AB052. SOH21AS116. Visceral fat as a tumour promotor: the role of adipose-derived factors in the immune-mediated chemoresistance of oesophageal adenocarcinoma

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Background: Visceral obesity is a key risk factor for development of oesophageal adenocarcinoma (OAC). Greater than 70% of OAC patients are resistant to chemoradiotherapy and the visceral fat has been implicated in therapy-resistance, via secretion of tumour-promoting mediators into the periphery enhancing OAC cell survival/growth. This study investigates the effect of the secretome from visceral fat of OAC patients on chemo-sensitivity and anti-tumour T-cell immunity, with potential implications for therapy resistance.

Methods: The effect of visceral adipose conditioned media (ACM) on OAC cell viability and FLOT-chemotherapy induced-toxicity was assessed by crystal violet assay (n=16). The effect of ACM on immune checkpoint (IC) expression was also assessed on OAC cells and T-cells by flow cytometry (n=20). Anti-tumour cytokine profiles (IFN-γ, TNF-α and IL-2), cytotoxicity (CD107a), activation markers (CD27, CD69) and T-cell subsets (naïve, effector and central memory) were also investigated following treatment with ACM by flow cytometry (n=12).

Results: ACM increased OAC cell growth and decreased the toxicity of FLOT (P<0.05). Anti-tumour cytokine production was enhanced following treatment with ACM, however, ACM generated from patients with early-stage tumours enhanced T-cell cytotoxicity more substantially than ACM generated from patients with advanced tumours. Markers of T cell activation were decreased and ICs were increased by ACM generated from patients with more advanced stage tumours.

Conclusions: The visceral fat from OAC patients protected OAC cells from FLOT chemotherapy via secretion of soluble mediators. ACM from patients with more advanced stage tumours exhibited a more immunosuppressive profile highlighting the role of the tumour in subverting distal organs toward a tumour-promoting milieu.

Keywords: Visceral fat; adipose tissue; oesophageal adenocarcinoma immunosuppression; chemoresistance

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/map-21-ab052). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/map-21-ab052