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BAP1 immunohistochemistry and p16 FISH in the diagnosis of malignant peritoneal mesothelioma

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Objective

Peritoneal malignant mesothelioma (PMM) is an un- common tumor, only 7-9% of all mesothelioma in Japan. Differential diagnosis between PMM and primary peritoneal serous carcinoma **(**PPSC), a high-grade serous carcinoma, may be difficult, and separating reactive mesothelial hyperplasia (RMH) from PMM can be even more challenging.

Methods

To help differentiate PMM from PPSC and RMH, we used immunohistochemistry to examine BAP1, and FISH to examine for homozygous deletion of p16, 9p21. We used formalin-fixed, paraffin-embedded blocks from 22 PMMs (M:F=18:4; subtypes: 16 epithelioid, 6 biphasic), 11 PPSCs, and 10 RMHs.

Results

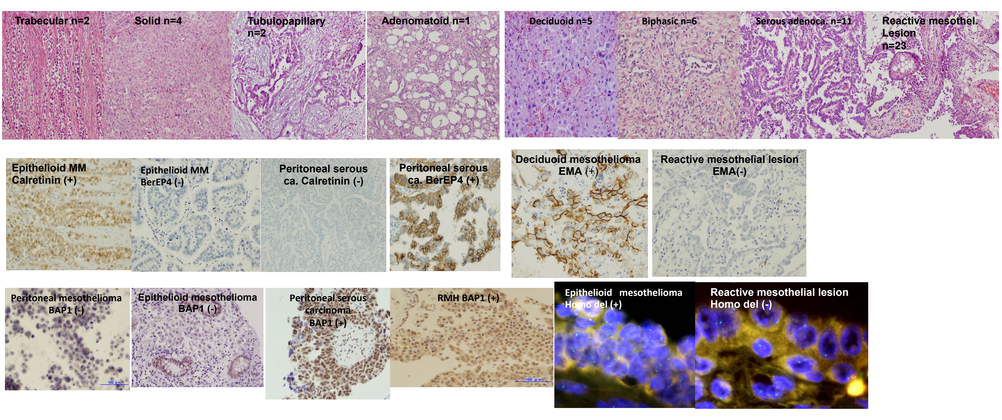
	calretinin	AE1/AE3	CK5/6	CAM5.2	D2-40	WT-1
Epithelioid PMM	16/16 (100%)	16/16 (100%)	15/16 (94%)	15/16 (94%)	14/16 (88%)	12/16 (75%)
Biphasic PMM	4/6 (67%)	6/6 (100%)	6/6 (100%)	6/6 (100%)	3/6 (50%)	3/6 (50%)
PPSC	0/11 (0%)	11/11 (100%)	8/11 (73%)	9/11 (82%)	3/11 (27%)	11/11 (100%)
Sensitivity	91%	100%	95%	95%	77%	68%
Specificity	100%	0%	27%	18%	73%	0%

	CEA	BerEP4	MOC31	ER	PgR
Epithelioid PMM	0	0	0	0	0
Biphasic PMM	0	0	0	0	0
PPSC	0	11/11 (100%)	8/11 (73%)	8/11 (73%)	3/11 (27%)
Sensitivity	0	100%	73%	73%	27%
Specificity	0	100%	100%	100%	100%

	EMA	Desmin	GLUT-1	CD146	IMP3	9p21del*	BAP1(-)
Epithelioid PMM	11/16 (69%)	1/16 (6%)	7/16 (44%)	4/16 (25%)	9/16 (56%)	8/10 (80%)	6/16 (38%)
Biphasic PMM	4/6 (67%)	0/6 (0%)	4/6 (67%)	1/6 (17%)	5/6 (83%)	3/3 (100%)	4/6 (67%)
RMH	0/23 (0%)	13/23 (57%)	0/23 (0%)	0/23 (0%)	1/23 (5%)	0/11 (0%)	0/10 (0%)
Sensitivity	68%	57%	50%	23%	64%	85%	45%
Specificity	100%	95%	100%	100%	95%	100%	100%

- At least 50 cells were scored for each case. Homozygous deletion was considered to be present if both 9p21 signals were lost in at least 20% of nuclei and at least one signal for the chromosome 9 copy number probe was shown in each nucleus.

Figures



Conclusions

BAP1 loss is not a sensitive test, although specificity is very high for differentiating PMM from both PPSC and RMH. Homozygous deletion of p16 may be helpful for differentiating PMM from RMH.

References

1. The prognostic significance of *BAP1, NF2*, and *CDKN2A* in malignant peritoneal mesothelioma. Singhi et al. Mod Pathol 2015 14-24
2. Peritoneal malignant mesothelioma, and primary peritoneal serous carcinoma and reactive mesothelial hyperplasia of thr peritoneum. Kawai et al. J Clin Pathol 2016;706-712