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КОМПЛЕКСНОЕ ОРТОПЕДИЧЕСКОЕ ЛЕЧЕНИЕ ПАЦИЕНТОВ С СИСТЕМНЫМИ ДИСПЛАЗИЯМИ СКЕЛЕТА

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Целью исследования являлось обоснование комплексного подхода к диагностике и хирургическому лечению системных дисплазий скелета.

Материал и методы. Представлена серия из 15 пациентов в возрасте 6–17 лет, обследование и лечение которых было проведено в рамках программы научного партнерства между Детским ортопедическим институтом им. Г.И. Турнера (Россия) и Ортопедической клиникой Шпайзинг (Австрия). Спектр заболеваний включал такие диагнозы, как множественная эпифизарная дисплазия, спондилоэпифизарная дисплазия, диастрофическая дисплазия, метафизарная дисплазия, спондилометафизарная дисплазия, синдром Стиклера, дисплазия Книста и анаукзетическая дисплазия. Комплексное ортопедическое лечение состояло в одномоментном или последовательном восстановлении соотношений в суставах и исправлении оси нижних конечностей. Оперативные методики включали корригирующие остеотомии, методики управляемого роста и применение аппаратов внешней фиксации.

Результаты. Отличные результаты (полная осевая коррекция и восстановление соотношений) достигнуты у 8 пациентов, включая 2 пациентов с метафизарной дисплазией, 2 пациентов со спондилоэпифизарной дисплазией, 2 пациентов с множественной эпифизарной дисплазией, пациента с синдромом Стиклера и пациентку со спондилометафизарной дисплазией. Хорошие результаты (частичная коррекция) были достигнуты у 4 пациентов (2 пациента с дисплазией Книста, 1 пациент с множественной эпифизарной дисплазией и пациент с анаукзетической дисплазией), удовлетворительные (прекращение прогрессирования деформации) – у 2 пациентов с диастрофической дисплазией и неудовлетворительные (прогрессирование деформаций) – у 1 пациента с диастрофической дисплазией.

Заключение. Таким образом, благодаря комплексному подходу положительные результаты были достигнуты в большинстве случаев, несмотря на тяжесть исходной патологии. Международная кооперация в области диагностики и лечения пациентов с редкими системными дисплазиями скелета позволяет накапливать и обобщать имеющийся опыт для оптимизации результатов.

Ключевые слова: скелетная дисплазия, комплексное ортопедическое лечение.

COMPLEX ORTHOPAEDIC MANAGEMENT OF PATIENTS WITH SKELETAL DYSPLASIAS

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Skeletal dysplasias are challenging for diagnostics and treatment. We present a series of fifteen patients with different forms of skeletal dysplasias with age ranged from 6 to 17 years with variable clinical presentations managed as a part of the project of scientific cooperation between Turner Paediatric Orthopaedic Institute and Orthopaedic Hospital Vienna-Speising. The spectrum of diagnoses included multiple epiphyseal dysplasia, spondyloepiphyseal dysplasia congenita, diastrophic dysplasia, metaphyseal dysplasia, spondylometaphyseal dysplasia, Stickler syndrome, Kniest dysplasia, and anauxetic dysplasia. Complex treatment, which included axial correction and juxta-articular realignment, was performed as a single-stage, or consecutive surgery. Surgical techniques included corrective osteotomies with internal fixation, guided growth technique and external fixation devices. Best results (full axial correction, normal alignment of the joint) were achieved in 8 patients, including 2 patients with metaphyseal dysplasia, 2 patients with multiple epyphyseal dysplasia, 2 patients with spondyloepyphyseal dysplasia, patient with Stickler syndrome and patient with spondylometaphyseal dysplasia. Good results (partial correction at the present time) were seen in 4 patients (2 patients with Kniest dysplasia, 1 – with multiple epyphyseal dysplasia and 1 – with anauxetic dysplasia). Satisfactory results (non-progressive condition in previous progression) were obtained in 2 patients with diastrophic dysplasia, and poor results (progression of the deformity) – in 1 patient with diastrophic dysplasia. Positive results in most of the cases of our series make promising future for usage of complex approach for orthopedic management of children with skeletal dysplasias; advanced international cooperation is productive and helpful for diagnostics and management of rare diseases.

Key words: skeletal dysplasia, complex orthopaedic treatment.

Skeletal dysplasia represents a major skeletal malformation complex characterized by wide spectrum and confusing clinical presentations of bone deformities encountered in paediatric orthopaedic practices [11]. In each of these conditions a structural abnormality in the bone itself leads to disturbances in growth of the appendicular and axial components. The aim of this study is to illustrate our methodology in managing children with skeletal dysplasia.

Diagnosis of skeletal dysplasia is complex though is empirical. Clinical and radiological data are crucial for basic diagnosis, laboratory tests, including genetic testing become more precise and important for final confirmation in the recent years. Nevertheless, proper phenotypic characterization still remains the corner stone for diagnosis of these children [2].

Management of patients with skeletal dysplasias remains challenging. Some authors recommend observational strategy with minimal interventions because of poor prognosis and high risk of complications. However, the demands of the patients and parents drive the surgeons to find the ways of more aggressive and effective treatment [3]. The latest advances in surgical techniques gave the possibility to improve results significantly. Among these advances three basic techniques should be mentioned: modern external fixators (including devices based on the principles of hexapod system with computed planning), locking-compression plates (paediatric systems for stable internal fixation) and guided growth technique (temporary epyphyseodesis with plates). Combination of these methods gives possibility of effective correction even in severe cases of rare skeletal dysplasias with multilevel involvement. We define "complex management" in this study as simultaneous or following application of axial correction and realignment of the joints in the treatment protocol of a patient. We postulated that this approach can give more satisfactory results.

Material and methods

In 2009 it was established the project of scientific cooperation between Turner Paediatric Orthopaedic Institute from Saint-Petersburg, Russia(TI) and Orthopaedic Hospital Vienna-Speising, Austria (OHS). The aim of the project was to join the efforts of both clinics in order to improve knowledge and clinical practice in the field of orthopaedic management of children with rare musculoskeletal conditions. From the period of 2009–2013, forty children with different forms of skeletal dysplasia were clinically documented. Surgical corrections were carried out in these two clinics, and were included in the database. The inclusion criteria were mutual participation of the physicians from the both clinics (TI and OHS) in diagnostics and treatment of the patient. Most of the patients underwent staged diagnostic processes with data exchange and scientific emails discussions. The outcome was publication of several papers as case reports and recently as research papers in peer-reviewed journals.

Consent forms were signed by parents for all the data transferred and published. Thence fore, surgical interventions were performed in one of these clinics (TI or OHS), or in both the clinics consecutively. As we mentioned above, complex management included simultaneous or following axial correction and realignment of the joints in the treatment protocol of patients in accordance with their clinical presentation and diagnosis.

From out of 40 patients, included in the database, we selected 15 children who were compatible to the scientific criterion of classification and diagnosis, which were included in the present study. The spectrum of diagnoses included multiple epiphyseal dysplasia (autosomal dominant type), spondyloepiphyseal dysplasia congenita, diastrophic dysplasia, metaphyseal dysplasia (Schmid type), spondylometaphyseal dysplasia (Kozlowski type), Stickler syndrome, Kniest dysplasia, and anauxetic dysplasia (table).

Table

List of diagnoses and number of patients

Diagnosis	Abbreviation	Number of cases
Multiple epyphyseal dysplasia	MED	3
Diastrophic dysplasia	DD	3
Metaphyseal dysplasia, Schmid type	MDS	2
Spondyloepyphyseal dysplasia congenital	SEDC	2
Kniest dysplasia	KD	2
Spondylometaphyseal dysplasia, Kozlowski type	SMDK	1
Stickler syndrome	SS	1
Anauxetic dysplasia	AD	1
Total		15

In a series of fifteen patients with different forms of skeletal dysplasias with age ranged from 6 to 17 years (6 girls and 9 boys) respectively, variable clinical presentations were the landmark. Short stature was readily identified and was a common clinical presentation and chief complaint of the parents. Phenotypic characterizations include careful reading of dysmorphic craniofacial features as well as other physical signs. The latter were usually enforced by proper radiographic interpretations. All these measures are considered as the baseline

tool of diagnosis. Genotypic correlations have been performed in some of our patients. Surgical interventions are usually based primarily on definite diagnosis of every given disorder encompassed by distinctive clinical calculations and precautions.

A constellation of syndromic entities have been diagnosed and surgical interventions have been carried out accordingly.

The most paramount indications for surgery in our group of patients were malalignment of the joints and axial deformities of the lower limbs, interfering with postural and walking abilities.

Though in patients with skeletal dysplasia we usually following certain steps which have been carefully considered prior to any surgical interventions; we usually assess the craniocervical junction and the possibility of C1-2 instability, in fact, these are not uncommon manifestations. In some patients and because of the narrow foramen magnum and to avoid unintentional spinal cord compression, special care has to be taken in manipulation the neck. We also avoid spinal anaesthesia especially in patients with severe lumbar lordosis because of the limited space within the canal.

Surgical techniques included corrective osteotomies with internal fixation (mostly with paediatric locking-compression plates – LCP), guided growth technique with "eight-plates" and external hexapod fixation devices for fixation and lengthening of the bones.

We considered excellent results if full axial correction and normal alignment of the joint were achieved; good results – if partial correction was seen; satisfactory results – in non-progressive condition with previous progression; and poor results – in the cases of progression of the deformity.

Results

Complex treatment, which included axial correction and juxta-articular realignment, was performed as a single-stage, or consecutive surgery. Most of the cases were treated consecutively. The consequence of the procedures was defined by predominant deformity: if the amount of axial deformity was substantively more than juxta-articular malalignment, we considered axial correction first. In the contrast situation articular realignment was performed first.

The results were followed 12–36 months after achievement of correction or hardware removal (in the cases of incomplete correction).

Best results (full axial correction, normal alignment of the joint) were achieved in 8 patients, including 2 patients with metaphyseal dysplasia, 2 patients with multiple epyphyseal dysplasia, 2 patients with spondyloepyphyseal dysplasia, patient with Stickler dysplasia and patient with spondylometaphyseal dysplasia.

Good results (partial correction at the present time) were seen in 4 patients (2 patients with Kniest dysplasia, 1 – with multiple epyphyseal dysplasia and 1 – with anauxetic dysplasia).

Satisfactory results (non-progressive condition in previous progression) were obtained in 2 patients with diastrophic dysplasia, and poor results (progression of the deformity) - in 1 patient with diastrophic dysplasia.

Progressive deterioration of the hips resulting in limitation of adduction associated with adverse influence upon the deformity of the long axes of the limbs (genua valga) (Fig. 1 a). After the mutual consultancies at the both clinics this was estimated as a key-point which warrants surgical correction at first place. Simultaneous bilateral proximal femoral valgus osteotomies were performed in The Turner Institute (Fig. 1 b). Fixation with angular plates was added by spica cast for 6 weeks for the reason of confirmed intraoperatively poor bone quality. We achieved acute correction up to 95° (changing of the NSA – from 40° to 135°) with removal of bone wedge with lateral base height of 12 mm. This osteotomy gave us the possibility to approach to absolute lengthening of the femora of 15 mm by valgization along with changes in the tension of the gluteal muscles which is important factor in gait and posture. After removal of the plaster cast and achievement of painless movement (8 weeks after hip surgery) temporary hemiepiphyseodesis with the "8-plates" of distal femoral and proximal tibial physes on the both sides was performed (Fig. 1 c). The aim of this procedure was to perform some sort of gradual correction of the valgus knee deformity. We choose this technique as an alternative to acute correction to avoid shortening of the bones by closing-wedge osteotomy. Gradual correction with possible limb lengthening in external fixation devises was unprofitable because of poor bone quality associated with delayed callus formation.

Valgus knee deformities (35° on the both sides) have been encountered in a patient with Stickler syndrome. Interestingly, in standing position he exhibited valgus deformity mimicking fixed flexion deformity of the knee because of excessive external rotation of the thighs (Fig. 2 a). Computed tomography of the hips revealed severe femoral retrotorsion which is unusual in Stickler syndrome in presence of coxa valga. This retrotorsion was compensated during standing and walking by external rotation of the both femora.

After the mutual consultancies at the both clinics it was decided to perform staged surgical correction of the lower extremities. The first stage (guided growth for bilateral valgus knee deformity) was done in TI (Fig. 2 b, c), and the second stage (correction of the rotational alignment) – in OHS (Fig. 2 d)

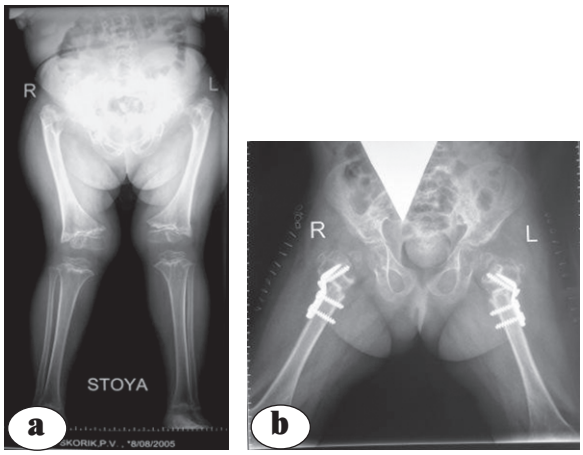

Fig. 1. Pre- and postoperative radiographs of the girl with anauxetic dysplasia: a – anteroposterior radiographs of the pelvis and lower legs before surgery: abnormal ossification of the epiphyses, coxa vara, genua valga; b – anteroposterior radiographs of the hip joints after corrective subtrochanteric valgus osteotomy on the both sides

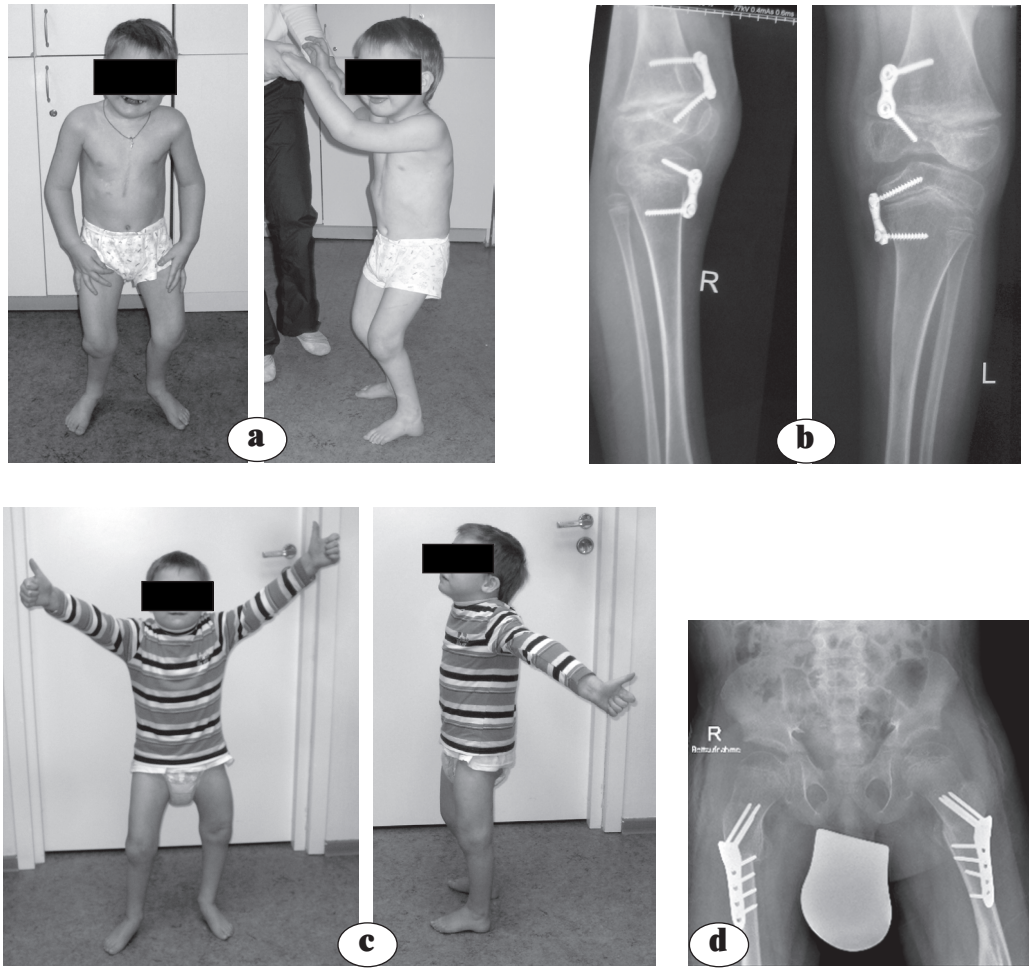

Fig. 2. Clinical appearance, pre- and postoperative radiographs of the boy with Stickler syndrome: a – frontal and lateral view of the boy before surgery: assisted standing, flexion and external rotation of the femora, kyphosis, genua valga mimicking flexion of the knees; b – radiographs of the knee joints after first stage of surgery: valgus deformities are corrected with guided growth technique; c – frontal and lateral view of the boy after first stage of surgery: independent standing, valgus deformities are corrected, residual external rotation of the femora; d – anteroposterior radiographs of the hip joints after corrective subtrochanteric derotational osteotomy on the both sides, fixation with LCH-PHP

A girl was seen at the Orthopaedic Hospital Vienna-Speising with a definite diagnosis of spondyloepyphyseal dysplasia congenita. The girl underwent staged surgical procedures aimed to the joint realignment and axial correction in OHS. First stage included corrective subtrochanteric valgus osteotomy combined with acetabular "shelf" procedure for correction of coxa vara and acetabular dysplasia (Fig. 3 a, b). The procedure was done consequentially on the both sides. Second stage included consequential correction of valgus deformities by corrective supracondilar osteotomy with fixation in hexapod external fixator (Fig. 3 c). The staged surgery resulted in restoration of the alignment of the hip joints with improvement of the range of motion and postural ability, followed by axial correction of the lower limbs in the frontal plane.

The presented series of the cases demonstrates that complex approach to management of the patients with severe skeletal dysplasias, including axial correction and realignment of the joints gives excellent and good results in most of the cases.

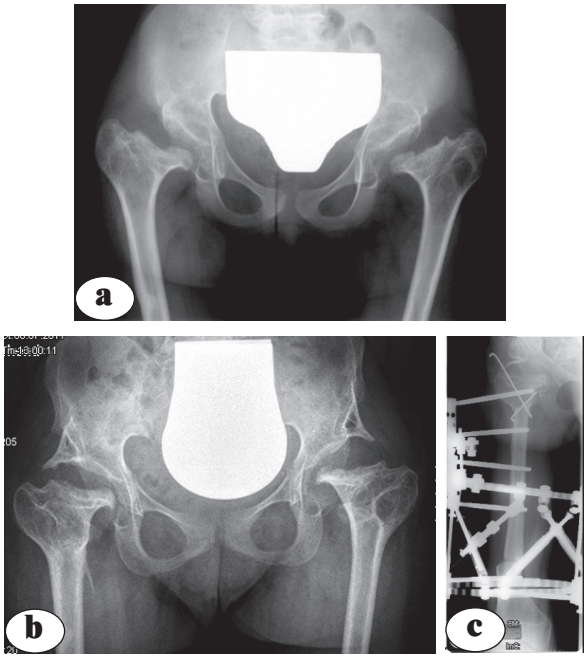

Fig. 3. Pre- and postoperative radiographs of the girl with congenital spondyloepyphyseal dysplasia: a – anteroposterior radiographs of the hip joints before surgery: abnormal ossification of the epiphyses, metaphyseal widening, coxa vara, and acetabular dysplasia; b – anteroposterior radiographs of the hip joints after corrective subtrochanteric valgus osteotomy and acetabular "shelf" procedure on the both sides; c – anteroposterior radiographs of right hip and femur after correction of valgus deformity by corrective supracondilar osteotomy with fixation in hexapod external fixator

Discussion

Skeletal dysplasias is a heterogenic group of inherited conditions, mostly expressed clinically by growth disturbances, limb and spine deformities, premature degeneration of articular cartilage with early osteoarthritis, as well as numerous extraskeletal signs. Most of the disorders, included in this group are resulted from monogenic mutations, responsible for abnormal synthesis of collagen or other proteins and proteoglycans of extracellular matrix

The new generation of the plates for internal fixation with angular stability gives excellent possibility for correction and fixation of the bone fragments, especially in presence of osteopenia, which is usual for children with skeletal dysplasias [7]. Locking screws placed and locked in different directions provide maximal stability and minimal damage of the bone. Comparing the time of surgery and blood loss we did not reveal significant difference between patients, operated with locking plates and blade plates. The number of intraoperative complications and length of postoperative immobilization were lower among patients, operated with LCP. If the acetabular coverage was insufficient, additional pelvic procedure can be necessary to prevent progressive migration and subluxation. The technique of pelvic correction depends on the severity, age of the patient and preference of the surgeon [8].

Guided growth technique becomes more and more popular in the recent years. The idea of temporary hemiepiphyseodesis, which is well known from the classical works of Blount [4] have got "second birth" with invention of new hardware, known as "8-plate". The method includes extraperiosteal application of small, low-profile two-hole plate, overpassing growth plate [10]. This technique has the benefits comparing to previously described, which are widely discussed in the literature. These advantages lead to wide spreading of the method for different indications, including skeletal dysplasias [5]. As an alternative to acute correction of axial deformities (osteotomies) in growing patients, guided growth technique demonstrates less complications, less invasion and more patients' tolerance. As a specific disadvantage of the method in children with skeletal dysplasia slow speed of correction should be mentioned for the reason of generally retarded growth in many types of these disorders.

Hexapod system is a new generation of external fixation devices, which is based on classical principles of Ilizarov method, and provides three-dimensional correction by usage of special hardware and computer-assisted calculation. That gives better accuracy of correction and reduction of the time in a frame [9].

Anauxetic dysplasia is a spondylometaphyseal dysplasia with extreme dwarfism, caused by mutations in the untranslated RMRP gene, which forms the RNA subunit of the RNase MRP complex. Developmental coxa vara which is one of the characteristic deformities for anauxetic dysplasia as well as for other skeletal dysplasias, is a hip deformity characterized by a defect in endochondral ossification of the medial portion of the femoral neck, together with progressive vertical inclination of the proximal femoral physeal plate and shortening and decrease of neck shaft angle [6].

Stickler syndrome includes wide phenotypic variability, which often resulted in delayed or missed diagnosis in many cases [11]. Certain clinical findings, however, are consistent: 95% ocular problems (retinal detachment, myopia and blindness); 84% facial abnormalities (flat nose, small mandible, or cleft palate); 70% hearing loss; 90% degenerative joint disease and pain. There is great diversity and severity of pathologic articular conditions in patients with Stickler syndrome. Most patients are recognized in childhood if they present with cleft palate or severe ocular findings or have a positive family history. Fibrillar collagen mutations associated with the syndrome (COL2A1, COL11A1, and COL11A2) presumably lead to malformation and weakening of the bones, articular cartilage, intervertebral disks and vertebral end plates. Arthritic changes and adult age were associated with hip pain in adult patients with all types of Stickler syndrome. Al Kaissi et al described the correlation of severe undermineralization of the bone matrix and the compromised mechanical competence in a patient with Stickler syndrome type I. The diminished mineral deposition may be attributable to a fundamental defect in bone development and mineralization that is related to the connective tissue disorder, which is a direct consequence of the presumed genetic mutation in COL2A1 [1].

Congenital spondyloepyphyseal dysplasia is a rare skeletal dysplasia which resembles to the COL2A1-spectrum of disorders, as well as the above mentioned Stickler syndrome. Characteristic features of the disorder include short-trunk and short-limb dwarfism with more prominent deformities and contractures of the limbs, progressive infantile scoliosis, and less severe vision and hearing impairment if compare with Stickler syndrome.

We believe that correct diagnosis of the pathological condition is crucial for successful treatment. In most of the cases thorough clinical and radiological investigation is enough for the exact diagnosis. Genetic testing is ideal for the further confirmation. The diagnoses like “unidentified skeletal dysplasia” or “genetic-related condition” should be avoided wherever it is possible in favour of accurate diagnostics of the basic genetic syndrome.

We use guided growth technique as an alternative to acute correction to avoid shortening of the bones by closing-wedge osteotomy. Gradual correction with possible limb lengthening in external fixation devises was less often used for the reason of poor bone quality, unpredictable callus formation and progressive degenerative changes of the joints in patients with skeletal dysplasias. Nevertheless, the usage of hexapod external fixators for the selected cases gives enough stability with good results, as well as permits more precise primary and secondary correction in the device. Acute correction with internal fixation

Conclusion

Skeletal dysplasias remain challenging for paediatric orthopaedists in terms of diagnostics and treatment. The recent advancements in surgical techniques and better understanding of underlying pathological conditions occurred in the recent decade gave us more practical solutions, and changed results of surgical treatment significantly. Our current study has two folds; firstly erroneous management of patients with skeletal dysplasia is mostly originated from misconception and inaccurate diagnosis. And secondly, diagnostic errors with subsequent application of inappropriate surgical procedures might be a reason behind unexpected damage instead of corrections.

One more crucial point, which is demonstrated by this study, is the effectiveness of international scientific cooperation. Thank to the project of scientific cooperation between Turner Paediatric Orthopaedic Institute and Orthopaedic Hospital Vienna-Speising more than 40 children with different types of skeletal dysplasias got consultancy and treatment from high-level experts from both the clinics. This cooperation definitely improved knowledge and clinical practice in the field of orthopaedic management of children with rare musculoskeletal conditions. Positive results in most of the cases of our series make promising future for usage of complex approach for orthopedic management of children with skeletal dysplasias; advanced international cooperation is productive and helpful for diagnostics and management of rare diseases.

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