in DMC. In mucopolysaccharidosis IV, Morquio disease, there is anterior pointing and thoracolumbar hypoplasia of vertebrae as well as distal radial and ulnar obliquity at the wrist articulation with proximal metacarpal pointing [5].

The current mechanism of hip dysplasia in DMC syndrome is thought to be epiphyseal in origin. Spondyloepimetaphyseal dysplasia leads to progressively abnormal development of the hip epiphysis and growth of the hip joint [8]. The abnormal femoral head can later develop osteonecrosis and major arthrosis as a

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sequela of DMC [9]. Suggested treatment options include realignment of the proximal femur and/or acetabulum, realignment osteotomy, cheilectomy of the hip, and/or total hip replacement [5,6,9].

We aim to review the complex hip pathology associated with DMC syndrome and its treatment options, as well as report on a case of successful bilateral total hip arthroplasties (THAs) in a patient with this rare syndrome.

Case history

The patient gave written, informed consent to have this case report published. The patient was a 30-year-old male measuring 3 ft 10 inches with history of DMC syndrome, bilateral acetabular dysplasia, and severe bilateral hip arthrosis who presented for preoperative medical assessment for left THA in September 2022. He had a surgical history of a right proximal femur osteotomy with associated screw fixation, curettage, and grafting of a right knee nonossifying fibroma, craniectomy decompression, and a C1 laminectomy. He reported no other medical problems. He experienced severe left groin pain that limited his activities of daily living and ambulation, refractory to pain medication and physical therapy. Physical examination revealed left hip pain, exacerbated by internal and external rotation of the hip. Radiographic images revealed significant bilateral hip dysplasia, advanced arthritic changes in both hips, and right hip hardware from a previous proximal femoral osteotomy (Figs. 1-3). A computed tomography (CT) scan was obtained for further bony evaluation. In addition to a shallow acetabulum, the CT scan displayed a flattened femoral head with lateral subluxation, excessive anteversion of the femoral neck, and a small-diameter femoral canal.

The preop planning for the case required radiographs of both hips, full-length radiograph for limb length and alignment as well as a CT scan of both hips and pelvis with 3-dimensional reconstructions to evaluate the need for custom implants. Using the standard radiograph films, both hips were templated using a software templating system (TraumaCad, Brainlab, Germany). The templating software demonstrated that the anatomy would tolerate an 8-mm stem. This was verified on the CT scan. Using this information, the surgical plan was made for an S-ROM stem and Pinnacle Bantam acetabular cup (DePuy Synthes, Warsaw, IN). A custom-made stem was not required as the S-ROM stem can accommodate a 7-mm canal and larger. A similar sized cemented option was also made available in the event that proximal femur was not suitable for cementless fixation; however, this was not necessary.

He underwent a complex left THA in October of 2022 after informed consent for the procedure was obtained. He was positioned in the lateral position using a pegboard hip positioner, with careful attention to protect his cervical spine. A posterolateral approach to the hip was performed. During dissection down to the hip, there were no identifiable short external rotators other than the quadratus, and a thickened capsule was consistent with advanced capsular dysplasia. His femoral head was noted to be flattened and extremely high riding, and the femoral neck displayed significant anteversion. After osteotomy of the femoral neck was performed, the head was measured to be 34 mm in diameter. Fluoroscopic imaging was used to identify the desired anatomic hip center, and reaming was begun. Small reamers were used to ensure full medialization of the shallow acetabulum. A 40-mm porous cup (Pinnacle Bantam, DePuy Synthes, Warsaw, IN) was impacted into position and a 15mm screw was added for additional fixation. In light of his small-diameter canal and significant proximal femur anteversion, we elected for a ream and broach stem which allowed control of the version (S-ROM, DePuy Synthes, Warsaw, IN). The proximal sleeve was impacted into position, and a 6-mm $\times$ 115-mm stem was inserted with the version set at 20 degrees of anteversion. Finally, a 22 + 0 head was impacted onto the trunnion to engage the morse taper. Postoperatively, he recovered well with no complications. Active and passive forward flexion quickly improved to 90 degrees without pain. By 3 months postoperatively, he was weight-bearing with no pain in his left lower extremity, limited to a rolling walker only due to right hip pain. Post-operative radiographs demonstrated left THA in a good position with no sign of hardware failure, lysis, or loosening (Fig. 4).

He underwent a right THA in June of 2023. A THA was performed through the posterolateral approach with a similar technique to the left hip. Femoral head deformation with a proximal femoral screw was consistent with previous proximal femur osteotomy (Fig. 5). His prior hardware was successfully removed, and he was fitted with a right total hip using a 44-mm porous cup and a similarly sized femoral component to his contralateral hip. He was discharged with the plan of weight-bearing as tolerated, pain medications as needed, deep vein thrombosis prophylaxis, and was discharged home.

At his 6-week follow-up from his right total hip replacement, he was comfortably walking with a walker and demonstrated significant improvement from preoperative status. He denied pain and has progressed well with physical therapy. Physical examination revealed well-healed surgical incisions with a painless hip range of motion and a straight leg raise with good strength. Knee range of motion was still limited to 90 degrees bilaterally, which was consistent with his baseline. Post-operative radiographs demonstrated bilateral THAs in a good position with no signs of hardware failure, lysis, or loosening (Fig. 6). Our patient was seen for his 1-year follow-up from his left total hip replacement and 3 months from his complex conversion THA. He has no pain in his left hip but continues to have slight discomfort on his right hip around surgical site that may be secondary to surgical exposure. Since his last visit,

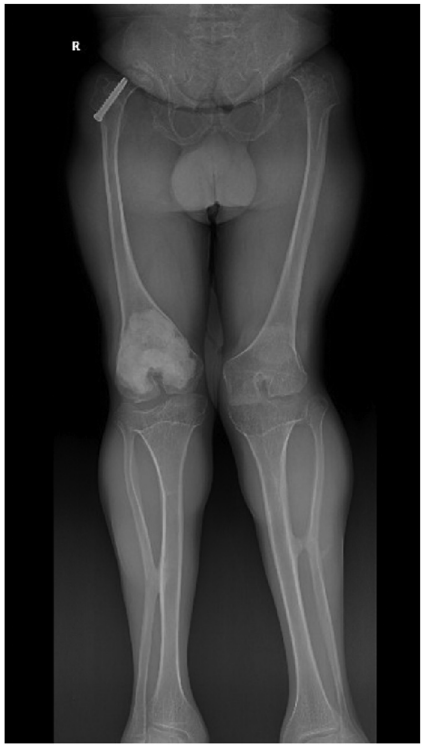

Figure 1. Bilateral lower extremity preoperative radiograph before left total hip arthroplasty. Full-length standing radiograph displays bilateral hip dysplasia with valgus knees, left worse than right, as well as bilateral degenerative changes of the knees. Right distal femur had cementing from prior surgery.

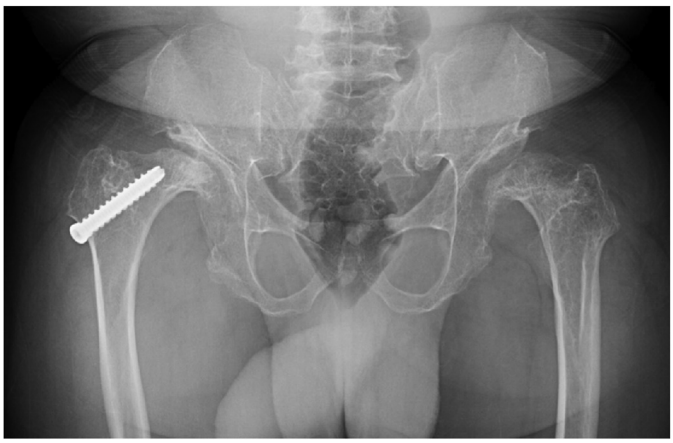

Figure 2. Bilateral hip preoperative radiograph with a demonstration of right femoral screw. Imaging of the pelvis redemonstrates bilateral hip dysplasia and lacy pelvis.

his status has improved significantly walking comfortably with a walker. He has demonstrated improved strength in leg raise and bilateral hip range of motion for flexion was 110 degrees, internal rotation of 15 degrees, and external rotation of 30 degrees.

Regarding both procedures, the surgeries were done using a posterior approach with the patient positioned in a lateral decubitus position. Three-dimensional reconstructions were made of the pelvis given the patients difficult anatomy. The acetabulum and proximal femurs behaved very similar to a Crowe 3 hip dysplasia. Similar to a dysplastic hip, the acetabulum was carefully positioned and cup stability was achieved with medializing to an appropriate depth to reestablish the nip center of rotation and create superior coverage. The unique challenge in this case is the short femur of 26 centimeters. This pathologically small femur makes a shortening subtrochanteric osteotomy problematic as the stem would have to traverse greater than 50% of the femoral length making anterior perforation very likely. For this reason, a low femoral neck cut was selected just above the level of the lesser trochanter and the implant was seated at this level. Soft-tissues releases were completed at the level of the joint capsule including an anterior capsular release to allow for successful hip reduction. The gluteus maximus tendon was also released off of its insertion on the proximal femur. In addition, the sciatic nerve was carefully dissected out for easy inspection throughout the case as the planned lengthening of the lower extremity was approximately 2

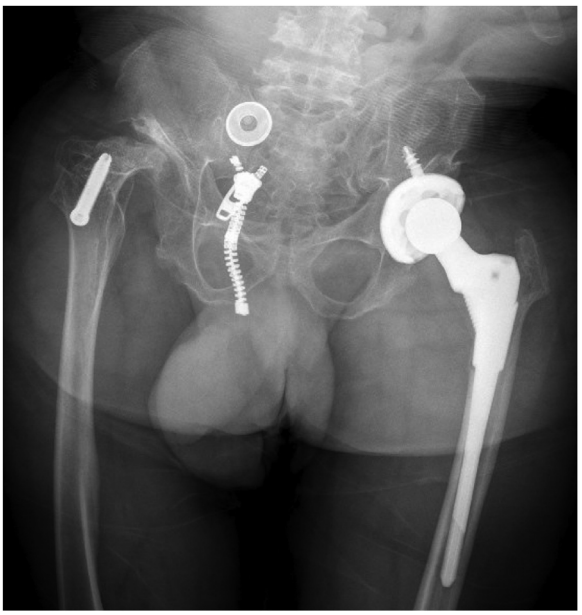

Figure 4. Postoperative left total hip arthroplasty that demonstrates intact hardware. Nonhardware artifacts (zipper and coin) are seen in the center.

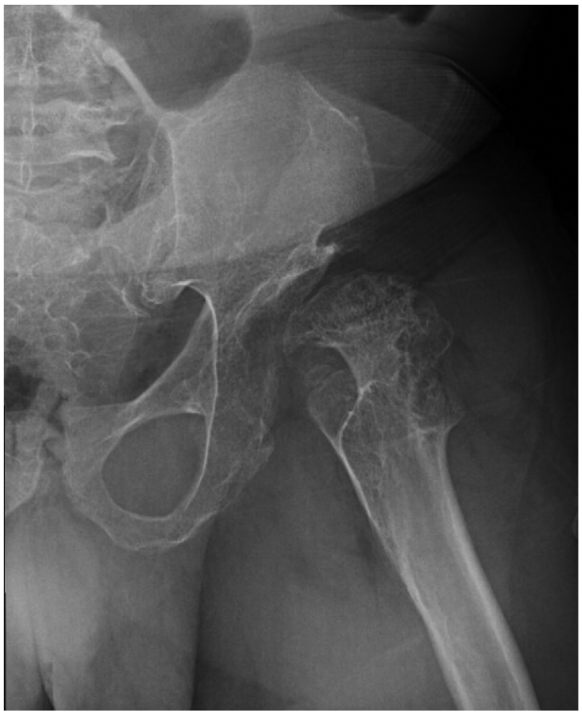

Figure 3. PA of left femur shows a necrotic, degenerative femoral head.

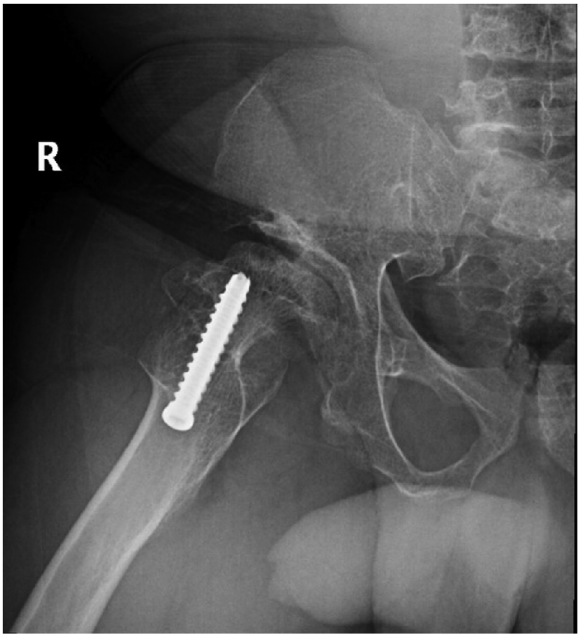

Figure 5. Advanced degenerative changes of the femoral head and acetabulum. Osteonecrotic right femoral head secondary to prior femoral osteotomy, femoral head deformation with subluxation and collapse. Significant superiolateral bone loss in the right acetabulum.

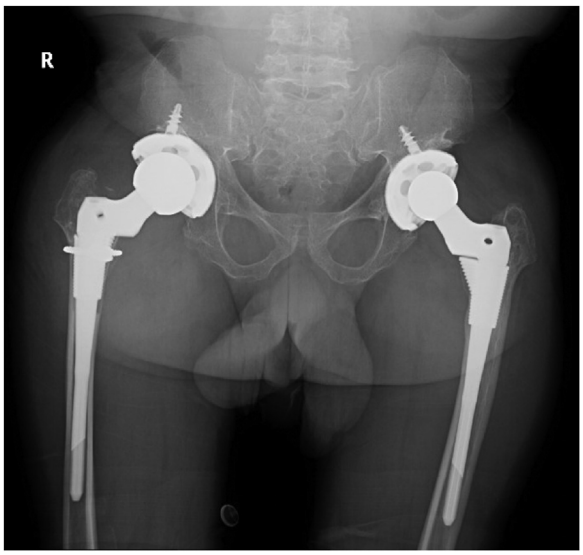

Figure 6. AP imaging of hips demonstrating intact bilateral total hip arthroplasty without hardware failure. AP, anterior-posterior.

centimeters and given that no shortening osteotomy was possible all care had to be taken to preserve sciatic nerve function.

His postoperative deep vein thrombosis prophylaxis was the standard prophylaxis for standard postoperative risk patients in our institution and he was given Aspirin 81 mg twice daily for 4 weeks. The postoperative protocol was slightly more complex as patients with DMC syndrome have some level of developmental delay and for this reason in home physical therapy after discharge was the best method of care for him. These needs were met by the social work department. A robust social work presence is necessary when dealing with patients with DMC syndrome as many times they will require in-home care and significant family support.

Discussion

DMC is a very rare condition and orthopedic treatment has not been frequently documented. This patient had a history of right hip osteotomy with screw fixation and our team noted that it was not successful in halting the progression of the patient's symptoms, ultimately necessitating a right total hip replacement. There is a scarcity of publications on orthopedic care for patients with DMC syndrome. A literature review on PubMed using the search criteria of ((Dyggve-Melchior-Clausen)) AND ((Orthopedics) OR (Orthopedics)) yields 9 publications. Of these, 4 articles mention osteotomies as a treatment for lower extremity skeletal dysplasia.

There has been a case report of a Chiari pelvic osteotomy performed to halt hip subluxation in a Belgian patient with DMC syndrome. The osteotomy did not affect the outcome of the hip subluxation, with progressive lateral migration of the femoral head [10]. This may be one of the earliest documentations of pelvic osteotomies demonstrating ineffectiveness in halting the migration of the femoral head.

The largest case series we found describing the musculoskeletal pathology of DMC was a study of 15 Egyptian patients from 9 unrelated families. All patients had clinical findings such as a pigeon-shaped chest, flaring of lower ribs, exaggerated lumbar lordosis, broad metaphyses of long bones, broad interphalangeal joints, and brachydactyly. Of 15, 14 had genu valgum, with 5 cases demonstrating various degrees of asymmetry. Radiographically, all patients had findings such as misshaped long bones, small irregular delayed ossification of epiphyses, medially deviated femoral necks with abnormally pointed femoral heads, irregular iliac bones, and irregular shallow acetabular roof. Of 15, 8 patients had hip subluxation or dislocated femoral heads [5]. Our patient is consistent with the clinical findings described in the case series above and had a history of hip subluxation, which was treated with an osteotomy at the time. Aglan et al. [5] posited that DMC syndrome may require femoral osteotomy, THA, early meniscectomy, realignment osteotomy, or posterior cervical spine fusion.

Burns et al. described 2 siblings who received THA as a result of the severity of joint degeneration from their DMC syndrome. The first patient had a Sugioka trans-trochanteric rotational osteotomy and cheilectomy for severe hip dysplasia accompanied by femoral neck osteonecrosis, which prompted bilateral THA. The second patient received a total hip replacement for their severe joint degeneration. There is no mention of how these patients recovered [6].

Kenis et al. presented a child with progressive genu varum with a similar constellation of symptoms—short stature, spinal deformity, pelvic dysplasia with lacy iliac crests, subnormal intelligence, and so on. The patient's progressive nature of lower limb deformities and low-quality osseous tissue led the team against performing extensive bone surgery, such as osteotomies with internal or external fixation. The team opted for minimally invasive surgery of a guided growth technique, or hemiepiphysiodesis, without long-lasting immobilization and immediate full weight-bearing after the procedure. Six months after the treatment protocol, there was no further progression of the deformity [11]. Similarly, Yadav et al. present a case report of bilateral severe genu varum in a DMC syndrome patient. The six-year-old male presented with bilateral, progressive genu varum over the course of 4 years. Radiographs revealed genu varum with platyspondyly of the dorsolumbar spine and semilunar lacy appearance around the iliac crest [2].

Another case report is of a 9-year-old patient with DMC syndrome with painful wrists and bilateral hip subluxation [9]. The subluxation of the right hip became painful at age 17, and varisation of the upper femur with triple pelvic osteotomy of the right hip was performed. While short-term quality of life was improved, both hips progressively evolved toward degeneration with major arthrosis after a 5-year follow-up. The right femoral head developed subtotal avascular necrosis, while the left hip developed coxofemoral fusion with no range of motion. The patient's younger brother also had DMC syndrome and developed bilateral hip subluxation at age 9, with right hip pain. The patient received bilateral femoral varisation with Pemberton osteotomies at age 11. Over 3 years, the patient rapidly developed progressive articular degeneration with subsequent subluxation of the right hip [9].

As DMC is a rare subtype of SEDs, there is a scarcity in the literature of how well THAs will serve DMC patients. There is a study by Wyles et al. of over 50 THAs performed in 29 patients with SED, which may suggest that THA can be used to treat spondyloepiphyseal dysplasias. In a long-term outcome study of 50 cases, the authors found that THA provided significant pain reduction and improvement of function, with a majority of patients independently ambulating following the procedure. Mean implant survival of these implants at 5, 10, and 20 years were 96%, 85%, and 55%, respectively, with use of gait aids in their patients reduced from 64% to 34%. As DMC syndrome is a type of SED, there is a precedent for THAs being effective in conditions of similar pathophysiology. These results could serve as baseline for future investigation of how DMC patients treated with THA compare post-operatively with a pool of all SED patients treated with THA [12]. Thus, there is precedent in THAs being used to treat SEDs. Given that DMC is a type of SED and shares similar skeletal abnormalities of SEDs, it is transitive that THAs may be beneficial to DMC patients as it has helped SED patients.

Current controversies and future considerations

Few articles in the literature discuss the results of osteotomies with DMC patients. While Aglan et al. posited osteotomies as a potential treatment for these patients, Hosny et al. and Nectoux et al. demonstrated that hip osteotomies do not prevent further hip subluxation and femoral head migration. Thus, a review of the current literature suggests that osteotomies performed on individuals with DMC do not halt the progression of hip subluxation, and the patient will likely subsequently develop articular degeneration over several years. Additionally, our patient's right femoral osteotomy did not change the progression of the disease, with hip subluxation and femoral head migration noted on subsequent radiographs, eventually leading to THA.

DMC patients greatly benefit from THA as adults. However, prior pediatric femoral osteotomies could pose challenges due to anatomical changes in the hip. Based on current evidence, the use of osteotomies for patients with DMC may not prevent the need for THA. While further research is needed, patients could consider receiving total hip replacements for improvement of ambulation for symptomatic relief, as evidenced by our patient's surgeries and improvement of symptoms.

There are technical difficulties in performing THA in this patient population. Preoperative planning with a CT scan is strongly advised to better understand the complex acetabular and proximal femur deformities. Due to dwarfism, small or custom implants may be required for a successful arthroplasty procedure, which may be challenging to obtain, measure, and insert. We believe the use of small cups with a focus on initial medialization reaming, as well as the use of a small-version control stem allows the surgeon to overcome some of the technical difficulties associated with the patient's unique anatomy. It is also important to ensure excellent stability constructs with these patients, as falls and lack of precautionary adherence may be common as a result of intellectual disability.

The hip dysplasia associated with this disorder is combined with pathologically short stature resulting in several challenges that must be overcome for successful arthroplasty. Technology can be very helpful in assisting in making effective intraoperative decisions. In this case preoperative CT scan was employed with 3-dimensional reconstruction to allow for accurate measurements. Most importantly accurate length of the femur as well as intra-medullary canal width are essential to ensure that implants can be successfully placed within the intramedullary space. In this case, the patient's anatomy could successfully accommodate standard implants using a standard, modular press-fit stem. If the anatomy is not accommodating, then custom implants must be considered. As far as intraoperative decision making, robotic assistance was not used; however, several studies have demonstrated that it can be successfully used for implant positioning in similar pathologies [13,14].

Summary

In summary, DMC is a rare condition characterized by a plethora of orthopaedic abnormalities, primarily in the skeletal axis and hips. To our knowledge, this is the second case report to document a THA on a patient with DMC syndrome. We present a patient with DMC syndrome with a history of a right femoral osteotomy with screw fixation. He is approximately 1 year out from his left total hip and almost 3 months from his right total hip. The progression of his disease continued despite the osteotomy, and he received bilateral THAs. Our patient is recovering well from both arthroplasties. In conclusion, we consider total hip replacement in DMC syndrome to be a safe and effective operation to address a challenging hip pathology.

Key Points

1. Hip osteotomies do not appear to prevent the progression of femoral head subluxation and subsequent arthrosis in patients with DMC syndrome.
2. Total hip arthroplasties are safe, improve mobility, and alleviate symptoms in patients with Dyggve-Melchior-Clausen syndrome.
3. Close follow-up with routine radiographic documentation should be made to track the syndrome and evaluate treatment efficacy.

Conflicts of interest

The authors declare there are no conflicts of interest.

For full disclosure statements refer to [please insert article DOI link here].

Informed patient consent

The author(s) confirm that written informed consent has been obtained from the involved patient(s) or if appropriate from the parent, guardian, power of attorney of the involved patient(s); and, they have given approval for this information to be published in this case report (series).

CRediT authorship contribution statement

Vahe Yacoubian: Writing – review & editing, Writing – original draft, Investigation. **Brenden Cutter:** Writing – review & editing, Writing – original draft, Supervision, Investigation. **Carlos Alvarado:** Writing – review & editing, Supervision, Investigation.

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