

Majewski syndrome, Short Rib Polydactyly Syndrome (SRPS) Type II - A rare case report, with review of literature

ABSTRACT

Short Rib Polydactyly Syndrome (SRPS) type II also known as Majewski syndrome, is the rarest of the four subtypes of SRPS which is a rare inherited skeletal dysplasia. We report a case of Majewski syndrome in a neonate with brief review of literature. A 24 years old primigravida, with history of second degree consanguineous marriage underwent a Prenatal USG which revealed anhydramnios, bilateral enlarged kidneys, extremely narrow thorax and bilateral short limbs with polydactyly. Based on these findings a probable diagnosis of lethal skeletal dysplasia was made and termination of pregnancy advised. Refusing termination the mother delivered a male foetus at 30 weeks with severe respiratory distress and gross anomalies. The foetus succumbed to respiratory failure inspite of resuscitation. Gross findings were a male foetus with enlarged head, hydropic face, hypertelorism, short nose, depressed nasal bridge, pseudo cleft lip, cleft palate, low set posterior rotated ears, cystic hygroma, micrognathia, short and narrow chest, all the limbs showed mesomelic limb shortening, postaxial polydactyly, syndactyly and brachydactyly. Postnatal X-ray, CT scan and USG confirmed the above mentioned features and additional findings were extremely short horizontal ribs and disproportionately shortened ovoid tibia. Autopsy revealed a bell shaped thorax, small hypoplastic lungs, bilateral enlarged kidneys, atrial septal defect, hypoplastic epiglottis and larynx and short small intestine. Microscopic findings of pulmonary hypoplasia, renal cystic dysplasia, hepatic fibrosis and markedly retarded endochondral ossification correlate with the clinical, radiological and pathological findings of Short Rib Polydactyly Syndrome Type II -Majewski Syndrome.

Keywords: Short Rib Polydactyly Syndrome Type II, Majewski Syndrome

1. INTRODUCTION

Short rib-polydactyly syndromes (SRPS) are a heterogeneous group of recessively inherited lethal osteochondrodysplasias, the prevalence rate is reported to be about 2.1 to 2.3/10,000 births and the rate of lethal osteochondrodysplasia is about 0.95/10,000 births.¹ There are four classical subtypes of SRPS with a common finding of small and narrow thorax with short ribs and hypoplastic lungs alongwith pre/postaxial polydactyly. Apart from these findings in all the four subtypes, Type I - Saldino-Noonan is characterized by severely shortened flipper like extremities, polycystic kidneys and pointed metaphyses, Type II- Majewski is characterized by cleft lip, cleft palate, epiglottis/laryngeal hypoplasia, renal cystic disease and short, ovoid tibia, Type III -Verma-Naumoff is characterized by extreme micromelia with severely dysplastic widened metaphyses and occasionally situs inversus, Type IV -Beemer-Langer is characterized by extreme micromelia with smooth metaphyseal margins, macrocephaly with frontal bossing, cleft lip, cleft palate and CNS abnormalities.

We report a case of SRPS type II – Majewski syndrome; the rarest out of the 4 types of SRPS, which itself is an extremely rare group of syndromes with less than 100 published cases in the literature.²

2. PRESENTATION OF CASE

24 years old primigravida with a history of consanguinity was antenatally diagnosed with multiple congenital fetal anomalies on USG scan at 28 weeks of gestation. The USG scan revealed a single live intrauterine fetus with bilateral echogenic enlarged kidneys, minimal fetal ascites, bilateral short limbs and anhydramnios. Based on these findings a probable diagnosis of a lethal skeletal dysplasia was made and termination of pregnancy advised. Refusing termination, the mother delivered a male neonate at 30 weeks of gestation with severe respiratory distress and gross anomalies. The neonate succumbed to respiratory failure in spite of resuscitation and was sent for perinatal autopsy.

A male neonate with attached umbilical cord, without placenta and weighing 1.9kgs was received. All external orifices were patent. Significant anthropometric findings were an increased upper segment: lower segment ratio of 2.5:1(normal for the age is 1.7:1), arm span of 30cms (normal = 2-3cms less than total length) and a total length of 43cms, which suggested short limb short stature. Also noted were a decreased chest circumference and an increased abdominal circumference.

Postnatal X-ray and CT scan revealed extremely short horizontal ribs, normal pelvis and vertebrae, extreme micromelia, disproportionately shortened ovoid tibia and postaxial polydactyly in all the four limbs (Figures-I&II). Postnatal USG-abdomen showed bilateral enlarged kidneys.



Figure I- XRay Infantogram- Pelvis&Lower limbs- shows a normal pelvis, disproportionately shortened ovoid shaped tibiae and polydactyly.



Figure II- Whole body CT scan- shows extremely short horizontal ribs, extreme micromelia, disproportionately shortened ovoid shaped tibiae and polydactyly.

51 External examination of the neonate revealed macrocephaly, a prominent forehead, hydropic facies, hypertelorism, short
52 nose, depressed nasal bridge, pseudocleft lip, extremely short and narrow chest, protuberant abdomen and
53 hypospadias (Figure-III).



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55 **Figure III- Neonate with hydrops, macrocephaly, hypertelorism, pseudocleft lip, extremely short&narrow chest,**
56 **protuberant abdomen& short limbs.**
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58 Additional findings were a cleft palate, posteriorly rotated low set ears, micrognathia and cystic hygroma (Figures-IV&V).



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60 **Figure IV- Cleft palate in the same neonate**



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62 **Figure V- Posteriorly rotated low-set ears, micrognathia and cystic hygroma in the same neonate**

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64 **All the four limbs showed micromelia, mesomelic limb shortening, postaxial polydactyly, syndactyly, brachydactyly and**
65 **nail dysplasia (Figures-VI&VII).**



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67 **Figure VI- Both hands of the same neonate show postaxial polydactyly, brachydactyly&syndactyly**



Figure VII- Both feet of the same neonate show postaxial polydactyly, brachydactyly&syndactyly

Autopsy findings revealed short, horizontal ribs and a characteristic bell shaped thorax. Gross findings were extremely small bilateral hypoplastic lungs i.e. 20gms/1900gms= 0.0105 (normal > 0.015) and bilateral enlarged kidneys (Figure-VIII).

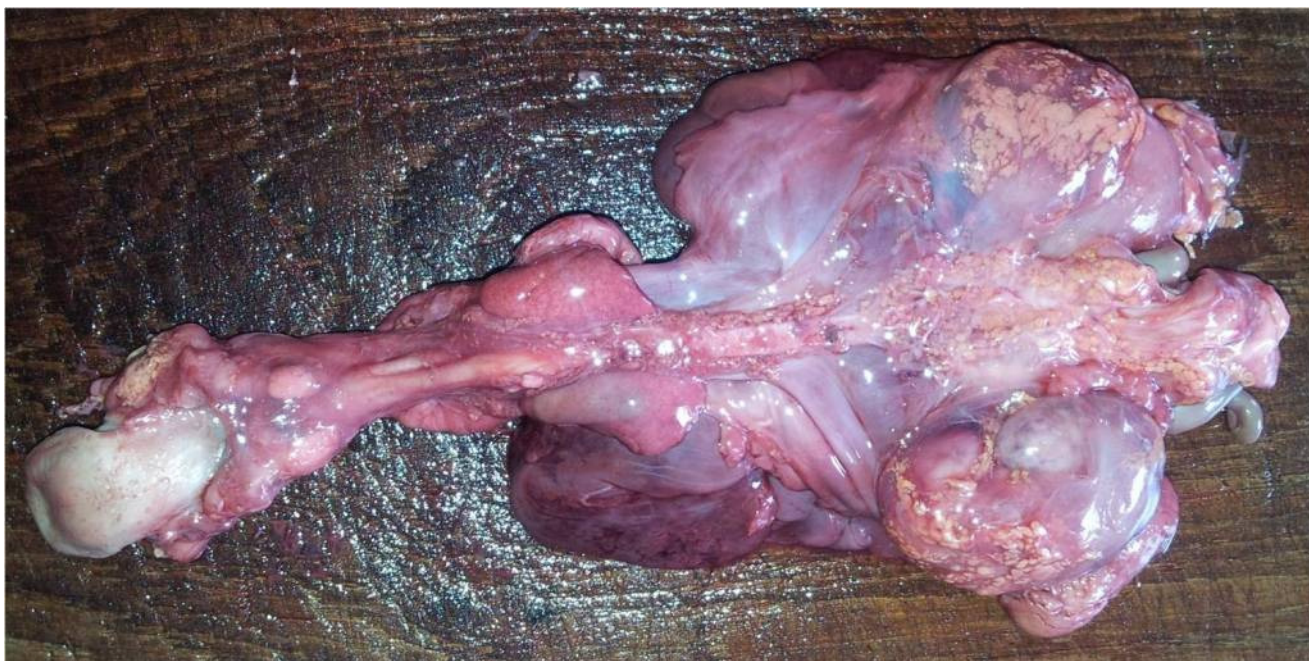


Figure VIII- Enbloc removed on autopsy (posterior view) shows small lungs&enlarged kidneys

Additional findings were an atrial septal defect, short small intestine i.e. 90cms in length (normal >200cms), hypoplastic epiglottis and larynx. Microscopically bilateral pulmonary hypoplasia was noted (Figure-IX).

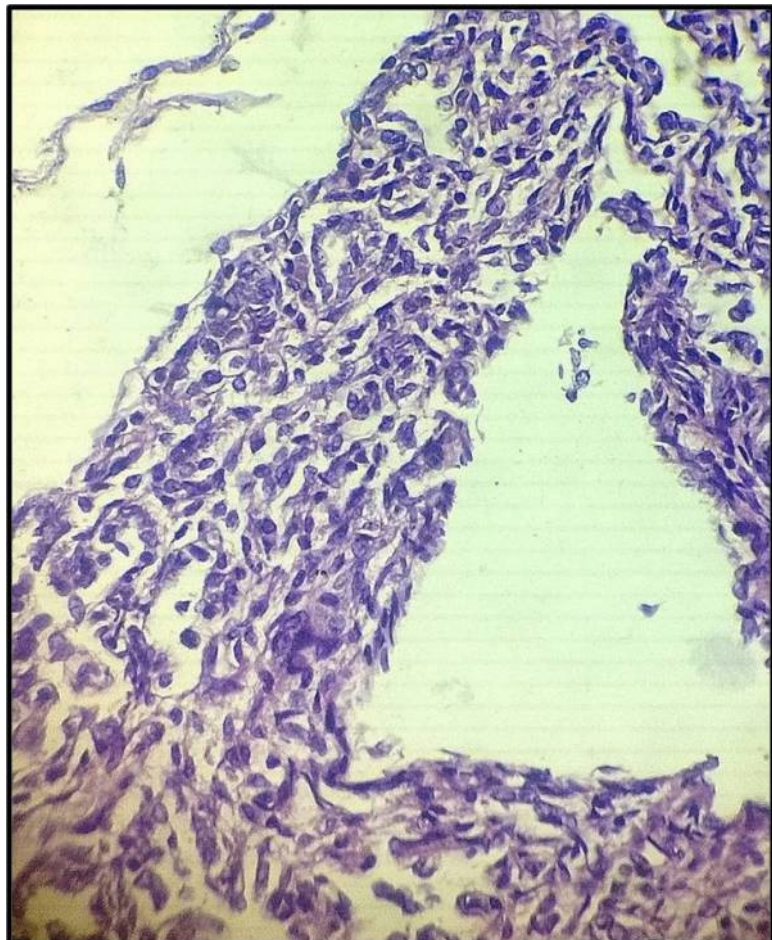


Figure IX-Photomicrograph of Lungs-H&E x400-Pulmonary hypoplasia

Bilateral kidneys showed microcystic spaces, premature collecting ducts, immature mesenchyme, dysplastic changes, cystic dilatation of the tubules both in the cortex and medulla; occasional glomeruli in the cortex also showed cystic dilatation (Figure-X).

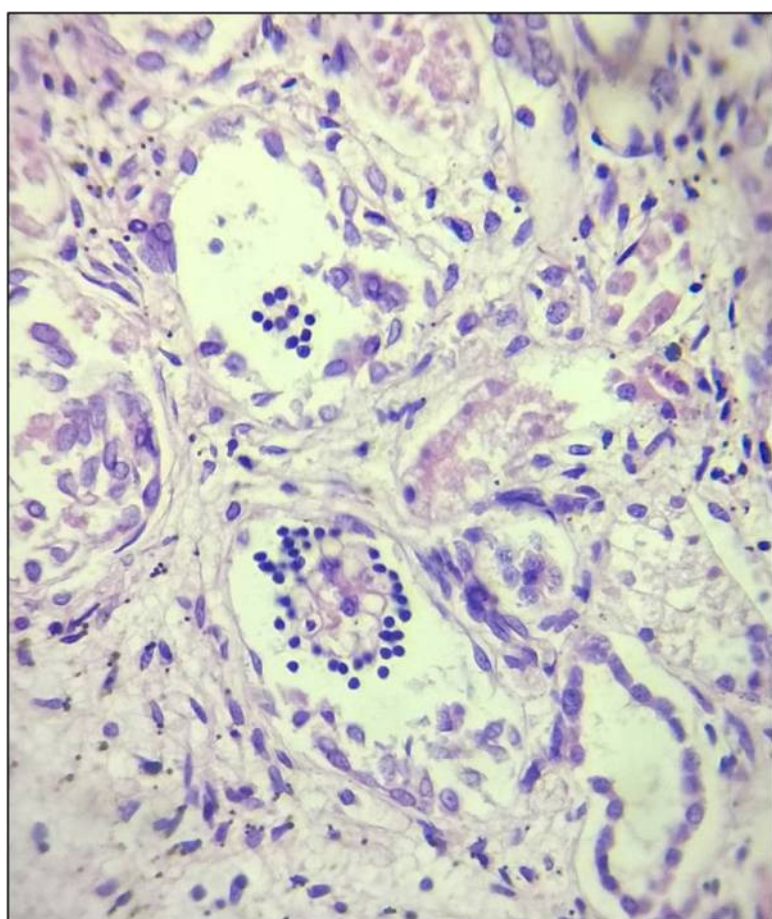
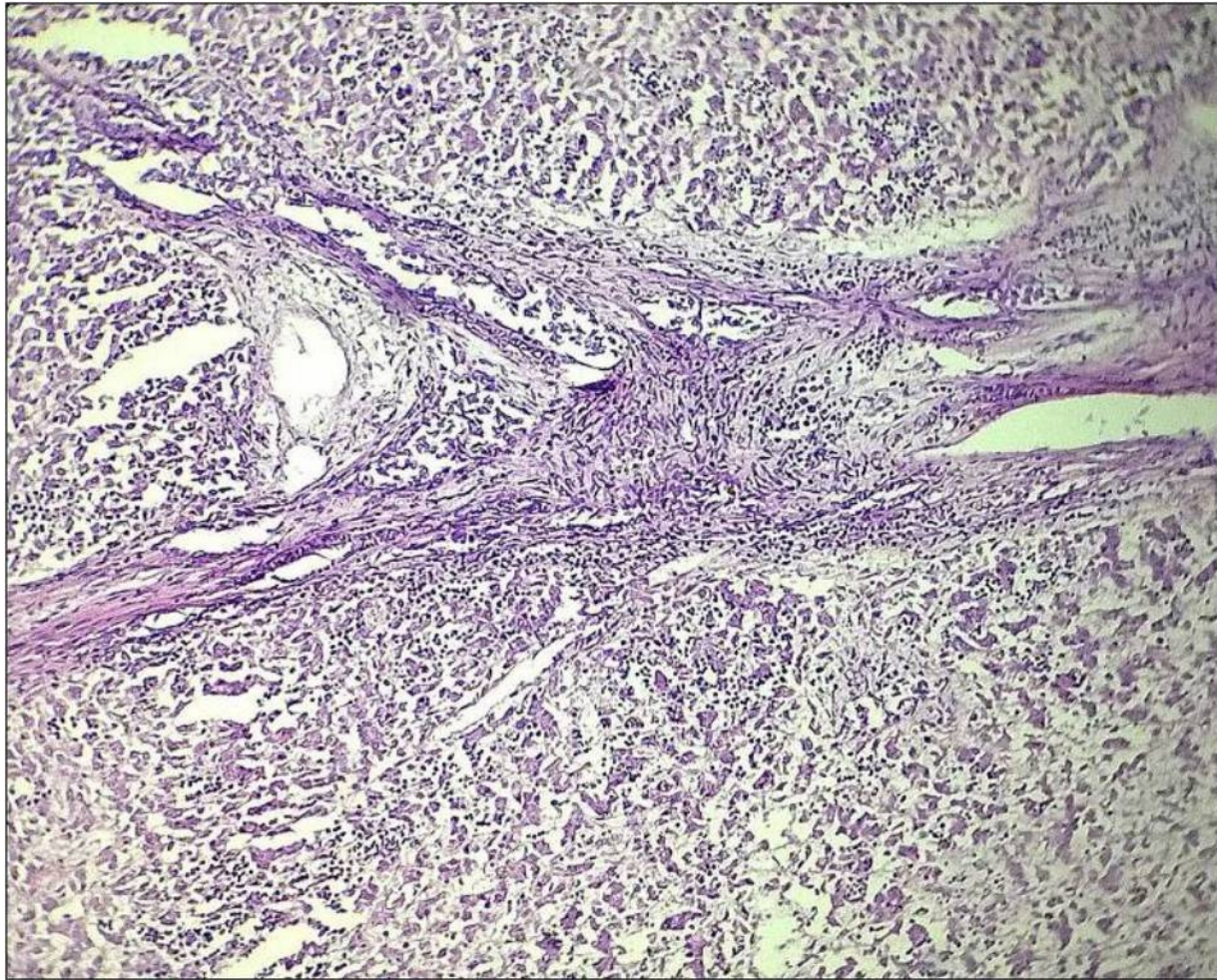


Figure X- Photomicrograph of Kidneys-H&E x400-Renal cysts&primitive glomeruli

Liver showed band like periportal fibrosis and extramedullary haematopoiesis (Figure-XI).



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90 **Figure XI- Photomicrograph of Liver-H&E x400-Periportal fibrosis**

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92 **Sections from tibial metaphyses and costochondral junction showed markedly retarded endochondral ossification with**
93 **chondrocytes in the growth zone markedly reduced in number and disorderly arranged (Figure-XII).**

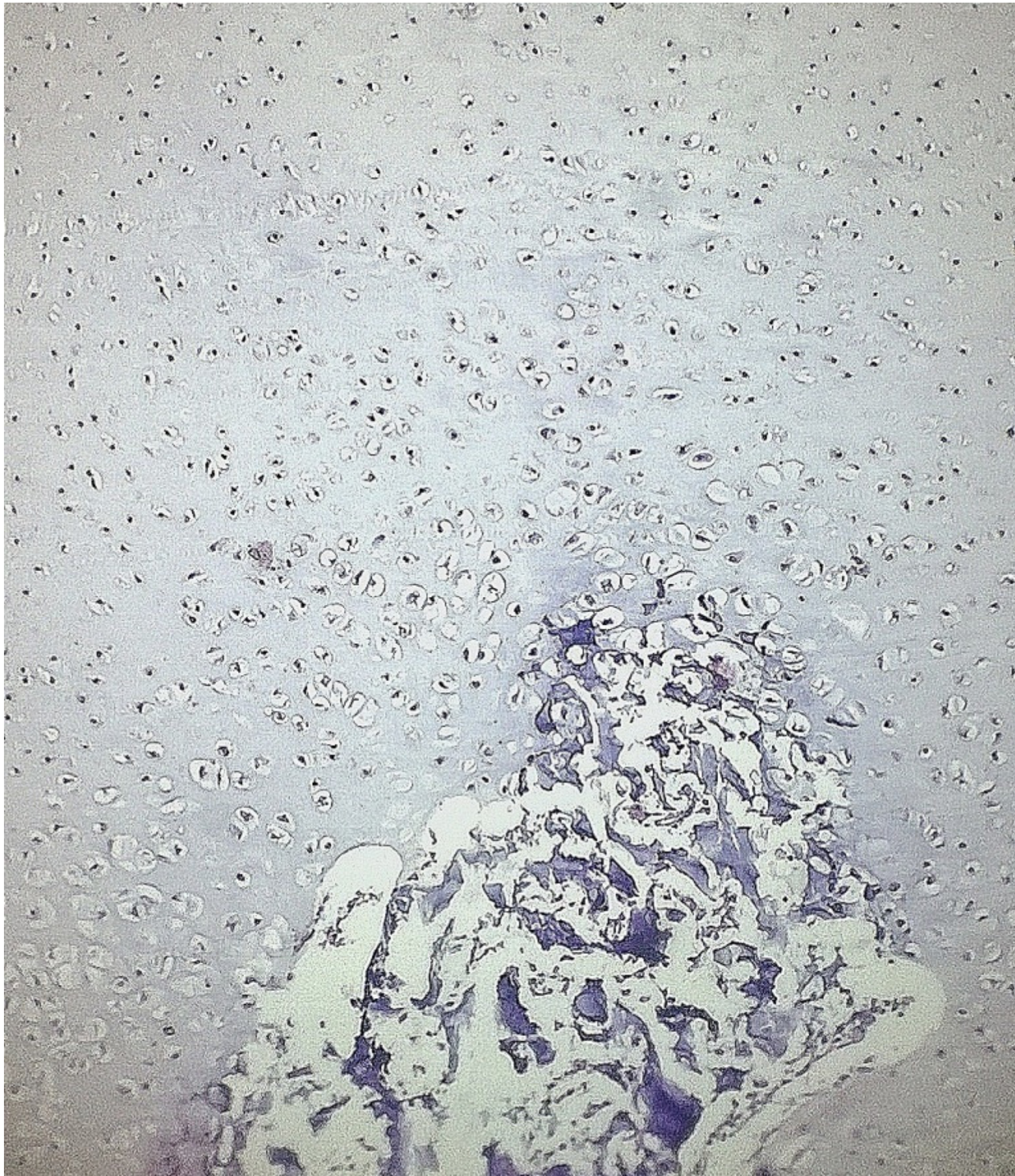


Figure XII- Photomicrograph of Tibia&Costochondral junction-H&E x100- Markedly retarded endochondral ossification with chondrocytes in the growth zone markedly reduced in number and disorderly arranged

All other organs were normal grossly with normal histology.

Hence, based on these radiological, clinical and pathological findings a diagnosis of Short Rib Polydactyly Syndrome type II- Majewski Syndrome was made.

3. DISCUSSION

Majewski syndrome was first described in 1971 by Majewski et al who reported 4 cases which was later labelled as Short Rib Polydactyly Syndrome (SRPS) type II - Majewski syndrome. A comparative study of the present case to those of earlier authors and demonstrating the differences between the 4 types of SRPS is shown in Table-I.

TABLE- I

Comparative study of Short Rib Polydactyly Syndromes

SRPS	TYPE	TYPE	TYPE	TYPE	MAJEWSKI et al ^[3] (1971)	BEEMER et al ^[4] (1983)	PRAMILA P et al ^[5] (2009)	PRESENT CASE (2014)
TYPE	I	II	III	IV	II	IV	II	II
SHORT HORIZONTAL RIBS	+	+	+	+	+	+	+	+
SHORT LIMBS	+	+	+	+	+	+	+	+
PRE/POST AXIAL POLYDACTYLY	+	+	+	+/-	+	+	+	+
AMBIGUOUS GENITALIA	-	+	+	+	+	+	+	+
HYDROPS FETALIS	+	+	+	+		+	-	+
POLYHYDRAMNIOS	+	+	-	-		+	-	-
MEDIAN CLEFT LIP/PALATE	-	+	+	+	+	+	+	+
SITUS INVERSUS	+	-	+	-		-	-	-
COARCTATION OF AORTA	-	+	-	-		+	-	-
VERTEBRAL ABNORMALITIES	+	-	+	+/-		-	-	-
HYPOPLASTIC EPIGLOTTIS	-	+	-	-	+	+	+	+
CNS ABNORMALITIES	-	+	-	+		+	+	-
OVAL TIBIA	-	+	-	-		-	+	+
SMOOTH METAPHYSES	-	+	+	+		+	+	+
GI/ GENITAL ABNORMALITIES	+	+	+	+/-		+	+	+
PROTUBERANT ABDOMEN	+	+			+			+
RENAL CYSTS		+	+		+			+

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The present case demonstrated all of the constant clinical findings and most of the common and occasional clinical findings, radiological findings and all of the histopathological findings of SRPS type II – Majewski syndrome mentioned in the literature. ^[6]
In 2012, C.P Chen et al reported that SRPS has been found to be caused by mutations in the genes of IFT80, DYNC2H1, NEK1 or WDR35. ^[7]

Genetic counseling in these cases is of great importance because the recurrence risk in siblings is 25% since it is an autosomal recessive condition. Management of this universally lethal entity comprises of supportive therapy only. Early diagnosis can be made prenatally by Ultrasonography although it is not always possible to differentiate the subtype of SRPS. ^[8]

4. CONCLUSION

In conclusion, the present case report draws attention to the various aspects of diagnosing SRPS type II- Majewski syndrome from the clinical, radiological and histopathological aspects. As the condition is invariably fatal during the neonatal period, the antenatal diagnosis is very important. Termination of pregnancy regardless of the period of gestation and genetic counseling for recurrence risk after confirmation of the diagnosis is advised.

CONSENT (WHERE EVER APPLICABLE)

"All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Informed consent was taken from the neonate's parents before conducting the autopsy and all measures have been taken to protect the privacy of the subject.

REFERENCES

1. Praveen Kumar, Barbara K. Burton. Congenital malformations-Evidence Based Evaluation and Management; 1st edition. The McGraw-Hill Companies, Inc.:2008.
2. Alessandro Castriota-Scanderbeg, Bruno Dallapiccola. Abnormal Skeletal Phenotypes- Medical -976pages: From Simple Signs to Complex Diagnoses: Short Rib-Polydactyly Syndrome, Type II-page 868: Springer Science & Business Media. Google eBook. 20-Mar-2006.
3. Majewski, F., Pfeiffer, R. A., Lenz, W., Muller, R., Feil, G., Seiler, R. Polysyndaktylie, verkuerzte Gliedmassen, und Genitalfehlbildungen: Kennzeichen eines selbstaendigen Syndrome? Z. Kinderheilk.1971; 111: 118-138.
4. Beemer FA, Langer LO Jr, Klep-de Pater JM, et al: A new short rib syndrome. Report of two cases. Am J Med Genet. 1983; 14: 115-23.
5. M. Pramila Padmini, B. Narasinga Rao, R. Ramana Rao : An investigation into Short Rib Polydactyly Syndrome . J.Anat.Soc.India.2009; 58(1): 29-34.
6. Harold Chen: Atlas of genetic diagnosis and counseling; 1st edition. Humana Press Inc.:2006.
7. C.P. Chen et al: Short rib polydactyly syndrome type II (Majewski) - Prenatal diagnosis, perinatal imaging findings and molecular analysis of NEK1 gene; Taiwanese Journal of Obstetrics & Gynecology .2012; 51: 100-105.
8. Pramod Setty Jutur,chandan Pramod Kumar, Shetteppa Goroshi : Case Report-Short Rib Polydactyly Syndrome-type 2 (Majewski Syndrome). Indian Journal of Radiology and imaging. May 2010; 20(2): 138-142.