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Mesothelin as a marker of response in malignant pleural mesothelioma.

Background

Malignant pleural mesothelioma (MPM) is a rare malignancy related to asbestos exposure. Radiological assessment of disease status and treatment response using RECIST is often difficult, therefore blood markers of disease burden may be useful adjunctively. Soluble mesothelin related peptide (sMRP) can distinguish between MPM and benign pleural disease. We performed an exploratory analysis to determine whether sMRP correlates with MPM disease course.

Methods

From December 2006 to August 2008 blood samples were collected from MPM patients during clinic visits. Plasma sMRP levels were measured using the MESOMARK® assay (Fujirebio diagnostics). Changes in sMRP levels were compared with corresponding radiological tests, scored as progression, stable or disease shrinkage.

Results

From 41 patients, 165 samples were collected (median 4/patient; range 2-10). At study entry 34/37 (92%) patients with measurable disease had elevated sMRP (>9ng/ml, range 14–60). In 22 patients receiving chemotherapy or biologic therapy, relative (Fisher's exact test, $p=3.2 \times 10^{-6}$) and absolute ($p=2.6 \times 10^{-5}$) changes in sMRP correlated with radiological assessment (Table). All 4 post-surgery surveillance patients, with no evidence of

recurrence, had normal sMRP levels (1.8–4.9). Of 8 patients who underwent surgical resection, 7 had elevated pre-operative sMRP that fell to normal post-operatively (Wilcoxon rank (WR) $p=0.02$). Absolute sMRP rose in all patients with radiological progression (systemic therapy, $n=9$, WR $p=0.004$; supportive care, $n=10$, WR $p=0.02$).

Conclusion

sMRP levels not only correlate with surgical debulking but we report, for the first time, that they also correlate with treatment response and radiological progression in MPM patients undergoing systemic therapy or supportive care. sMRP may be a clinically useful biomarker in MPM clinical trials and in patient management. These findings should be validated prospectively.

Radiological assessment	Frequency of Relative ¹ (Absolute ²) Change in sMRP			Total
	Falling	Stable ³	Rising	
Progression	0 (0)	1 (2)	8 (7)	9
Stable	0 (0)	5 (6)	1 (0)	6
Response	6 (5)	0 (1)	1 (1)	7
Total	6 (5)	6 (9)	10 (8)	22

¹ Relative = $\geq 10\%$ change; ² Absolute = $\geq 5\text{ng/ml}$ change
³ Stable refers to any change in sMRP $< 10\%$ relative or $< 5\text{ng/ml}$ absolute

Key words

Mesothelioma, mesothelin, biomarker