Supplementary

Supplementary Table S1. Classification and interpretation of the genetic variants identified in the present case.

Variant	**Classification**	**Somatic variant interpretation criteria (ComPerMed/AMP-ASCO-CAP framework)**	**ACMG classification criteria**
IDH1; c.394C>T; p.(Arg132Cys)	Pathogenic	Oncogenic hotspot, ComPerMed Consensus Pathogenic Variants list (CPV), tumour recurrence (>500 COSMIC entries), Pathogenic in ClinVar, deleterious missense prediction tools; REVEL score: 0.814.	PM1_Moderate; PM2_Moderate; PP3_supporting; PP5_Supporting
DNMT3A; c.2645G>A; p.(Arg882His)	Pathogenic	Oncogenic hotspot, ComPerMed Consensus Pathogenic Variants list (CPV), tumour recurrence (>1000 COSMIC entries), Pathogenic in ClinVar, deleterious missense prediction tools; REVEL score: 0.742.	
CEBPA; c.619C>T; p.(Gln207*)	Likely pathogenic	Clear loss-of-function (LOF) variant: premature stop codon in Tumour Suppressor Gene	
CEBPA; c.230del; p.(Phe77Serfs*83)	Likely pathogenic	Clear loss-of-function (LOF) variant: frameshift and premature stop codon in Tumour Suppressor Gene	
EZH2; c.1876G>A; p.(Val626Met)	Likely pathogenic	Tumour recurrence (>10 COSMIC entries); Pathogenic in ClinVar; deleterious missense prediction tools; REVEL score: 0.817.	

Supplementary table S2: Methodological characteristics and molecular results for the detection of the *IDH1* c.394C>T; p.(Arg132Cys) variant across the different tissues analysed.

Sample	**Molecular assay**	**Depth at *IDH1* c.394C>T**	**Limit of detection (LOD)**	**Variant allele frequency (VAF)**	**Notes**
Bone marrow at AML diagnosis	Targeted NGS (AML gene panel; SOPHiA Genetics), MiSeq (Illumina)	3,411×	2%	37%	Diagnostic AML sample
Enchondroma 1	ddPCR (*IDH1* c.394C>T Variant Detection Assay)	Not available	1%	41%	
Enchondroma 2	ddPCR (*IDH1* c.394C>T Variant Detection Assay)	Not available	1%	Inconclusive	Insufficient DNA for reliable analysis
Parathyroid adenoma	Targeted NGS (thyroid gene panel; SOPHiA Genetics), MiSeq (Illumina)	5,487×	6%	44%	
Skin biopsy DNA	Targeted NGS (HaloPlex panel; Agilent), MiSeq (Illumina)	7,420×	5%	3%	Low-level variant signal below the validated limit of detection; not considered a confirmed positive result
Cultured skin fibroblasts	Whole-exome sequencing (SureSelect Human All Exon v6; Agilent), NovaSeq (Illumina)	Not available	30–50%	Not detected	Fibroblast culture removes contaminating blood cells that may be present in the original skin biopsy, which may explain the absence of the low-level signal observed in biopsy DNA. Whole-exome sequencing is not designed to detect low-level mosaic variants
Peripheral blood after HSCT	Not analysed				Not suitable for constitutional testing because haematopoiesis was donor-derived following allogeneic HSCT

Table S3. Clinical spectrum of patients with mosaic *IDH1* p.Arg132Cys variant

Nejo et al. (2019)	Male	Maffucci syndrome	Adulthood (age not specified in available data)	Maffucci syndrome with adenoma, diffuse astrocytoma, and chondrosarcoma	*IDH1* p.(Arg132Cys) detected in pituitary adenoma, diffuse astrocytoma and clival chondrosarcoma; blood negative	NR	One of the strongest demonstrations of p.(Arg132Cys) mosaicism affecting multiple independent tissues. Shows that absence of pathogenic variant in blood does not exclude widespread tissue mosaicism.
Al Rumeh et al. (2020)	Male	Ollier disease history	Glioma diagnosed at 23 years	Ollier disease associated diffuse astrocytoma	*IDH1* p.(Arg132Cys) detected in astrocytoma tissue	NR	Supports association between p.(Arg132Cys) mosaicism and glioma development in Ollier disease.
Srinivasan et al. (2020)	Male	Early childhood metaphyseal chondromatosis with D-2-hydroxyglutaric aciduria	3 years (AML presentation)	*IDH1*-associated enchondromatosis phenotype with D-2-hydroxyglutaric aciduria	*IDH1* p.(Arg132Cys) detected in AML cells (and reported in association with cartilage phenotype)	Elevated	First report linking p.(Arg132Cys) mosaicism with AML and increased D-2HG levels. Highly relevant to present case because of overlap between haematological malignancy and *IDH1*-driven metabolic phenotype.
Govalan et al. (2021)	Male	Ollier disease history	29 years	Ollier disease with liver tumour	*IDH1* p.(Arg132Cys) detected in liver tumour tissue	NR	Suggests that p.(Arg132Cys) mosaicism may predispose to rare visceral neoplasms such as liver tumour.
Littrell et al. (2022)	Female	Ollier disease during childhood	Juvenile granulosa cell tumour diagnosed at 15 years	Ollier disease associated juvenile granulosa cell tumour	*IDH1* p.(Arg132Cys) detected in ovarian tumour tissue	NR	Further illustrates ovarian tumour susceptibility in patients carrying p.(Arg132Cys) mosaicism.

Haiyan Lv et al. (2022)	Male	Maffucci syndrome diagnosed at 19 years	Chondrosarcoma diagnosed at 45 years	Maffucci syndrome with chondrosarcoma	*IDH1* p.(Arg132Cys) detected in chondrosarcoma tissue, absent from blood	NR	Documents tumour-restricted mosaicism and malignant transformation driven by p.(Arg132Cys) variant clones.
Zhang et al. (2023)	Female	Ollier disease during childhood	Juvenile granulosa cell tumour diagnosed at 4 years	Ollier disease associated juvenile granulosa cell tumour	*IDH1* p.(Arg132Cys) detected in both ovarian juvenile granulosa cell tumour and enchondroma	NR	Demonstrated identical p.(Arg132Cys) variant in cartilage and ovarian tumour, supporting a common embryonic mosaic clone and expansion beyond skeletal tissues.
Watanabe et al. (2024)	Male	Ollier disease diagnosed at 1 year	Multiple gliomas diagnosed at 15 years	Ollier disease with multiple gliomas	*IDH1* p.(Arg132Cys) detected in multiple gliomas	NR	First detailed p.(Arg132Cys) Ollier case with malignant transformation of gliomas. Highlights that the variant may predispose to both cartilage and CNS neoplasms.
Devins et al. (2024)	Female	Ollier disease during childhood	Ovarian tumour diagnosed at 10 years	Ollier disease with ovarian sex cord stromal tumour	*IDH1* p.(Arg132Cys) detected in ovarian tumour by NGS	NR	Expands p.(Arg132Cys) associated tumour spectrum to ovarian mesenchymal tumours.
Amary et al. (2011)	Cohort: Not individually reported	Not individually reported	Not available	Ollier disease and Maffucci syndrome	Enchondromas ± chondrosarcomas and soft tissue haemangiomas	Increased in tumour tissue in 4 participants	40 subjects (19 with tumour samples available). One subject developed brain tumour. p.(Arg132Cys) represented ~65% of variants with *IDH1* alteration.
Pansuriya et al. (2011)	Cohort: Not individually reported	Not individually reported	Not available	Ollier disease (n=43), Maffucci syndrome (n=13)	Enchondromas, chondrosarcomas	NR	*IDH1* p.(Arg132Cys) was the predominant *IDH1* variant.

					and spindle cell haemangiomas		
Chen et al. (2022)	Cohort: 5 patients (3 females, 2 males)	Childhood to early adulthood (individual data available but heterogeneous)	Variable	Ollier disease (n = 3) and Maffucci syndrome (n = 2)	Enchondromas, chondrosarcomas, spindle cell haemangiomas, ovarian juvenile granulosa cell tumour, ovarian serous cystadenoma, breast carcinoma†	NR	Single-institution clinicopathological series demonstrating identical *IDH1* p.(Arg132Cys) variants across multiple neoplastic lesions within the same patients, supporting a common post-zygotic mosaic origin and expanding the tumour spectrum beyond cartilage.
Present case	Female	Ollier disease diagnosed at 11 years	AML and parathyroid adenoma diagnosed at 18 years	Ollier disease with AML and parathyroid adenoma	*IDH1* p.(Arg132Cys) detected in enchondroma, AML and parathyroid adenoma	Elevated urinary D-2HG	First reported case demonstrating the same *IDH1* p.(Arg132Cys) variant in enchondroma, acute myeloid leukaemia and parathyroid adenoma. This case further expands the recognised tumour spectrum associated with post-zygotic *IDH1* p.(Arg132Cys) mosaicism.