

Case Report**A Rare Case of Spondyloepiphyseal Dysplasia with Ocular Manifestations***MuthuKrishnan Vallinayagam¹, Pugazhendhi Sambath², Manibharathi Asokan³*¹MS, DNB, FRCS, FICO, Assistant Professor, Department of Ophthalmology, Sri Lakshmi Narayana Institute of Medical Sciences (SLIMS), Puducherry² MBBS, SLIMS, Puducherry.³MBBS, SLIMS, Puducherry.

ABSTRACT: Spondyloepiphyseal dysplasia (SED) is a rare heterogenous form of chondrodysplasia characterized by congenital dwarfism with a short trunk and epiphyseal dysplasia in the long bones and vertebral bodies. There is a defect in type II collagen, resulting in stunted growth and premature degenerative arthropathy. We report a twelve year old child who presented with polyarthritis of knee and ankle joints, developmental delay, syndromic facies, short neck, pectus carinatum, hypertrichosis and hyperpigmentation. There were recurrent painful episodes with remissions and exacerbations. Ocular manifestations in our patient included prominent eyeballs, telecanthus, euryblepharon, myopia, vitreous membranes, arcus juvenilis and xerophthalmia. SED is frequently misdiagnosed as Juvenile Idiopathic Arthritis (JIA) or Rheumatoid arthritis. The most common ophthalmic features seen in Spondyloepiphyseal dysplasia are vitreoretinopathy, myopia, corneal opacities, subcapsular cataract, subluxated lens, blepharoptosis, retinal tears and retinal detachment. The constellation of systemic and ocular features have to be borne in mind to make an accurate diagnosis of this rare entity.

Keywords: Spondyloepiphyseal Dysplasia, Ocular manifestations, vitreoretinopathy, myopia.

INTRODUCTION

Spondylo-epiphyseal dysplasia (SED) is a rare heterogeneous form of skeletal systemic disease characterized by congenital dwarfism with a short trunk, and epiphyseal dysplasia in the long bones and vertebral bodies. [1] It results in stunting of growth and premature degenerative arthropathy, due to incongruity of joint surfaces. The underlying defect lies in type II collagen and is classified into two clinical types namely SED congenita and SED tarda. [2] SED congenita presents at birth with predominant involvement of knees and hips, short neck and vertebral abnormalities at the base of skull. [1] SED tarda is an entity where the major abnormality is in the spine, which becomes shortened and stiff. There is often an abnormal curvature of the spine and hands may reach down to the knees. [2] We report a child with polyarthritis with a cluster of features such as developmental delay, syndromic facies, vertebral abnormalities, hypertrichosis and hyperpigmentation. Ocular manifestations were prominent eyeballs, euryblepharon, telecanthus, myopia, vitreous membranes, arcus juvenilis and xerophthalmia.

case report

A twelve year old girl presented with fever and painful swelling in bilateral knee and ankle joints for a month.

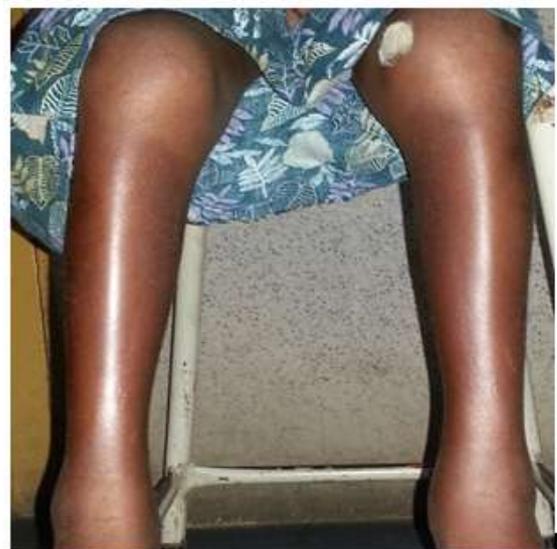


Fig 1: Bilateral Knee and ankle swelling

(Fig 1) She was deaf mute with developmental delay. There was a particular pattern of occurrence of pain, which seemed to increase during morning hours. There was incessant crying at night and pain in the sacral region. She had similar episodes of joint pains for 6 years. There were recurrent painful episodes with remissions and exacerbations. The family history was insignificant. Physical examination revealed short stature, syndromic facies, depressed nasal bridge, frontal bossing, short neck and pectus carinatum (pigeon chest)



Fig 2: Syndromic Facies, Frontal bossing, Prominent eyes, Telecanthus, Euryblepharon, Depressed nasal bridge and Short neck



Fig 3: Pectus carinatum (Pigeon chest)

(Fig 2 and 3) Neurological examination exposed her inability to speak and to hear. There was no focal neurological deficit. Few indurated hyperpigmented plaques with hypertrichosis on the medial aspect of both lower limbs were noticed.



Fig 4: Knee swelling with hyperpigmented plaques and hypertrichosis

(Fig 4) Dental examination disclosed irregular teeth. Radiological examination of spine showed flattened vertebral bodies. There were no signs of rickets. On ocular examination, she was found to have downward slant of both eyes with prominent eyeballs, euryblepharon and pseudoesotropia. The temporal aspect of bulbar conjunctiva showed Bitot's spots suggesting xerophthalmia. Examination of cornea revealed prominent arcus juvenilis.



Fig 5: Arcus juvenilis

(Fig 5) Fundus examination revealed degenerated vitreous and membranes in the vitreous. Retina was within normal limits. Refraction revealed myopia of -5 dioptres in both eyes. Laboratory investigations showed microcytic hypochromic anaemia. C Reactive protein was positive. Rheumatoid factor (RA) and Antinuclear Antibody (ANA) assay were negative. Fasting lipid profile was normal. Thyroid function tests were normal.

discussion

Spondyloepiphyseal dysplasia (SED) is a rare hereditary chondrodysplasia with a variable inheritance, characterised by disproportionate short stature, abnormal epiphysis and flattened vertebral bodies. [3] Genetic studies have shown mutation in COL2A1 gene resulting from the substitution of glycine by serine in $\alpha 1$ chains of Type II collagen. These changes were expected to cause permanent damage to the structural protein of the cartilage and the vitreous gel. [4,5] In our case, the girl presented with fever and painful swelling in joints with systemic clinical features suggestive of spondyloepiphyseal dysplasia. Short stature, flattened vertebral bodies, short neck and premature arthritic changes in major joints are the hallmark features of Spondyloepiphyseal dysplasia in our patient. The frequent presenting feature of Spondyloepiphyseal dysplasia - Tarda is premature osteoarthritis of major joints, especially affecting the hip joint. SED is commonly seen in males. [6] It is often confused with Juvenile Idiopathic Arthritis (JIA) because of the age group affected and similarity in presentation. More often than not, it has also been misdiagnosed and treated as rheumatoid arthritis. Non inflammatory joint involvement, absence of laboratory changes such as Rheumatoid factor and non-responsiveness to anti-inflammatory drugs helps in the diagnosis of SED. [2] The most common ophthalmic features seen in Spondyloepiphyseal Dysplasia are vitreoretinopathy and myopia. Vitreous abnormalities are a frequent association. Other features reported in literature include corneal opacity, subcapsular cataract, subluxated lens and blepharoptosis. [3,7] Vitreous abnormalities such as vitreous membranes, as observed in our patient, are an important feature in the majority of

SED. Type II collagen is abundant in cartilage and vitreous and it makes these sites vulnerable in Spondyloepiphyseal Dysplasia. A study was conducted in Cambridge University Hospital regarding ophthalmic features in a group of 14 subjects with SED, and showed membranous anomaly in vitreous in 13 subjects. 10 subjects were found to be myopic, ranging from -0.50 to -15.00 D. 4 subjects were noted to have retinal anomalies. [3] This study provides ample evidence to prove a strong association of ophthalmic findings in Spondyloepiphyseal dysplasia. Corneal opacity was noted to be a rare ocular anomaly in Spondyloepiphyseal dysplasia. Some cases were reported to have peripheral nodular, punctate, ground glass corneal opacities and central nebular opacities. [8] In our case, cornea was clear with a prominent corneal arcus. There were no retinal abnormalities in our patient. Retinal tear and retinal detachment have been reported to be associated with Spondyloepiphyseal dysplasia. The risk of ocular morbidity is high with an increased life time risk of retinal detachment, as seen in Stickler's syndrome, a type II collagenopathy. [3]

CONCLUSION

Spondyloepiphyseal Dysplasia can have a variable presentation. Ophthalmic features may be associated and may result in visual compromise in an unfortunate patient. The constellation of systemic and ocular features have to be borne in mind, to make a prompt diagnosis and to avoid misinterpretation as Juvenile Idiopathic Arthritis. Further research and genetic analysis are indicated to throw light into this enigmatic disease entity.

REFERENCES

- [1] Gembun Y, Nakayama Y, Shirai Y, Miyamoto M, Sawaizumi T, Kitamura S. 2001. A Case Report of Spondyloepiphyseal Dysplasia Congenita. *J Nippon Med Sch.* 68(2):186-9.
- [2] Gupta R, Gulati N, Hatimota P, Gulati M, Kumar M. 2002. Spondylo-epiphyseal Dysplasia Mimicking Juvenile Idiopathic Arthritis - A Case Report. *J Indian Rheumatol Assoc.* 10:22-3.
- [3] Meredith S P, Richards A J, Bearcroft P, Pouson A V, Snead M P. 2007. Significant ocular findings are a feature of heritable bone dysplasias resulting from defects in type II collagen. *Br J of Ophthalmol.* 91:1148-51.
- [4] Anderson I J, Goldberg R B, Marion R W, Upholt W B, Tsipouras P. 1990. Spondylo-epiphyseal Dysplasia Congenita: Genetic linkage to Type II Collagen (COL2A1). *Am. J. Hum. Genet.* 46:896-901.
- [5] Cole W G, Hall R K, Rogers J G. 1993. The Clinical Features of Spondyloepiphyseal dysplasia congenita resulting from the substitution of Glycine 997 by serine in the $\alpha 1(\text{II})$ chain of type II collagen. *J Med Genet.* 30:27-35.
- [6] Weinfield A, Ross W, Sarasohn S H. 1967. Spondyloepiphyseal Dysplasia Tarda – A cause of premature Ostoarthritis. *American journal of Roentgenology.* 101:851-9.
- [7] Yurdakul F G, Kocak R, Sivas F, Guvenir A A, Bodur H. 2015. Spondylo-epiphyseal dysplasia Tarda with Progressive Arthropathy associated with Osteoporosis and Cataract. *Clin Med Rev Case Rep.* 2:6.
- [8] Hirata Y, Watanabe H, Maeda N, Inoue Y, Shimomura Y, Tano Y. 2000 .Corneal Changes in Spondyloepiphyseal Dysplasia Tarda. *Jpn J Ophthalmol.* 44:29-32.