Cancer associated macrophage-like cells (CAMLs) are a recently described circulating stromal cell subtype commonly found in the peripheral blood of cancer patients. While CAMLs have been identified in all stage of solid malignancies and in a variety of cancer subtypes, no study has evaluated their clinical use as it relates to cancer prognosis. In an effort to elucidate the clinical utility of CAMLs as it relates to cancer progression, we ran a multi-institutional prospective 2-year study of 293 cancer patient samples in 6 types of solid tumors. CAMLs are specialized myeloid polyoid cells transiting the circulation of patients with various types of solid malignancies and appearing in multiple heterogeneous epithelial, myeloid, and endothelial markers.

INTRODUCTION

CAMLs are specialized myeloid polyoid cells transiting the circulation of patients with various types of solid malignancies and appearing in 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 marker expression. 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 disease.

MATERIALS & METHODS

This single blind study consisted of 293 stage I-IV patients; breast (n=59), esophageal (n=27), prostate (n=52), pancreatic (n=59), lung (n=59), and renal cell (n=37), in treated (n=123) and untreated baseline (n=170). 7.5ml of whole peripheral blood was filtered by CellSieve™ microfiltration. CAMLs were identified as giant polyoid cells that express cytokeratin 8, 18 & 19, CD45, and/or CD14, as previously described. Patients were grouped by CAML number (<5 or ≥6) and by size (<50 or ≥250 μm) to determine hazard ratios (HR) by censored univariate & multivariate analysis.

RESULTS

- In 7.5 ml blood, CAMLs were found in 91% of all cancer patients (n=266/293), but in none of the healthy control samples (Fig. 2).
- CAMLs were common, found in stage 1 (84%), stage 2 (94%), stage 3 (95%) or stage 4 (97%).
- Number of CAMLs was exponentially associated with disease stage averaging 4.7 (Stage I), 4.7 (Stage II), 8.7 (Stage 3), 12.0 (Stage IV).
- In a univariate analysis of CAML number, optimal HR stratification for progression free survival (PFS) and overall survival (OS) occurred in patients with ≥6 CAMLs per sample (Fig. 3): OS (HR=1.9, p=0.006) and PFS (HR=1.8, p=0.003).
- In a multivariate analysis CAML size of ≥250 μm was the most significant factor, Fig. 4: OS (HR=3.6, p<0.001) and PFS (HR=3.7, p<0.001).

CONCLUSIONS

- In a multivariate analysis CAML size was the most predictive variable for PFS & OS and was independent of other clinical variables tested, including CTCs.
- Our data suggests that in solid malignancies CAML number and size clinically correlate with OS and PFS in early and late stage solid malignancies.
- Additional studies are warranted to determine if CAMLs can serve as a general clinically prognostic blood based marker.

References


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