Cancer associated macrophage-like (CAMLs) cells in circulation predict progression and survival in all stages of solid tumors

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ABSTRACT

We have previously demonstrated that cancer associated macrophage-like cells (CAMLs) are a cancer specific giant polyloid cell that circulates in the blood of patients with solid tumors. Building on our initial discovery, others have shown that these hyperploid cells are an innate immune response that is associated with decreased survival. However to date, no study has been done to elucidate their clinical significance as in relation to the various stages of malignant disease. We established 2 year prospective study of 315 patients from a variety of solid tumors (breast, prostate, lung, renal cell, pancreas, and esophageal) comparing the morphological properties of CAMLs in both early and late stage disease as they relate to progression free (PFS) and overall survival (OS). These data suggest that large CAML size has a significant negative correlation with PFS and OS in a variety of solid tumor regardless of stage, which indicates their broad use as a non-invasive blood based biomarker in solid tumors.

MATERIALS & METHODS

A prospective multi-institutional study used anonymized peripheral blood (7.5 mL) from 315 cancer patients [stage I (n=62), stage II (n=73), stage III (n=67) & stage IV (n=103), unknown stage (n=10)] from subjects with breast (n=59), esophageal (n=27), lung (n=59), renal cell carcinoma (n=37), prostate (n=74), pancreas cancers (n=59). CAMLs were isolated by the CellSieve™ microfiltration technique at 5 institutions and stained for cytokeratin 8, 18, 19, CD14 and CD45. After imaging, a size based threshold <50µm was used to separate the patient cohorts.

RESULTS

CAMLs are specialized myeloid polyloid cells transiting the circulation of patients in various types of solid malignancies and appearing in all stages of cancer1-4. While CAMLs are easy to identify by their large size and polyloid nucleus, they appear to present as stem cell like phenotype with multiple heterogeneous epithelial, myeloid, and endothelial markers.

Size exclusion is the only known technique for isolating large cells from peripheral patient blood irrespective of their surface markers. CellSieve™ microfilters are size exclusion membranes which efficiently isolate CAMLs and circulating tumor cells (CTCs) from whole blood, making it possible to study both cell types in relation to malignant disease1-4.

CONCLUSIONS

In a large scale prospective study on the clinical utility of CAMLs, CAMLs were common in all stages of invasive solid cancers. Smaller CAML size appeared associated with improved survival outcome and longer PFS. In a multivariate analysis, CAML size was the most predictive variable for PFS & OS and independent of other clinical variables. CAMLs assessment may constitute a new real time predictor of progression, and survival in both early and late stage disease. Larger scale clinical validation studies are underway to determine predictive value of CAMLs in specific cohorts

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References