CASE REPORT

Management of Severe Obstructive Sleep Apnea in Pediatric Patients with Pycnodysostosis: A Report of Two Cases

Dhruv Jain¹^o, Sanjeev Datana², SS Agarwal³, Indranil D Roy⁴

ABSTRACT

Pycnodysostosis (PKND) is a rare autosomal recessive disorder caused by molecular mutation in cathepsin K (CTSK) gene, resulting in decreased bone turnover with enfeeblement of bone structure. This report addresses an array of systemic and craniofacial features of two siblings affected with PKND with an association of severe obstructive sleep apnea (OSA), managed conservatively with an oral mandibular advancement appliance. **Keywords:** Obstructive sleep apnea, Oral appliance therapy, Pycnodysostosis.

Indian Journal of Sleep Medicine (2022): 10.5005/jp-journals-10069-0091

INTRODUCTION

Pycnodysostosis (PKND), also known as Maroteaux–Lamy syndrome and Toulouse Lautrec syndrome, is a rare autosomal recessive disorder that presents with an array of clinical and radiographic manifestations: osteosclerosis with increased susceptibility to fracture, short stature, delayed closure of cranial sutures, craniofacial abnormalities, clavicular dysplasia, spondylolysis, acro-osteolysis of terminal phalanges, and dysplastic nails. Other findings may include ocular abnormalities, platybasia, stridor, and laryngomalacia. Respiratory resistance in the form of snoring and OSA are also common among affected patients. Intelligence is usually normal though psychomotor skills may be mildly deranged.^{1–3}

Craniofacial manifestations chiefly include brachydactyly, frontoparietal bossing, open fontanelles, proptosis, bluish sclera, convex nasal bridge, midface retrusion, and mandibular micrognathia with obtuse mandibular angle. Dental findings comprise delayed/abnormal tooth formation and eruption process, short or poorly shaped roots with narrowing of pulp chambers and root canals, hypercementosis, deep and grooved palate, and characteristic malocclusion, such as crossbite, anterior open bite, and crowding. Dental caries and periodontitis are frequently associated with poor oral hygiene.^{1–4}

Though this condition gained world academic attention in 1962 when Maroteaux and Lamy⁵ described PKND as a distinct entity as "diastrophic dwarfism," it remained an exceedingly rare diagnosis until 1996, when the mutant gene responsible for PKND was mapped to human chromosome 1q21 and was subsequently identified as encoding for CTSK by a positional cloning strategy.^{6–8}

Young patients presenting with PKND along with respiratory insufficiency require a multidisciplinary approach and pose a great challenge to an orthodontist with special emphasis on preventive and interceptive management.⁹ Currently, there have been no established guidelines pertaining to the orthodontic or orthopedic management of such patients. This paper addresses the systemic and craniofacial features of two siblings affected with PKND along with the conservative management of severe OSA with oral appliance therapy. ^{1–3}Department of Orthodontics and Dentofacial Orthopedics, Armed Forces Medical College, Pune, Maharashtra, India

⁴Department of Oral and Maxillofacial Surgery, Armed Forces Medical College, Pune, Maharashtra, India

Corresponding Author: Dhruv Jain, Department of Orthodontics and Dentofacial Orthopedics, Armed Forces Medical College, Pune, Maharashtra, India, Phone: +91 7060726831, e-mail: drdhruvjain08@ gmail.com

How to cite this article: Jain D, Datana S, Agarwal SS, *et al.* Management of Severe Obstructive Sleep Apnea in Pediatric Patients with Pycnodysostosis: A Report of Two Cases. Indian J Sleep Med 2022;17(1):22–31.

Source of support: Nil Conflict of interest: None

Case 1

Diagnosis and Etiology

A 7-year-old male patient reported with chief complaint of loud snoring and forceful awakening during sleep with no previous intervention. The patient was the eldest among three siblings of consanguineous parents, with normal birth history. He presented with brachycephaly, marked facial convexity, prominent forehead, high nasal bridge with bulbous nose tip, shallow orbits, potentially competent hypotonic lips with increased interlabial gap, shallow mentolabial sulcus, retrusive chin, and short neck. Intraoral examination revealed mixed dentition stage, poor oral hygiene, generalized gingivitis, multiple carious teeth, and anterior open bite with interposed tongue (Fig. 1).

Physical examination revealed disproportionate short stature with a height of 85 cm (<third percentile), weight of 15 kg (<third percentile), BMI of 20.8 kg/m², head circumference of 42 cm (<third percentile), short stubby digits with dysmorphic nails, and sandal foot deformity (Fig. 2). Liver function test and thyroid function test were within normal limits. Visual and neurological assessments were normal. However, 2D echocardiogram revealed tiny atrial septal defect, and chest examination revealed pectus excavatum.

[©] The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons. org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.



Fig. 1: Pretreatment facial and intraoral photographs



Figs 2A and B: Physical examination. (A) Short stubby digits with dysmorphic nails; (B) Sandal foot deformity

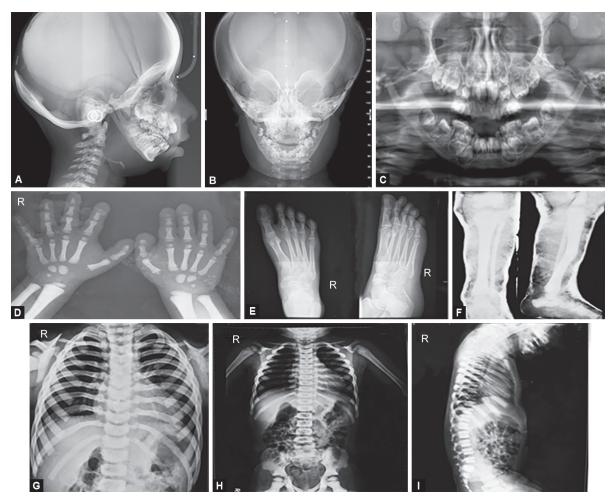
Skeletal survey revealed a generalized increase in bone density, persistent open fontanelles, wormian bones, hypoplastic paranasal sinuses, spur-shaped vertebrae, distal erosion of both clavicles, acro-osteolysis of distal phalanx, and radiolucent horizontal fracture line with cortical breach in mid-tibia (Fig. 3).

Lateral cephalogram revealed abnormal morphology of sella turcica, maxillomandibular hypoplasia, short mandibular ramus with long body, elongated condylar and coronoid process, obtuse mandibular angle, interdental alveolar crest resorption, and short dental roots. There was no evident facial asymmetry as evaluated by posteroanterior cephalogram. However, generalized sclerosis of facial skeleton, more pronounced in circumorbital region ("harlequin appearance"), was evident (Fig. 3). Cephalometric findings are presented in Table 1.

Since excessive day sleepiness, loud snoring, and forceful awakening during sleep were the chief concerns of the patient, a

thorough airway analysis was carried out along with a real-time recording of sleep (Video 1). Lateral cephalogram suggested severe compromise in airway dimension (Table 1). Otolaryngological evaluation revealed adenoid hypertrophy may be a contributing factor for snoring. Furthermore, polysomnography (PSG) was carried out to assess the severity as well as the underlying cause of airway disorder, which confirmed the diagnosis of severe OSA with apnea-hypopnea index (AHI) of 25.3 per hour, the lowest oxyhemoglobin saturation of 37% and 155 out of 190 total events of obstructive apnea (Fig. 4). Central cause of sleep apnea was ruled out. Video 1: Real-time sleep of case 1 (Above-mentioned video is available online on the website of www.ijsm.in.)

On consultation with pediatrician, the provisional diagnosis of PKND was formulated, which was confirmed through genetic testing revealing CTSK exon 6 homozygous mutation (c.749A > G p.Asp250Gly). Further, the youngest sibling and both the parents



Figs 3A to I: (A) Craniofacial radiographic manifestations as depicted by lateral cephalogram; (B) Posteroanterior cephalogram showing pronounced sclerosis in periorbital region ("harlequin appearance"); (C) Orthopantomogram; (D and E) Radiograph showing acro-osteolysis of terminal phalanges; (F) Radiograph of tibia and fibula demonstrating diffused sclerosis; (G) Chest radiograph revealing pectus excavatum; (H) Coxa valga deformity; (I) Lateral spine radiograph depicting vertebral deformity

Cephalometric parameter	Normal value	Case 1	Case 2
Sagittal measurements			
SNA	82°	74°	76°
SNB	80°	59°	63°
ANB	2°	15°	13°
Effective length of maxilla (Co-A)	81.7 ± 3.4 mm (M) 79.8 ± 2.2 mm (F)	67 mm	63 mm
Effective length of mandible (Co-Gn)	99.3 ± 3.6 mm (M) 97.7 ± 3.4 mm (F)	70 mm	68 mm
Maxillomandibular differential	$17.5 \pm 2.2 \text{ mm (F)}$ $17.9 \pm 8.1 \text{ mm (F)}$	3 mm	5 mm
Anterior cranial base length (S-N)	_	55 mm	57 mm
Vertical measurements			
Anterior facial height (N–Me)	_	81 mm	74 mm
Posterior facial height (S-G0)	—	20 mm	21 mm
Jarabak ratio (%)	62–65%	25%	28.3%
Lower anterior facial height (LAFH)/anterior facial height	65–70%	62%	55%
Go-Gn to SN	32°	66°	56°

were heterozygous for the CTSK gene variant, while the second sibling was homozygous for the same (Fig. 5).

Treatment Objectives

The primary treatment objective was to increase the upper airway volume through maxillomandibular advancement, thereby reducing the severity of OSA and improving the stomatognathic function along with the quality of life.

Treatment Plan

As an interdisciplinary approach, the case was thoroughly discussed conjointly with a team of pediatricians, otolaryngologist, oral and maxillofacial surgeons, and orthodontists regarding the comprehensive management of severely compromised airway of the patient. Distraction osteogenesis (DO) was given a serious thought to address the chief complaint; however, because of the associated potential risk factors, such as pathologic fracture and maxillary osteomyelitis, there was no general consensus on DO. Alternatively, conservative measurement with oral appliance therapy was adopted as a treatment mode.

Appliance and Treatment Progress

As an immediate therapy for airway improvement, oral appliance was fabricated comprising of maxillary and mandibular acrylic



SLE	SLEEP APNEA KEPOKI	AKE	PORI														
	Patient Information	aution .															
Name Rel	Are 7		Intern Phys.		Г												
	Ht-Cm 85 Wt-Kr 15		Referred By Technician														
Polysomrography was conducted on the night of 08-02-2020.	in the night of 09-02-2020.	The following	were monitored: o	The following were monitored: central and occipital EEG,	1			Resp	iratory	Summa	y by Boc	Respiratory Summary by Body Position					
electrocologram (EOG), submentals EMG, nasal and oral airfow, thoracic and abdominal wall motion, anterior tibials EMG, book notice and electroconforciam. Anterio corport contractor uns monitored with a orige number. The tractor was cored resonal	s EMG, nasal and oral airflow, th	oracic and abd	ominal wall motion	anterior tibialis EMG, bi torino una sonneri usino		-		-	-	Total				-	•	te Tota	3
second epochs. Hypopneas were scored per AASM definition	red per AASM definition			Automation and Automation	_	Apn Index, REM Apn Index, NREM	0.0		0.0	992	AHL NREW		215 16.8	8 22.6	0.0	26.3	
	4										The Party is a local dial of the party is a l						
Lights Out	10:00:01	800	Duration	% TST	1						ROL REM						,
Lights On:	07:48:01	N	31.0 min	0.0%	Î				40	4.7	RDI, NREW				0 18.0	0 25.3	3
Total Recording Time:	588.0 min	2	PA.5 min	21.0%	Î	Hyp Index, Total			40		-						2
Total Steep Time (TST):	450.5 min	2	325.0 min	72.1%	Š	Duration (min) 30	307.0 19.7	7 63.7	83.6	678.0	TST (min)	1	225.8 10.7	7 66.7	7 00.4	4 688.0	2
Sleep Period Tme:	578.0 min	œ	0.0 min	200													
Sleep Onset	10:10:01								Hea	Heart Rate Su	Viennu						
Steep Efficiency.	70.0%	Latencies	From Lights Out	ut From Steep Onset	X	Average Heart Rate During Direct	NO WENT	deard Due				mdq 1.64	6				
Steep Latency (from LOff):	10.0 min	N			Γ	Highest Heart Kate During Used	T Kate Dur	daac fu				100 0 pm			٦		
R Latency (from Sleep Onset):	NA	2	11.0 min	1.0 min				DIC			BECRIPTORY BAR ATCHES	00.010					
Wake After Steep Onset (WASO):	127.5 min	2	10.5 min	0.5 min													
Wake During Steep:	127,5 min	œ	NA	NA				1.1.1			001						
Total Wake Time:	137.5 min				_	Respiratory channels showed a foral of 190 events. I hose events included	curann	els snov	e pas	10 1010	120	vents.	10056 6	Vents 1	Doluge.		
% Wake Tme:	23.4					155 Obstructive apnea and 55 Hypopneas, 0 Mixed and 0 Central events.	active a	te coud	CS DI	lodith	neas, u	MIXed	o pue	centra	I event	~	
							I he A	The Apnea/ Hypopnea index was 25.3 per hour.	dodi	Del Est	ex was	1 5.52	er hou	4			
	Respiratory Summary	Kremmo															
By Event Classification	Central		:	Obstructive			An	A total of 450.5 min of the total sleep time.	450.5	min of	the tot	tal sleep	time.				
Court	Mean Max	Court Mean	Max	Court Mean Max												_	
Apress, NYEM	00 00			N/1 000 00		> Oxyhemoglobin saturation at baseline was 86 %	idolgot	a satura	tion a	t basel	ine wa	s 86 %					
Apreas, Total		00	0.0	155 30.5 77.0	•	> The Lowest oxyhemoglobin saturation was 37 %	vest ox	chemog	lobin	aturat	EW HOI	\$ 37 %					
Herman ABEM	"Hypopneas scored based on 0% or greater desuturation 28.3 As 0 DCD1. NOCU.	on 0% or great		00 00 0	_	DIAGNOSTIC IMPRESSION:	IMPRI	OISS									
		REP				OBSTRUCTIVE SUEEP APVEA AND HVPOPVEA SVNDROME (OSA)	TVF SI	FFPA	PNF	INT	HVPC	PNFA	SVND	ROVIE	VSO)		
Hypopress, Total 35	28.3 58.0	RER		0 00 00	-	Severity Criteria: Severe AHI 25.3 of with nadir oxygen of 37%	.ci.ia	Severe	HY	253	f with	o aline o	ueo.	of 27%			
Event Statistics	Total		With Arousal													Τ	
			Cont	Index	_												
Apreads. Total			8 :	25]	
Hypopheas, Total	8	г	2 2														
Acres + Hercines NEEV	150 MM 233	-	2 00	80	S	SNORING SUMMARY	VRY										
Acrea + Hoconea REM	AHENA	Т	0	00	Sn	Snoring Upisodesi			451								
RERAS, TODA	00	T	0	00	°,	Total Time with Snoring:	oring		49.4 m	(011.0)	49.4 min (11.0% of sleep)						_
Total Events (A+H+RERA) Total			8	10.9													
Total Events (A+H+RERA) NREM	150 ROI: 25.3	-		10.8													
Total Events (AuHuRSRA) REM	RDI- MA		9	00	٦												

Fig. 4: PSG report

Gene	Variant*	Chromoso		Exon	Zygosity	Cond	ition group	Significa	ince	Inheritance
стѕк	c.749A>G p.Asp250Gly	NM_000 chr1:150		6	Homozygous	Pycno	odysostosis	Variar Unkno Signific (VU	ance	Autosoma Recessive
Gene	Chromos Coordin		Tested Variant		Clinical Exon Proband an Zygosity		Sanger P and Zyg		co	omments
стѕк	chr1:15077		c.749A> p.Asp250		Baby CASE	1	Mr. S F	ATHER	The individual carries one copy (heterozygous)	
		350.5			Homozygou	ıs	Heterozygous		of t	he tested variant
Gene	Chromo Coordir		Testec Varian		Clinical Exon Proband an Zygosity		Sanger P and Zy		Co	omments
стѕк	chr1:15077		c.749A> p.Asp250		Baby CASE	≣ 1	Ms. A	OTHER	Car	individual rries one copy erozygous)
1					Homozygo	us	Heteroz	ygous	oft	he tested

Gene	Chromosomal Coordinates	Tested Variant	Clinical Exome Proband and Zygosity	Sanger Proband and Zygosity	Comments	
стѕк	chr1:150772055T>C NM_000396.3	c.749A>G; p.Asp250Gly	Baby CASE 1	Ms. M CASE 2	The individual carries two copies (homozygous)	
			Homozygous	Homozygous	of the tested variant	
Gene	Chromosomal Coordinates	Tested Variant	Clinical Exome Proband and Zygosity	Sanger Proband and Zygosity	Comments	
стѕк	chr1:150772055T>C	c.749A>G; p.Asp250Gly	Baby CASE 1	Master 2ND SIBLING	The individual carries one cop (heterozygous)	
NM_000396.3		p.Asp250Gly	Homozygous	Heterozygous	(heterozygous) of the tested variant	

Figs 5A to E: Sanger sequencing test report, (A) Case 1; (B and C) Parents of case 1 and case 2 heterozygous for CTSK gene variant; (D) Case 2, the younger sibling; (E) The youngest sibling heterozygous for CTSK gene variant

plate (similar to twin block) with auxiliary buttons for attachment of class II elastics to posture mandible in a forward position. However, because of compromised dental support, the appliance lacked stability. Thus, the two acrylic plates were attached, and a monoblock appliance was fabricated with mandible in forwardly advanced position (Fig. 6). Pharmacological approach with mometasone furoate intranasal spray 1 puff (50 μ g) twice daily in each nostril for 6 weeks was also prescribed in consultation with the otolaryngologist to regress hypertrophied adenoids. The total duration of oral appliance therapy has been 17 months, and the patient is still on periodic follow-up.

Treatment Results

Currently, at a follow-up period of 1.5 years, there has been a marked improvement in airway (Figs 7 and 8) (Table 2) with considerable reduction in initial symptoms (Video 2). The AHI score reduced from 25.3 to 14.2 with reduction in total obstructive events from 155 to 95 along with the reduction in total snoring time, indicating reduction in the severity of OSA. The treatment is still in progress.

Video 2: Real-time sleep of case 1 at follow-up (Above-mentioned video is available online on the website of www.ijsm.in.)

Case 2

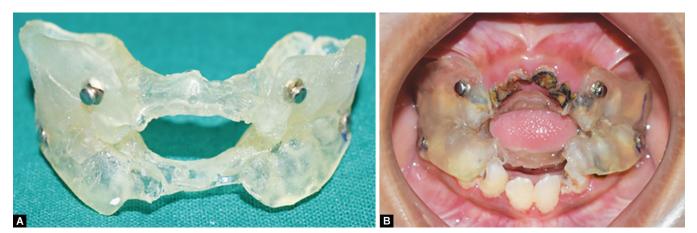
A 5-year-2-month-old female patient, younger sibling of the first case, presented with a chief complaint of loud snoring during sleep. However, there was negative history of excessive day sleepiness and forceful awakening during sleep.

Physical examination and radiographic assessment revealed typical findings of PKND similar to case 1 (Figs 9 and 10), which was confirmed through genetic testing (Fig. 5). Cephalometric findings are presented in Table 1. Airway was compromised though less severe in comparison with case 1. No active intervention other than mometasone furoate intranasal spray (similar to the first case) was prescribed to the patient since she was too young to show compliance with an oral appliance. Currently, at a follow-up of 1.5 years, there has been an improvement in airway (Fig. 11 and Table 3) with considerable improvement in initial symptoms. The patient is still on periodic follow-up.

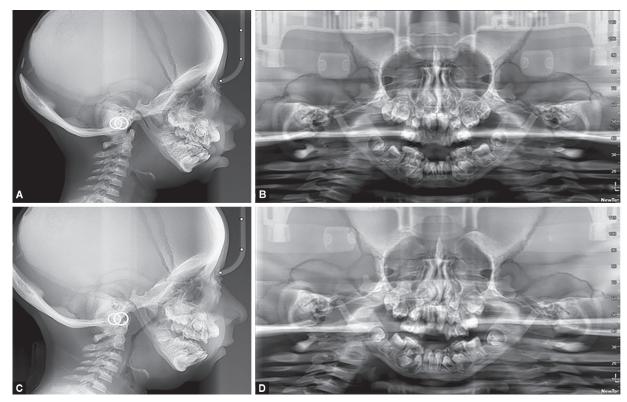
DISCUSSION

The term "pycnodysostosis" has been derived from Greek words—"pycnos" (dense), "dys" (defect), and "osteon" (bone).⁵ It is a rare genetic disorder that has been reported in patients ranging





Figs 6A and B: Oral appliance fabricated for mandibular advancement to enhance oropharyngeal volume



Figs 7A to D: Case 1, radiographs (A and B) Pretreatment; (C and D) At 1.5 years follow-up

from the age of 9 months up to an adult of 77 years of age.^{4,10} The prevalence has been estimated to be 1–1.7 per million with equal sex predilection affecting different ethnicities with approximately 200 cases reported till date in the medical literature.³ Most of the cases have been reported from Asian (39.3%), European (27.7%), and South American (16.6%) continents. Brazil, followed by India and Israel, is the most commonly affected country worldwide.¹¹

Parental consanguinity has been recognized as a cause of this autosomal recessive disorder¹² with underlying molecular mutation in the CTSK gene which maps to chromosome 1q21. Commonly occurring mutational hotspots are Arg241 in exon 6 and Ala277 in exon 7, both being located in the mature domain of CTSK. CTSK is a cysteine protease that plays an important role in osteoclast-mediated bone

resorption. Impaired enzymatic activity fails to degrade the organic matrix proteins, thereby resulting in increased volume and density of brittle bone with enhanced susceptibility to pathologic fractures.²

Currently, there are no specific guidelines in the literature to meet the aesthetic and functional demands of these patients. Since orthodontic and/or orthopedic treatment is entirely based on osteoclastic activity and associated bone remodeling, the efficacy as well as safety of these procedures is an issue of debate.

OSA is a common finding in children with PKND, which may occur due to obstruction at three levels, i.e., nasopharynx, oropharynx, and hypopharynx, each of which requires specific treatment.¹³ These patients must be diagnosed for OSA during the early childhood, since early intervention results in improved

Fig. 8: PSG report at follow-up

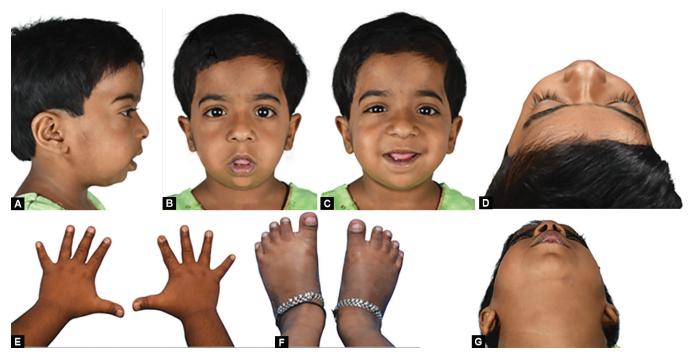
28

SLEEP APNEA REPORT

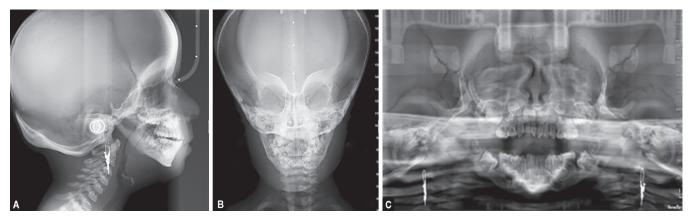
	Patient Information	rmation				
Name R h	Age 8.	8.5	Interp Phys			
	1		D. Contradio			
BUI 23.8		- 00	Technician			
			manual			
Polysomnography was conducted on the night	n the night of 12-06-2021.	The followin	g were montored ce	The following were montored certral and occipital EEG.		
electrococulogram (EOG) submertalis EMG, rasal and oral airflow, thoracic and abdominal wallmotion, arterior tibialis EMG, body	EMG, rasal and oral airflow, t	thoracic and a	ibdominal wall motion, a	Interior tibials EMG, body		
postion and electrocardiogram. Attental oxygen saturation was economic another Historican events economical Advintation	al orygen sauration was more	ntored with a	pulse oximeter. The tra	ong was scored using 30		
me a su seaudodí u suppla numas	incritication model and and					1
	Sleep Summary	Ammu				
Lights Out:	10:00:01	Stage	Duration	% TST		
Lights On:	07:30-01	ž	35 0 min	7.1%	Respiratory Summary by Body Position	
		1			Ru Rodu Dockiew Rack Laft Richt Denes Total Rack Laft Richt Denes Total	
10031 Mecording 11me:	um0.0/0	ZN	Um 0.001	1.0%		
Total Sleep Time (TST):	490.5 min	N3	350.0 min	71.4%		•
Steen Period Time:	560.0 min	α	0 0 min	0.0%		11
						1
Sieep Onset:	10:10:01				0.0 0.0 0.0 0.0 RDI, REM 0.0 0.0 0.0	
Sleep Efficiency:	S6.1%	Latenci	es From Lights Out	From Sleep Onset	A 1.8 0.0 5.9 1.9 2.6 RDI,NEM 11.2 7.8 12.6	ġ
Steen I steery from I Off-	10 0 min	IN I	L	0.0 min	0.0 5.9 1.9 2.6 RDI, Total 11.2 7.8 12.6 10.1	ņ
					Duration (min) 307.0 19.7 63.7 83.8 560.0 TST (min) 225.8 10.7 55.7 60.4 570.0	000
K Latency (from Skep Onset):	K N	ZN	10.0 min	umo.o		Γ
Wake After Sleep Onset (WASO):	69.5 min	N3	11.0 min	1.0 min	Heart Rate Summary	
Wake During Sleep:	69.5 min	α	NIA	NIA	Average Heart Rate During Sieed	
Total Webs Total	70 K min					
I OLGI VIAKE I ITTE.	um o.c.					
% Wake Time:	14.0					
					RESPIRATORY PARAMETERS	
	Respiratory Summ	Summary				
By Event Classification	Central	W	Mixed	Obstructive	Respiratory channels showed a total of 116 events. Those events included	
Count	t Mean Max	Count N	Mean Max Count	t Mean Max	95 Obstructive annea and 21 Hynomeas. 0 Mixed and 0 Central events	
Apreas, NREM	0.0 0.0		0.0 0.0	14.5 54.0		
Access DEM					The Appeal hypophea index was 14.2 per nour.	
Apneas, Total	0.0 0.0	•	0.0 0.0	14.0 04.0	A total of 490.5 min of the total sleep time.	
	"Hypopneas scored based on 0%	lon 0% or gr	or greater desaturation.			
Hypopneas, NREM 21	18.2 46.0	œ	RERAS, NREM 0	0.0 0.0		
Hypopneas, REM		œ	RERAS, REM			
Hypopneas, Total 21	18.2 46.0	œ	RERAs, Total 0	0.0 0.0	The Lowest oxyhemoglobin saturation was 58 %	
Event Statistics	Total		Weh Arousal		NI CULCTIC II III ECCLON.	
	Count Index		Count	Index	DLAGNOSTIC EMPRESSION:	
Access Total		1			0BSTRUCTIVE SLEEP APNEA AND HYPOPNEA SYNDROME (OSA)	
Disconces Total			2 0		Severity Criteria: Severe, AHI 14.2 of with nadir oxygen of 58%.	
mypopheas, rotai	0.7		0			
Apnea + Hypopnea Total	116 AHI: 14.2		51	6.3		
Apnea + Hypopnea NREM	116 AHI: 14.2			6.2		
Aonea + Hypoonea REM	AHI: N/A	Г		0.0		_
RERAS Total	00	I	c	00		
Tetal Control / A. U. DCDA/ Tetal	001140	Γ				
		Т	-			
Total Events (A+H+RERA) NREM	116 RDI: 14.2		8.	7.0		
Total Events (A+H+RERA) REM	RDI: N/A		0	0.0	Total Time with Smoring: 32.7 min (0.7% of sleep)	



Airway parameter	Description	Normal value (for male)	Pretreatment	At follow up
Nasopharyngeal airway space (NAS)	Measured from PNS to upper pharyngeal wall along palatal plane	25.9 <u>±</u> 2.6 mm	5.2 mm	6.2 mm
Superior pharyngeal airway space (SAS)	A horizontal distance from the tip of the soft palate to pharyngeal wall	9.9 ± 2.8	5.5 mm	6.4 mm
Oropharyngeal airway space (PAS)	A horizontal distance from the posterior margin of the tongue to pharyngeal wall measured on Go-B line	10.1 ± 3.1	1.7 mm	2.4 mm
Hypopharyngeal airway space (HAS)	Minimum horizontal distance in the hypopharyngeal area measured from point V (intersection of tongue and epiglottis)	18.71 ± 2.6	1 mm	3.2 mm



Figs 9A to G: Case 2, (A to E) Facial assessment; (F) Short stubby digits with dysmorphic nails; (G) Sandal foot deformity

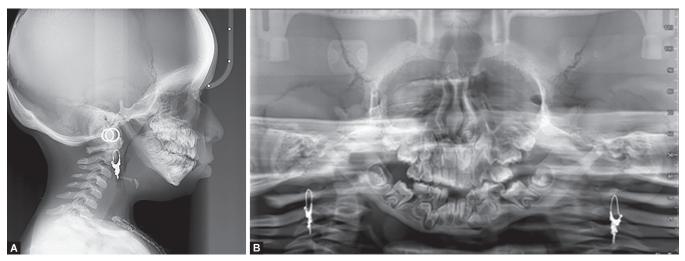


Figs 10A to C: Case 2, pretreatment radiographs (A) Lateral cephalogram; (B) Posteroanterior cephalogram; (C) Orthopantomogram

ventilation, which has a positive influence on the growth and development of craniofacial complex. Muto et al.¹⁴ suggested respiratory insufficiencies in forms of snoring or OSA as a common and underappreciated feature of PKND due to retrognathia leading

to glossoptosis and consequently narrowing of the airway space. Similar findings have been reported by various other authors.^{15,16}

OSA resulting from nasal obstruction may be due to nasal polyp, deviated nasal septum, or hypertrophied inferior turbinates.¹³



Figs 11A and B: Case 2, radiographs at 1.5 years-follow-up (A) Lateral cephalogram; (B) Orthopantomogram

Airway parameter	Description	Normal value (for female)	Pretreatment	At follow up
Nasopharyngeal airway space (NAS)	Measured from PNS to upper pharyngeal wall along palatal plane	$24.1\pm2.3~\text{mm}$	6.8 mm	7.2 mm
Superior pharyngeal airway space (SAS)	A horizontal distance from the tip of the soft palate to pharyngeal wall	$9.9 \pm 2.4 \text{ mm}$	4.5 mm	5.4 mm
Oropharyngeal airway space (PAS)	A horizontal distance from the posterior margin of the tongue to pharyngeal wall measured on Go-B line	10.0 ± 2.8 mm	2.8 mm	3.9 mm
Hypopharyngeal airway space (HAS)	Minimum horizontal distance in the hypopharyngeal area measured from point V (intersection of tongue and epiglottis)	16.5 ± 3.1 mm	12.3 mm	12.5 mm

Table 3: Airway analysis (lateral cephalogram) for case 2

Adenoid hypertrophy, being relatively more common in children, can be managed with adenoidectomy or conservatively with a pharmacological approach, which was in both of our cases. Oropharyngeal obstruction resulting from tonsillar hypertrophy can be managed with tonsillectomy,¹³ while the problem of long soft palate can be catered with uvulopalatopharyngoplasty,¹⁷ laser-assisted uvulopalatoplasty,¹⁸ or radiofrequency tissue ablation.¹⁹

Based on the severity of skeletal malocclusion, respiratory insufficiency due to hypoplastic maxilla and mandible can be managed with DO. However, due to frequently associated risk factors, such as pathologic fractures and maxillary osteomyelitis,²⁰ oral appliance therapy, which advances the mandible and tongue thereby increasing the oropharyngeal volume, was adopted in our first case. Both the patients are on periodic follow-up of every 3 months.

Besides the interceptive approach, special emphasis must be given to preventive dentistry since most of the PKND children present with poor oral hygiene, extensive dental caries, and generalized gingivitis or periodontitis. Periodic dental visits for topical fluoride application and enforcement of good oral hygiene are extremely important.

CONCLUSION

30

Respiratory needs are the primary determinants of an individual since the first day of life, which has a great influence on craniofacial growth and development as well as systemic wellbeing of an individual. Although PKND is a rare genetic disorder, many case reports are available in the literature highlighting the different aspects of the medical and dental condition. Although OSA is a frequently encountered feature among patients with PKND, the same has not been highlighted and addressed in the literature. Altered bone physiology among these patients along with poor oral hygiene and compromised dental condition poses great challenge to an orthodontist. A multidisciplinary approach with emphasis on preventive care is advocated, and a long-term follow-up is required for these patients.

ORCID

Dhruv Jain ⁽ⁱ⁾ https://orcid.org/0000-0003-1387-6768

REFERENCES

- 1. Bizaoui V, Michot C, Baujat G, et al. Pycnodysostosis: natural history and management guidelines from 27 French cases and a literature review. Clin Genet 2019;96(4):309–316. DOI: 10.1111/cge.13591.
- Xue Y, Cai T, Shi S, et al. Clinical and animal research findings in pycnodysostosis and gene mutations of cathepsin K from 1996 to 2011. Orphanet J Rare Dis 2011;6(1):1–10. DOI: 10.1186/1750-1172-6-20.
- LeBlanc S, Savarirayan R. Pycnodysostosis. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews[®] [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021 [Accessed July 19, 2021]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563694/.
- Muto T, Mishia H, Taira H, et al. Pyknodysostosis. Report of a case and review of Japanese literature, with emphasis on oral and maxillofacial findings. Oral Surg Oral Med Oral Pathol 1991;72(4):449–455. DOI: 10.1016/0030-4220(91)90559-u.

- 5. Maroteaux P, Lamy M. Pyknodysostosis. Presse Med 1962;70: 999-1002. PMID: 14470123.
- 6. Gelb BD, Moissoglu K, Zhang J, et al. Cathepsin K: isolation and characterization of the murine cDNA and genomic sequence, the homologue of the human pycnodysostosis gene. Biochem Mol Med 1996;59(2):200-206. DOI: 10.1006/bmme.1996.0088.
- 7. Polymeropoulos MH, Ortiz De Luna RI, Ide SE, et al. The gene for pycnodysostosis maps to human chromosome 1cen-q21. Nat Genet 1995;10(2):238-239. DOI: 10.1038/ng0695-238.
- 8. Gelb BD, Edelson JG, Desnick RJ. Linkage of pycnodysostosis to chromosome 1q21 by homozygosity mapping. Nat Genet 1995;10(2):235-237. DOI: 10.1038/ng0695-235.
- 9. Ortegosa MV, Bertola DR, Aguena M, et al. Challenges in the orthodontic treatment of a patient with pycnodysostosis. Cleft Palate Craniofac J 2014;51(6):735-739. DOI: 10.1597/12-233.
- 10. Elmore SM. Pyknodysostosis: a review. J Bone Joint Surg 1967; 49(1):153-162. https://scholar.google.com/scholar_lookup? journal=J+Bone+Joint+Surg+Am&title=Pycnodysostosis: +A+review&author=SM+Elmore&volume=49&publication_year= 1967&pages=153-62&.
- 11. Rodrigues C, Gomes FA, Arruda JA, et al. Clinical and radiographic features of pycnodysostosis: a case report. J Clin Exp Dent 2017;9(10):e1276-e1281. DOI: 10.4317/jced.54105.
- 12. Elmore SM, Nance WE, Macgee BJ, et al. Pyknodysostosis with a familial chromosome anomaly. Am J Med 1966;40(2):273-282. DOI: 10.1016/0002-9343(66)90108-2.

- 13. Ephros HD, Madani M, Yalamanchili SC. Surgical treatment of snoring and obstructive sleep apnoea. Indian J Med Res 2010;131:267-276. PMID: 20308752.
- 14. Muto T, Yamazaki A, Takeda S, et al. Pharyngeal narrowing as a common feature in pycnodysostosis—a cephalometric study. Int J Oral Maxillofac Surg 2005;34(6):680-685. DOI: 10.1016/ j.ijom.2004.10.024.
- 15. Ikizoglu NB, Gokdemir Y, Turan S, et al. Sleep disordered breathing in pycnodysostosis patients. Eur Respir J 2014;44(58):2277. https:// erj.ersjournals.com/content/44/Suppl_58/P2277.
- 16. Khirani S, Amaddeo A, Baujat G, et al. Sleep-disordered breathing in children with pycnodysostosis. Am J Med Genet A 2020;182(1): 122-129. DOI: 10.1002/ajmg.a.61393.
- 17. Fujita S, Conway W, Zorick F, et al. Surgical correction of anatomic abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 1981;89(6):923-934. DOI: 10.1177/019459988108900609.
- 18. Kamami YV. Laser CO₂ for snoring: preliminary results. Acta Oto-Rhino-Laryngol Belg 1990;44(4):451-456. PMID: 2128762.
- 19. Ellis P, Williams JE, Shneersan J. Surgical relief of snoring due to palatal flutter: a preliminary report. Ann R Coll Surg Engl 1993;75(4):286–290. PMID: 8379635.
- 20. Norholt SE, Bjerregaard J, Mosekilde L. Maxillary distraction osteogenesis in a patient with pycnodysostosis: a case report. J Oral Maxillofac Surg 2004;62(8):1037-1040. DOI: 10.1016/ j.joms.2004.02.012.