BCOR AND *TP53*-MUTATED CONVENTIONAL AND DEDIFFERENTIATED CHONDROSARCOMA: A CLINICOPATHOLOGIC STUDY

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INTRODUCTION

- Chondrosarcomas (CSAs) are a heterogeneous group of malignant neoplasms that arise within or on the surface of bone.
- *IDH1/2, COL2A1, and TP53* are the most commonly mutated genes in conventional chondrosarcomas (CCSA) and dedifferentiated chondrosarcomas (DCSA).
- One case of grade 2 CCSA with standalone *BCOR* mutation and aggressive clinical behavior was the impetus for this study.
- Mutations in *BCOR* are frequently acquired in other *IDH* driven neoplasms and it is unclear if they contribute to IDH inhibitor resistance.
- Recently, *TP53* mutations in CSA were shown to be associated with worse clinical outcome.
- Mutations of *BCL-6* transcriptional corepressor (*BCOR*) gene have been rarely described in CCSA or DCSA; the goal of this study is to describe the clinicopathological features of *BCOR*-mutated CSA.

DESIGN

- We interrogated the surgical pathology archives for CCSA and DCSA between 2019 and 2023 that underwent genomic analysis.
- All cases were sequenced using a commercial NGS panel (CARIS Life Sciences, Irving, Texas).
- Frequentist statistics were performed to stablish association between the presence of *BCOR* and *TP53* mutations and histological tumor grade, involvement of non-appendicular skeleton, T stage, mean tumor size and presence of metastases at diagnosis.

RESULTS

- A total of 27 cases of CCSA and DCSA were identified. Twelve and nine cases, harbored mutations of *BCOR* and *TP53,* respectively. Both genes were mutated in 4 cases. One case harboring *BCOR* mutation and *FN1::ACVR2A* fusion was excluded.

Table 1 Clinicopathological findings

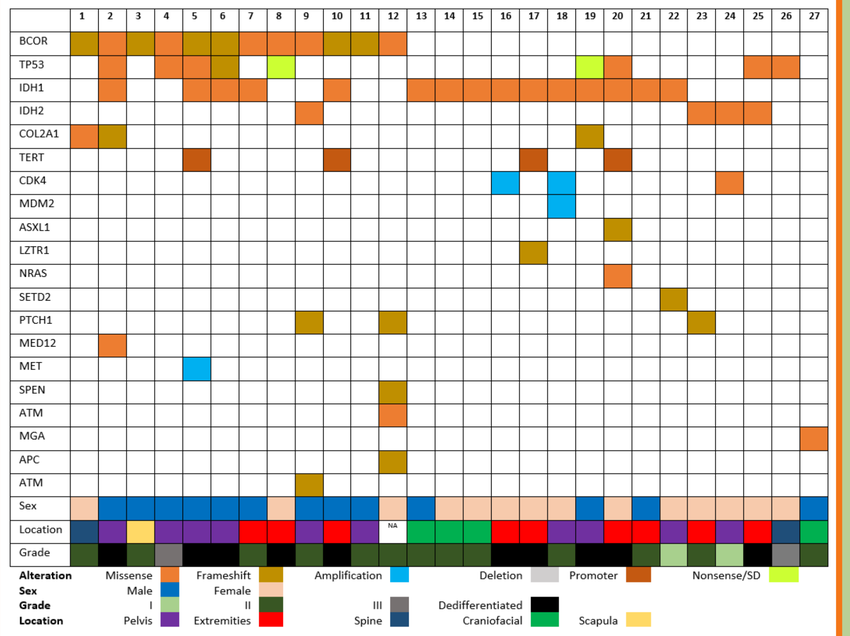
	BCOR MUT		BCOR WT		TP53 MUT		TP53 WT	
	n	%	n	%	n	%	n	%
Number of cases	12	-	15	-	9	-	18	-
M/F ratio	3	-	0.44	-	1.25	-	0.8	-
Mean age	55	-	55	-	55	-	55.5	-
CCSA Grade I	-	-	2	13	-	-	2	11
CCSA Grade II	6	50	7	47	-	-	13	72
CCSA Grade III	1	8	1	7	2	23	-	-
Dedifferentiated	5	42	5	33	7	77	3	17
Location								
Pelvis	6	50	4	27	5	56	5	29
Extremities	3	25	6	40	3	33	6	35
Spine	1	8	1	6	1	11	1	6
Craniofacial	-	-	4	27	-	-	4	24
Scapula	1	8	-	-	-	-	1	6
Metastasis at presentation	7/9	78	4/15	27	5/9	55	6/15	40
Mean size (cm)	11.7 (8)	-	7.8 (12)	-	8.7 (7)	-	9.7 (13)	-

Table 2 Relevant statistical analysis results

	Estimate	Lower CI	Upper CI	p
BCOR				
Tumor size	3.92	0.59	7.24	0.024[a]
Metastasis	0.42	0.25	0.6	<0.001[b]
Dedifferentiation	0.08	-0.28	0.44	0.441
TP53				
Tumor size	0.23	-3.62	4.08	0.902
Metastasis	0.15	-0.25	0.56	0.564
Dedifferentiation	0.61	0.28	0.93	<0.001[b]

[a] Mean difference, [b] Proportion difference

Fig. A. Mutational landscape and relevant clinicopathological features of 27 cases of CCSA and DCSA.



CONCLUSIONS

- This is the first study to establish the biological significance of *BCOR* mutations in CCSA and DCSA.
- *BCOR* and *TP53* can be present as unique mutations or concurrent with other driver mutations.
- Missense and frameshift mutations of *BCOR* are the genetic alterations in CCSA and DCSA without internal tandem duplication or rearrangements as in other sarcoma types.
- *BCOR* mutations in CCSA and DCSA are associated with larger tumor size and metastases at diagnosis while *TP53* mutations herald dedifferentiation.

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