

Steel syndrome: first reported case in Brazil harboring a novel variant in *COL27A1*

GIULIA ZOCCOLI BUENO¹; HELOÍSA AUGUSTA CASTRALI¹; RAFAEL AVELAR MACHADO¹; CARLA TONI MARCELINO MÜLLER DE SIAS¹; MARIA INEZ DA CORREGGIO LEAL¹; ALEXANDRE CHAVES FERNANDES¹; DERNIVAL DANTAS DIAS JÚNIOR¹; GABRIELA YUMI GOTO SALT¹; ÉRIKA PRISCILA MACHADO¹; CONSÓRCIO GENOMAS RAROS²; DÉBORA E SILVA DE LAZARI¹; MATHEUS AUGUSTO ARAÚJO CASTRO¹; RACHEL SAYURI HONJO¹; CHONG AE KIM¹; DÉBORA ROMEO BERTOLA¹

1-INSTITUTO DA CRIANÇA - HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO
2-HOSPITAL ISRAELITA ALBERT EINSTEIN

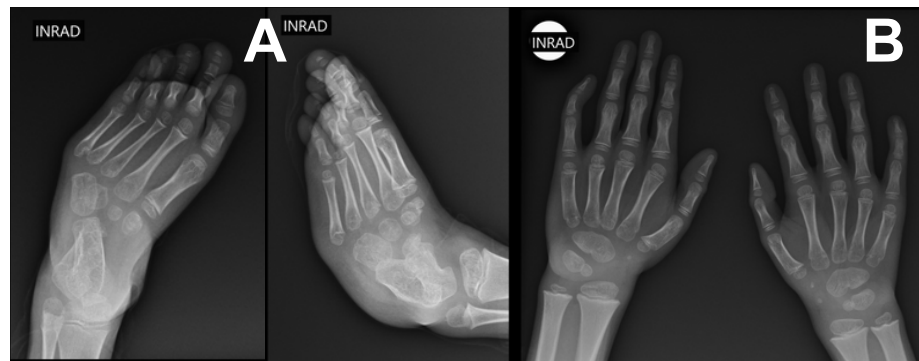
giulia.zoccoli@hc.fm.usp.br

INTRODUCTION

Steel syndrome (OMIM #615155, NOS 13–0300) is a rare autosomal recessive skeletal dysplasia caused by biallelic *COL27A1* variants. It is characterized by short stature, bilateral hip and radial head dislocations, scoliosis, carpal coalitions and pes cavus. To date, around 55 cases have been reported, predominantly in individuals of Puerto Rican ancestry. We report the first Brazilian case, contributing to the global data of this condition.

CASE REPORT

The proband is a 6-year-old girl, born to healthy first-cousin Brazilian parents. She was delivered at 39 weeks due to oligohydramnios. At birth, she presented with short stature (length 44 cm, $z = -3.43$), scoliosis, right knee dislocation and clubfoot. Respiratory stridor due to laryngotracheomalacia developed shortly after. Neonatal hearing screening showed abnormal otoacoustic emissions. She underwent calcaneal tenotomy at 3 months and reoperation at 6 months. Growth remains below the 1st centile. Kyphoscoliosis progressed severely, accompanied by developmental delay. She has never walked independently and uses a wheelchair. Physical findings include thoracolumbar scoliosis with gibbus, pectus carinatum, bilateral hip and patellar dislocations, clubfeet, joint limitations in the lower limbs, and dysmorphic features (broad nasal base, mild midface hypoplasia, broad forehead). Hearing aids were recently indicated. Spine X-ray revealed left coronal imbalance and thoracolumbar "S-shaped" scoliosis (Cobb angle: 115°), T9-T10 laterolisthesis to the right, straightened costal arches and thoracic kyphosis, accentuated lumbar lordosis, and a ~90° kyphotic angle at the thoracolumbar junction. Hand X-ray showed hamate-capitate coalition and bilateral clinodactyly of the 5th digits. Foot X-ray revealed tarsal coalition and lateral deviation of the talus, more marked on the right. Due to the suspicion of skeletal dysplasia with multiple dislocations, genome sequencing (via research protocol) identified a homozygous *COL27A1* missense variant: c.2549G>A (p.Gly850Glu), classified as likely pathogenic.



A - Foot X-Ray demonstrating tarsal coalition

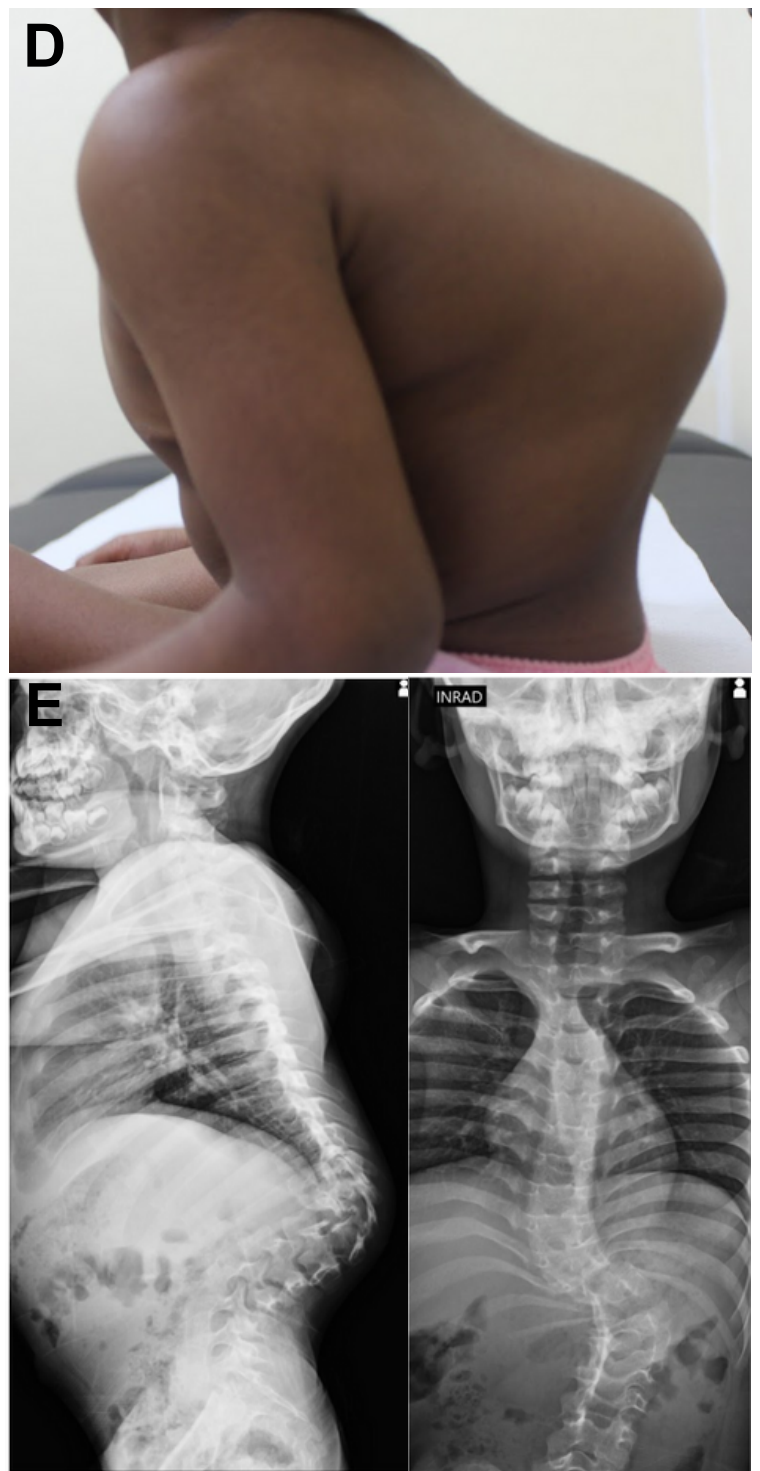
B - Hand X-Ray revealing coalition of the hamate and capitate bones bilaterally



C - Typical facial dysmorphisms observed in Steel Syndrome: broad nasal base, mild midface hypoplasia, broad forehead

DISCUSSION

This is the 16th case reported outside Puerto Rico and involves a novel *COL27A1* variant. Previously described variants include loss-of-function and several missense changes, notably the recurrent p.Gly697Arg in Puerto Rican patients. The p.Gly850Glu variant is absent from control populations of mostly European ancestry (GnomAD/AbraOM), contrasting with the proband's African ancestry. The phenotype in this case is notable for severe, progressive kyphoscoliosis, only previously reported in one Syrian patient with two loss-of-function variants. This report expands the phenotypic and variant spectrum of Steel syndrome and highlights the importance of molecular testing in rare skeletal disorders. Continued research is critical to better understand the pathophysiology of *COL27A1*-related conditions and to guide future diagnostics and therapies.



D - Lateral view of kyphoscoliosis

E - Panoramic X-Ray showing severe kyphoscoliosis

REFERENCES

