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Supplementary material

Supplement to: Y Cao, YKY Cheng, TY Leung, et al. Early prenatal detection of autosomal dominant skeletal dysplasia using first-trimester ultrasound and cell-free fetal DNA screening: three case reports. Hong Kong Med J 2026;Epub 28 Jan 2026. https://doi.org/10.12809/hkmj2513462.

SUPPLEMENTARY TABLE 1. Genetic conditions included in COATE-seq based comprehensive non-invasive prenatal screening

Aneuploidies	**Microdeletions**	**Monogenic disorders**					
Trisomy 21	22q11.2	*ASXL1*	*EFNB1*	*KAT6B*	*NSD1*	*SMC1A*	*TSC1*
Trisomy 18	1p36	*BRAF*	*ERF*	*KMT2D*	*NSDHL*	*SMC3*	*TSC2*
Trisomy 13	2q33	*CBL*	*FBN1*	*KRAS*	*PKD1*	*SNRPB*	*TWIST1*
Trisomy 15	4p16	*CD96*	*FGFR1*	*LMNA*	*PKD2*	*SOS1*	*ZIC1*
Trisomy 16	5p15	*CDKL5*	*FGFR2*	*MAP2K11*	*PTPN11*	*SOS2*	
Trisomy 22	8q23q24	*CHD7*	*FGFR3*	*MAP2K2*	*RAD21*	*SOX9*	
45,X	9p	*COL10A1*	*FLNB*	*MECP2*	*RAF1*	*SPECC1L*	
47,XXX	11q23q25	*COL11A1*	*FREM1*	*MSX2*	*RIT1*	*STAT3*	
47,XXY	15q11.2-q13	*COL1A1*	*GLI3*	*NF1*	*RUNX2*	*TCF12*	
47,XYY	18p	*COL1A2*	*HDAC8*	*NF2*	*SHOC2*	*TGFBR1*	
	18q22q23	*COL2A1*	*HNRNPK*	*NIPBL*	*SKI*	*TGFBR2*	
	17p11.2	*EBP*	*HRAS*	*NRAS*	*SLC25A24*	*TRAF7*	

Abbreviation: COATE-seq = coordinative allele-aware target enrichment sequencing

SUPPLEMENTARY TABLE 2. Ultrasound features and genetic findings of reported cases of prenatally detected cleidocranial dysplasia

Publication	**Affected family members**	**GA**	**Clavicles**	**Cranium**	**Nasal bone**	**Long bones**	**Spine and others**	**Post-delivery additional findings**	**Genetic findings**
Hamner et al[1]	Mother Grandmother	15.4	Absent	-	-	-	-	Large fontanelles Wide sutures	NA
Bowerman[2]	Mother Multiple members	15	-4 SD	-	-	-2 SD	-		NA
Hassan et al[3]	Mother*	19	Markedly shortened	Abnormal ossification	-	<5%	-	Large fontanelles Wide sutures	46,XX
Stewart et al[4]	Father Brother	14.6	Short	Poorly ossified	-	-	-	Extremely wide and communicating fontanelles Opened sutures	NA
Paladini et al[5]	Mother*	37	Hypoplastic	Hypomineralised	-	<5%	-	-	NA
Winer et al[6]		24	Poorly ossified	Very poorly ossified	-	<3%	Iliac wings hypoplasia	-	De novo balanced translocation 46,XY, t(2q:6q)(q36;q16)
Chen et al[7]		20	-	-	Absent	10%	-	Absent clavicles Large fontanelles Wide sutures Skull	46,XX

								hypomineralisation	
Zheng et al[8]		19	Absent	Hypomineralised	-	Smaller by 1 week	-	-	*RUNX2*, c.1228dupC, p.Leu410fs, heterozygous, de novo
Soto et al[9]	Mother* Sister	18.4	Fractured	Hypomineralised Absent squamous temporal bone Wide sutures	Absent	-	-	Open and communicating fontanelles	46,XX *RUNX2* gene sequencing negative
Hove et al[10]	Mother Sister Grandfather (*RUNX2* negative)	13.9	Barely seen	Severe delayed ossification	-	Short femur	Severe delayed ossification	-	NA
Hermann et al[11]	Mother 3 generations (*RUNX2* negative)	15.6	Short	Severe delayed Ossification Large fontanelle	Absent	5%	-	-	NA
Broeks et al[12]		T2	-	Incomplete mineralisation	-	-	-	Clavicles aplasia and hypoplasia Pubic bones delayed	*RUNX2* gene heterozygous nonsense mutation at nucleotide 1113 in

								ossification	exon 7
Waelti et al[13]	Half brothers	24	Hypoplastic	Large fontanelle Wide sutures	Absent	-	-	-	*RUNX2* gene mutation
Delgado et al[14]	Mother Grandfather Great grandfather	20	Hypoplastic	Large fontanelle Wide sutures	Absent	-	-	-	NA
Dufke et al[15]		23	Short	Large sutures	Absent	Short femur	-	-	*RUNX2* c.1208dup, p.Val404Serfs*86 heterozygous, de novo
Moczulska et al[16]	Mother	19	Short	-	Hypoplasia	Short	-	-	CMA normal
Roy and Dey[17]		16	Short	-	-	-	Rudimentary cervical rib	Wide fontanelle and sutures Pubic and ischial bones delayed ossification	~1Mb microdeletion at 6p21.2p12.3 involving *RUNX2* gene arr[GRch37] 6p21.2p12.3(37,520, 993 48,467,869)x1
Han et al[18] Case 1		13.3	-	Poorly ossified	Absent	<10%	Poorly ossified	-	*RUNX2,* c.931_946del, p.Thr311fs
Han et al[18] Case 2		32	Poorly ossified	Inadequate ossification	Absent	-	-	-	*RUNX2,* c.911-914delinsTTT

Present study Case 1		12	-	Non-ossified parietal bone	Absent	Short	11 pairs of ribs	Absent clavicles	*RUNX2* , c.674G>A, p.Arg225Gln, heterozygous, de novo
Present study Family 2: Case 2	Father* Grandfather Aunt	12	Mildly shortened	Non-ossified (normal from 16 weeks) Widened sutures	-	-	Reduced ossification (normal from 16 weeks)	11 pairs of ribs	NIPS: high risk of *RUNX2* gene pathogenic c.577C>T, p.Arg193Ter, heterozygous. Confirmed by Sanger sequencing
Present study Family 2: Case 3	Father Grandfather Aunt Brother	12	Hypoplastic	Non-ossified Wide sutures and fontanelle	Thin	Mildly shortened	Reduced ossification 11 pairs of ribs	-	NIPS: high risk of *RUNX2* gene pathogenic c.577C>T, p.Arg193Ter, heterozygous. Confirmed by Sanger sequencing
Total (22 cases)	**Familial: 13 (59%) De novo: 9 (41%)**	**T1: 5 (23%) T2: 17 (77%)**	**18 (82%)**	**17 (77%)**	**11 (50%)**	**13 (59%)**			***RUNX2*-related: 10 (45%) *RUNX2* negative: 3 (14%) Others: 1 (5%)**

* Affected family member discovered after fetal presentation

Abbreviations: GA = gestational age at presentation; NA = not available; NIPS = non-invasive prenatal screening; *RUNX2*: NM_001024630.4; T1 = first trimester; T2 = second trimester

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