Circulating tumour cell clusters in the metastatic development of prostate cancer

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Background & objectives

Circulating tumour cells (CTCs) have been observed to travel individually or as part of a CTC-cluster in the circulation. The significance of CTC-clusters in cancer metastasis is a relatively new field of discovery, with CTC-clusters demonstrating a metastatic potential of 23-50 times greater than that of single-CTCs. The ability of these cells to enter the circulation involves subpopulations of primary tumour cells gaining a migratory and more invasive phenotype in a process known as epithelial to mesenchymal transition (EMT) resulting in down-regulation of epithelial markers and up-regulation of mesenchymal markers. Non-EMT mediated invasion can also occur whereby cells enter the circulation through passive infiltration, retaining their epithelial phenotype. Many of the CTC-cluster studies to date have focused on CTC-clusters of an epithelial nature, resulting in limited understanding of these transitioned, mesenchymal CTC-clusters.

Objective

To investigate the abundance, size and phenotype of CTC-clusters in metastatic and localised prostate cancer in order to further understand the biological basis of CTC-clusters in metastasis.

Methods

Whole blood from histologically confirmed prostate cancer patients of metastatic and non-metastatic status was enriched for CTC-clusters using an epitope independent microfluidic filtration technology, the Parsortix system from ANGLE Europe Ltd. Down-stream immunofluorescence was performed to identify epithelial and mesenchymal CTC-clusters.

Results

In a cohort of 64 metastatic and 156 non-metastatic prostate cancer patients, more (p=0.0018) and larger (p=0.0119) CTC-clusters were observed in metastatic cases. Metastatic prostate cancer patients also displayed significantly more (p=<0.0001) mesenchymal CTC-clusters compared to epithelial CTC-clusters. In addition, these mesenchymal CTC-clusters were observed to associate with white blood cells (WBCs), in a significantly greater abundance (p=0.0004) than mesenchymal CTC-clusters without WBC accompaniment.

Conclusion

Mesenchymal CTC-clusters are highly significantly observed in metastatic prostate cancer. Their association with immune cells may be an important insight into the increased metastatic potential of CTC-clusters and their immune evasive abilities.