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CASE REPORT

Multiple pterygium syndrome with marked pterygia of the fingers and MRI changes in the spine

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KEYWORDS

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Abstract We report a two years old Egyptian girl, the first birth of consanguineous marriage with clinical findings consistent with the diagnosis of the autosomal recessive multiple pterygium syndrome (Escobar) (growth retardation, craniofacial dysmorphism, multiple pterygia, kyphoscoliosis, multiple joint contractures especially affecting the lower limbs). What characterizes out patient was the extensive pterygia of the fingers which kept them permanently flexed, while they were very mild in the neck, axillary folds and knee joints.

Our patient suffered also from mental retardation although mentality is commonly reported to be normal in this syndrome. MRI of the spine revealed widened spinal canal and engorged intraspinal vessels, which were not reported before.

1. Introduction

Multiple pterygium syndromes (MPSs) are phenotypically and genetically heterogeneous. They can be broadly divided into lethal and nonlethal forms (Escobar syndrome) [1]. The lethal form is characterized by prenatal growth deficiency, contractures, pterygia, and dysmorphic facies. Patients are usually stillborn or do not survive beyond the newborn period. Pulmonary hypoplasia is likely to be the primary cause of mortality [1]. It has been previously described under the nonspecific names of arthrogryposis multiplex congenita [2], or Bonnevie–Ullrich syndrome [3,4] and more recently multiple pterygium syndrome [5]. It is characterized by multiple congenital joint contractures, multiple skin webs (pterygia) across the neck and various joints (across every flexion crease in the extremities most notably the popliteal space) [6]. In addition the syndrome is associated with camptodactyly with or without syndactyly, distinct facial appearance with ptosis and antemongoloid eye slant, short stature, kyphoscoliosis and vertebral segmentation anomalies [7]. Also cleft palate, deafness, short stature and genital anomalies are frequently present as well as widespread musculoskeletal deformities [8].

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There are also reports about the association of some cases with microphthalmia, low set ears, small mouth and high arched palate [8]. Congenital vertical talus is a rare foot deformity which is commonly present in patients with MPS. If left untreated it can cause pain and morbidity which affect the patients' ambulation and quality of life [9]. Extrinsic extensor tendon hypoplasia of right index finger was also reported [10].

MPS is a rare syndrome; however, data from other countries in the Middle East showed that MPS is relatively common among Arabs in particular or even among other communities in the Middle East [11].

Most cases are inherited in an autosomal recessive pattern; however, autosomal dominant and sporadic cases have been reported [12].

The disease process is progressive with about 20% developing decreased pulmonary capacity and increasing spinal deformity [13].

Here we report an Egyptian child with MPS who had some characteristic features, after taking informed consent from the parents.

2. Case report

A two years old female patient was born after uncomplicated term pregnancy except for decreased fetal kicks and C.S. delivery. There was no history of medication taken by the mother during pregnancy. The mother was 24 years old and the father was 25 years old at time of conception and both are healthy and first cousins. This was the mothers' first and only pregnancy, with no history of previous abortions or still births. The child was referred to the genetics clinic for delayed motor and mental development with dysmorphic features. Her birth weight was 2.250 kg and suffered from physiological jaundice for which she was admitted to ICU for 3 days under phototherapy.

On examination the child weight was 7 kg (< third percentile), length was 68 (< third percentile), occipitofrontal circumference was 45 cm (< third percentile) and with frontal and parietal bossing and low posterior hairline. The child had hypertelorism, downslanting palpebral fissures, medial epicanthic folds, bilateral ptosis more marked on left eye. She had also depressed nasal bridge, retromicrognathia, high arched palate, small low set ears with rudimentary lobules. She had also short neck with slight webbing and limited extension and bilateral prominent sternomastoid muscles (Fig 1).

There was limited extension of both shoulder joints with wasting of shoulder girdle muscles more marked on the right side and mild pterygia of posterior and anterior axillary folds. There were no anticubital pterygia, so both elbows can be fully extended while limited movement of both wrist joints was observed.

As regards the hands there were bilateral flexion contractures of interphalangeal and metacorpophalangeal joints of the second to fifth fingers, with well developed and marked pterygia of these fingers which kept them flexed at the metacarpophalangeal joints with camptodactyly and bilateral simian creases. The thumbs were extended (Figs. 2 and 3).

As regards the lower limbs there was inability to abduct both hip joints, campomelia of both femora with bilateral flexure contractures of hips, knees and ankles, with mild pterygia of both knees. There was also marked rocker-bottom heels

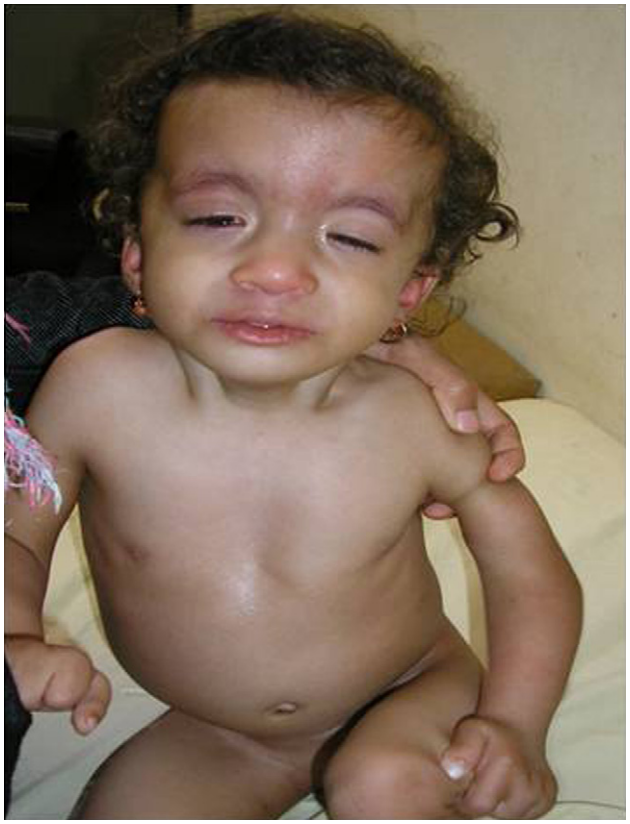

Figure 1 Typical facie of Escobar syndrome with ptosis, medial epicanthal folds, antimongoloid slant and bilateral prominent sternomastoid.

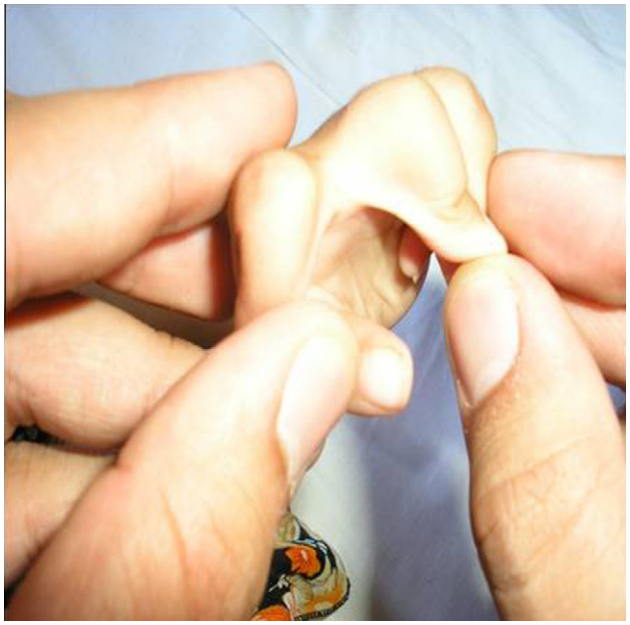

Figure 2 Pterygia of fingers and partial syndactyly.

with bilateral short halluces and lateral deviation of all toes (Figs. 4 and 5).

There was also dorsolumbar kyphoscoliosis with right convexity (Fig 6), and depressed lower part of the sternum.

Figure 3 Camptodactyly of hands

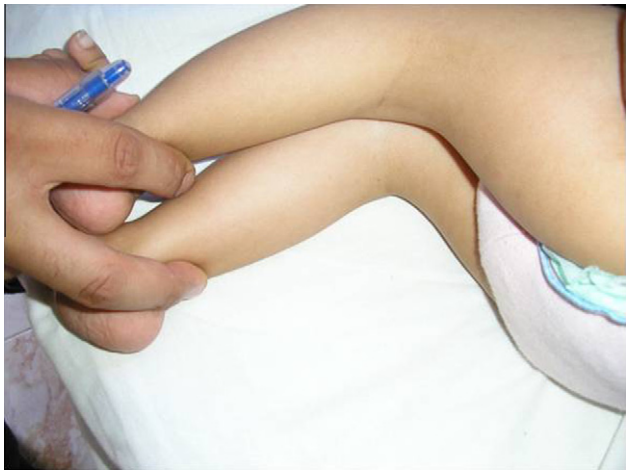

Figure 4 Mild popliteal pterygium, with bilateral flexure contractures of knee joints.

Abdominal examination revealed no organomegaly. Cardiovascular and chest examinations were clinically free.

Abdominal ultrasonography showed no abnormalities. X-ray dorsolumbar spine showed kyphoscaliosis. X-ray of both hips and knee joints showed destruction of head of both femur and/or new born formation, (Figs. 7 and 8).

MRI of the spine revealed rightword convexity of dosal scoliosis with widened spinal canal and engorged intraspinal vessels, yet with no MRI evidence of vascular malformations or any meningocele/meningiomyelocele. There was also normal MRI appearance of vertebral bodies with no evidence of wedging malformations, fractures, or under or oversized vertebrae (Figs. 9 and 10). Karyotype was normal.

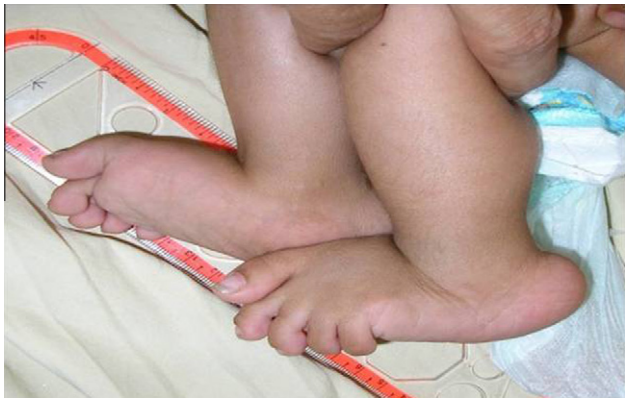

Figure 5 Rocker-bottom heels, short halluces and lateral deviation of all toes.

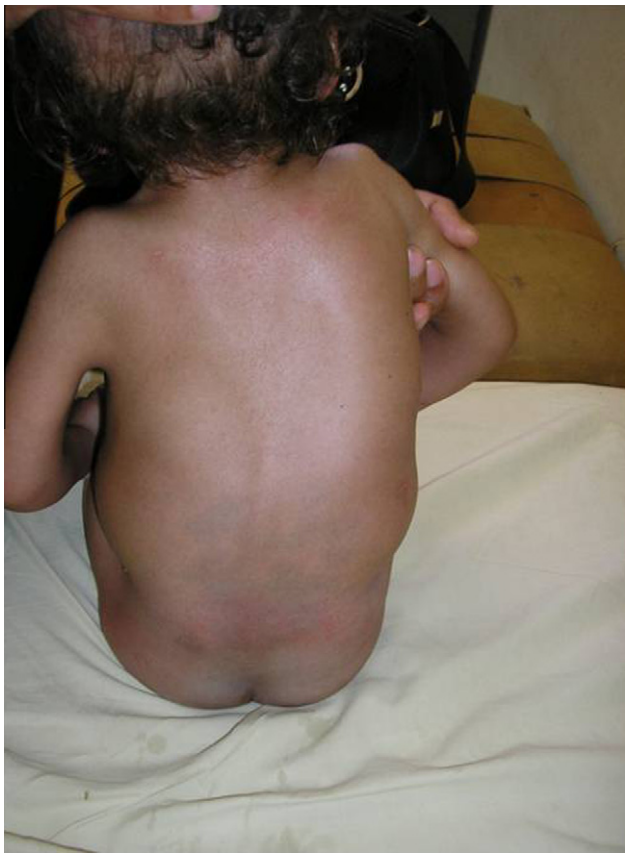

Figure 6 Axillary pterygium and dorsolumbar kyphoscoliosis.

3. Discussion

The clinical findings in our patient are consistent with the diagnosis of MPS (Escobar) (growth retardation, craniofacial dysmorphism, multiple pterygia, kyphoscoliosis, and multiple joint contractures). The main features of the condition were initially described by Matolcsy [14] and its phenotypic spectrum was described thereafter in several reports [2,3,14–16]. It is clear that the phenotypic spectrum is wide. What characterize our patient are the marked and well developed pterygia of the fingers with mild pterygia of neck, axillary folds and knees, together with mental retardation.

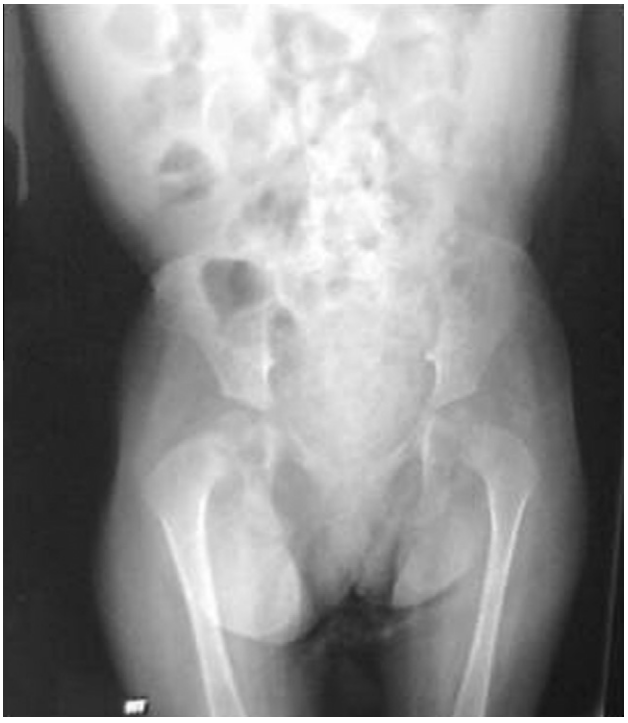

Figure 7 Joint destruction of head of both femur.

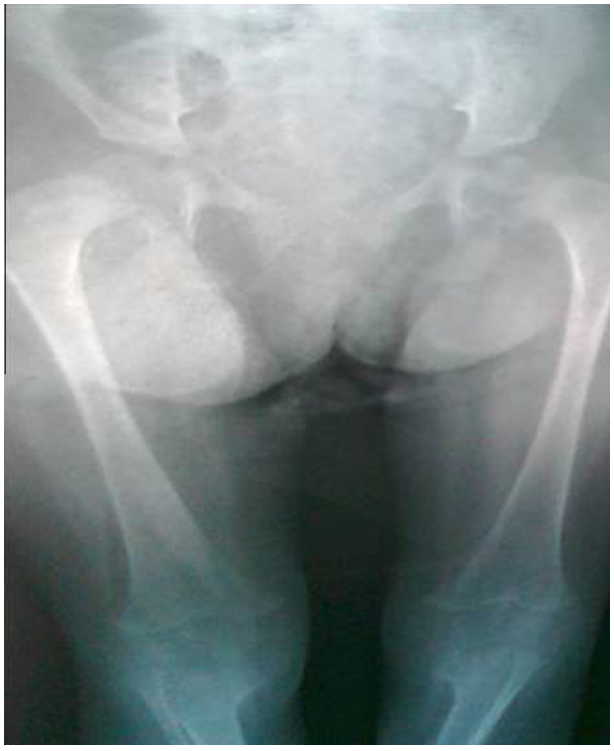

Figure 8 Bony change of hip and knee joints.

This child has normal external genitalia, although there are reports of aplasia of labia majora and small clitoris in females and small penis and scrotum with cryptochidism in males. [17]

Multiple pterygium syndrome is genetically heterogeneous, where autosomal recessive, autosomal dominant and sporadic cases are reported; however, most cases have been sporadic [12], although familial occurrence in sibs have been reported [2,14,16–18]. In our patient there was no family history but parental consanguinity was present which indicated autosomal recessive inheritance.

Our patient also suffered from mental retardation. Karyotype was done for this patient and it was normal. The same was also reported in other patients [9,15,16,18,19] although 47, XXY/48,XXXY mosaicism was reported previously in one patient which most probably was coincidental [20].

Autosomal dominant MPS was also reported with and without mental retardation [21]; however, this was not the case in our patient.

MRI of the spine revealed rightword convexity of dossal scoliosis which was previously reported [12]. However, in contrast to our patient, fusion of cervical vertebrae and narrowing of intervertebral disc spaces were not evident in our patient [12]. What was striking is the widening of spinal canal and engorged intraspinal vessels by MRI which were not reported previously and could not be explained.

The underlying abnormality in this disorder is unknown. In some cases biopsy showed muscle degeneration and disorganization of myofibrils [22–24]. However, this was not found in a necropied case [20] and more over in two additional patients, no histological abnormality was detected in skin, skeletal muscle fibers, peripheral nerves, or anterior horn cells. The proposed pathogenic mechanism involving decreased fetal joint movement remains a possibility still to be proved [16].

Nonlethal MPS (Escobar) can be caused by mutations in the CHRNG gene, encoding the gamma subunit of the acetylcholine receptor (AChR). Mutations in this gene can also cause the lethal (MPS/fetal akinesia) variant of this phenotype [25]. This gene is expressed before the 33rd week of gestation in humans, and replaced by the epsilon subunit in the late fetal and perinatal period, there by forming the adult AChR. Fetal and adult AChR are essential for neuromuscular signal transduction. In addition, the fetal AChRs seem to be the guide for the primary encounter of axon and muscle and Pterygia resulted from fetal akinesia. Congenital contractures may be caused by reduced fetal movements at sensitive times of development, due to transient inactivation of the neuromuscular endplate [26].

There are only few reports in the literature describing surgical treatment of scoliosis in MPS [27]. Sometimes there is a need for early surgical intervention to prevent progression of deformity. On the other hand management of MPS with severe spinal deformity and restrictive lung disease which was initially managed conservatively needs preoperative planning, with a multidisciplinary team (including the pediatrician, neurologist, orthopedic, surgeon, geneticist, physical and occupational therapist) and meticulous surgical technique, can result in balanced spinal correction and restoration of faction while arresting eventual pulmonary compromise and early demise [6].

In Escobar syndrome an operation may be needed for correction of cleft palate, scoliosis or other congenital anomalies and since, the gamma subunit of acetylcholine receptor which has a role in the muscle relaxant-effect was mutated, the use of any muscle relaxant is resented and anesthesia was deepened by inhalation anesthesia and as intubation is difficult, LMA insertion is a reliable method for security for the anesthetist and the patient [28].

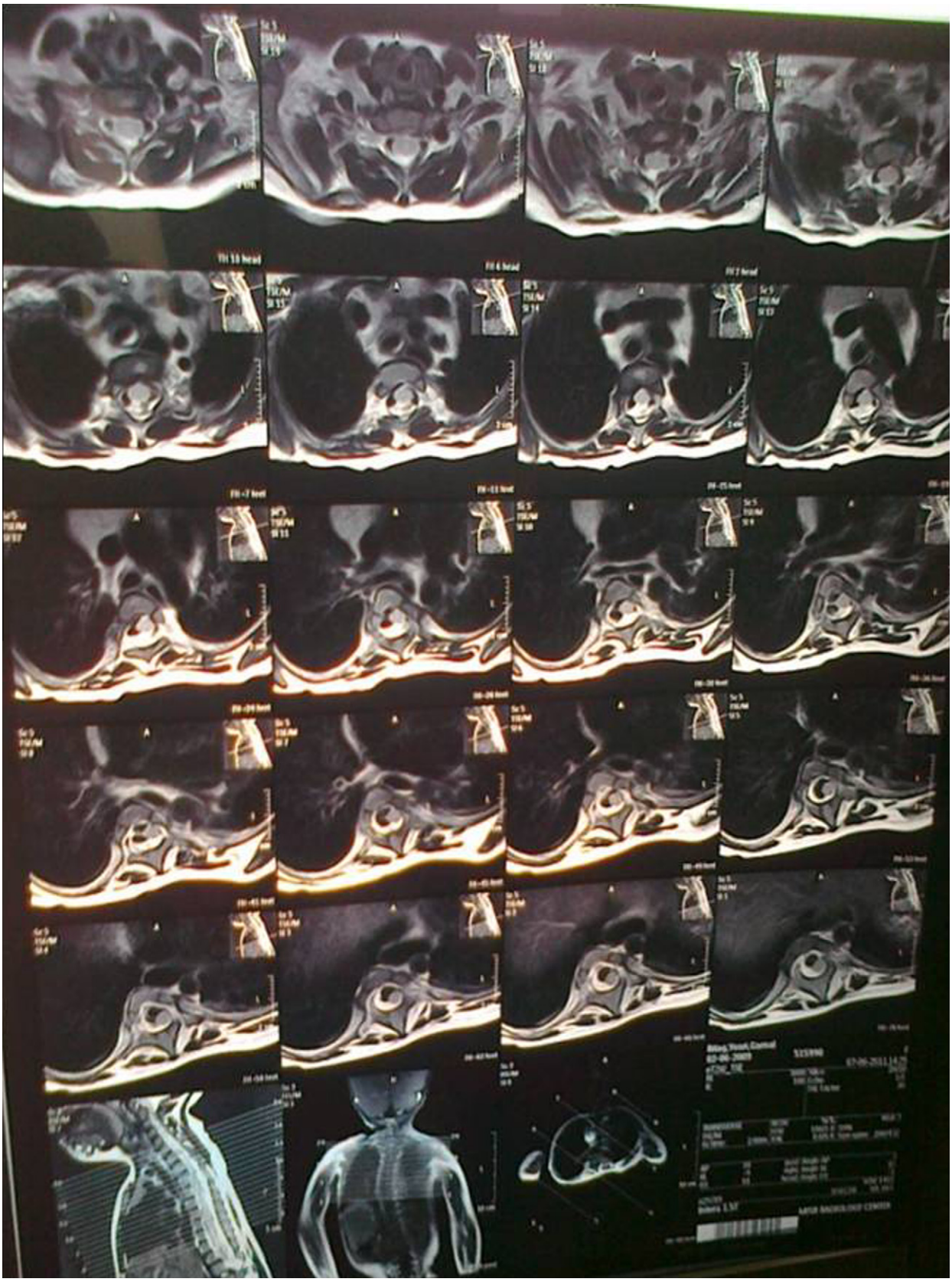

Figure 9 MRI shows widening of spinal canal and engorged intraspinal vessels.

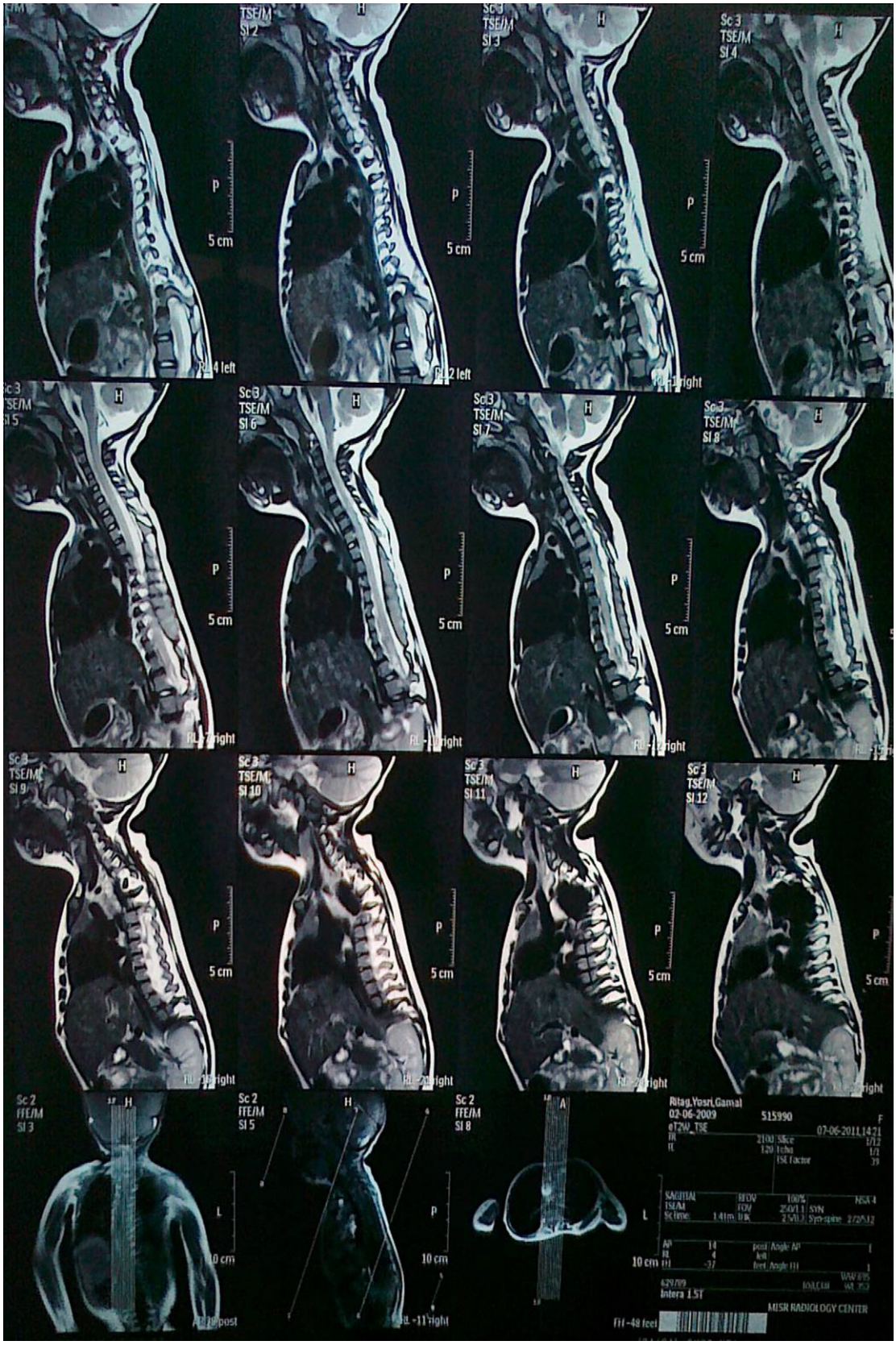

Figure 10 Convexity of dorsal scoliosis.

4. Conclusion

Signs and symptoms of MPS may vary on an individual basis for each patient and only the experienced physician can provide adequate diagnosis of any signs and symptoms and whether they are indeed MPS symptoms. Also a multidisciplinary team is needed to take care of these patients.

References

[1] Winder TL. Multiple pterygium syndromes via CHRNAI, CHRND and CHRNG gene sequencing (Test # 415). ton winder@preventiongenetics.com, www.preventiongenetics.com, version 1.23, March 21, 2011.

[2] Srivastava RN. Arthrogryposis multiplex congenita: case report of two siblings. Clin Pediatr 1968;7:691–4.

[3] Guinand-Doniol J. Observations nouvelles Sur le status Bonnevie–Ullrich (case 1). Ann Pediatr 1947;169:317–24.

[4] Rossi E, Caflisch A. Le syndrome du pterigium: status Bonnevie–Ullrich dystrophia brevicolli congenita. Helv Pediatr Acta 1951;6:119–48.

[5] Goh A, Lim KW, RajaLingam V. Multiple pterygium syndrome (Escobar syndrome) – a case report. Singapore Med J 1994;35:208–10.

[6] Dodson CC, Boachie-Adjei O. Escobar syndrome (multiple pterigium syndrome) associated with thoracic kyphoscoliosis, lordoscoliosis and severe restrictive lung disease: a case report. HSS J 2005;1(1):35–9.

[7] Hall JG, Reed SD, Rosenbaum KN, Gershanik J, Chem H, Wilson KM. Limb pterigium syndrome. A review and report of eleven patients. Am J Med Genet 1982;12:377–409.

[8] Kim GH, Kim JY, Song ES, Woo YJ, Choi YY. A case of Escobar syndrome (multiple pterigium syndrome). J Korean Soc Neonat 2006;13(1):189–93.

[9] Chanika A, Murat O, Laurens H, Kenneth R, Marnie KM, Maireen D, et al. Congenital vertical talus in multiple pterygium syndrome. J Pediatr Orthop 2011;31(5):564–9.

[10] Aslani A, Kleiner U, Noah EM, Pailuo N, Rudnik- Schoneborn S. Extensor-tendon hypoplasia and multiple pterygia: escobar syndrome in a 7 year-old boy. JPRAS 2002;55(6):516–9.

[11] Teebi AS, Daoud AS. Multiple pterygium syndrome: a relatively common disorder among Arabs. J Med Genet 1990;27:791–2.

[12] Penchaszadeh VB, Salszberg B. Multiple pterygium syndrome. J Med Genet 1981;18:451–5.

[13] Hall J. Arthrogryposis and associated anomalies. In: Rimons Emery, editor. Principles and practice of medical genetics, vol. 3. New York, NY: Churchil Livingstone; 1977. p. 2905–7.

[14] Matolcsy T. Uber-ein chirugische Behandlung der angeborene Klughaut. Arch Klin Chir 1936;185:675–81.

[15] Escobar V, Bixler D, Gleiser S, Weaver DD, Gibbs T. Multiple pterigium syndrome. Am J Dis Child 1978;132:609–11.

[16] Gillin ME, Pryse-Davis J. Pterigium syndrome. J Med Genet 1976;13:249–51.

[17] Chen H, Chang CH, Misra RP, Peters HA, Grijalva NS, Opitz JM. Am J Med Genet 1980;7(2):91–102.

[18] Norum RA, James VL, Mabry CC. Pterygium syndrome in three children in a recessive pedigree pattern. Birth Defects 1969;5:233–5.

[19] Scott CI. Pterygium syndrome. Birth Defects 1969;5:231–2.

[20] Pashayan H, Dallaire L, Macleod P. Bilateral aniridia, multiple webs and severe mental retardation in a 47 xxy/48 xxxy mosaic. Clin Genet 1973;4:126–9.

[21] Staheli LT, Hall JG, Jaffe KM, Paholke DO, editors. Overview of arthrogryposis, limbsplus other body areas. Arthrogryposis, a text atlas. 1998. p. 8–14.

[22] Herbich VJ. Zur Frage der Arthrogryposis multiplex congenita und des status Bonnevie-Ullrich. Monatsschr Kinderheilkd 1952;100:25–7.

[23] Kanof A, Aronson SM, Volk BW. Arthrogryposis: a clinical and pathologic study of three cases (case 1). Pediatrics 1956;17:532–40.

[24] Lang K, Lelbach WK, Colmat HJ. Beitrag Zum Bilde (Pterygoerthromyodysplasia congenita). Monatsschr Kinderheilkd 1960;108:248–52.

[25] Vogt J, Harrison BJ, Spearman H, Cossins J, Vermeer S, ten Cate LN, et al.. Mutation analysis of CHRNA1, CHNB1, CHRND and RAPSN genes in multiple pterygium syndrome/fetal akinesia patients. Am J Hum Genet 2008;82(1):222–7.

[26] Hoffman K, Muller JS, Stricker S, Megarbane A, Rajab A, et al. Escobar syndrome is a prenatal myasthenia caused by disruption of the acetylcholine receptor fetal Y subunit. Am J Hum Genet 2006;79(2):303–12.

[27] Yokochi K, Suzuki S, Tanaka T, et al. Skeletal muscle involvement in Escobar syndrome. Brain Dev 1985;7(6):585–9.

[28] Arpaci AH, Bozkirli F, Konuk O. Anesthesic management for Escobar syndrome: case report. Case Rep Med 2011;2011, 3pp [Article ID 515719].