Brain stereotactic biopsy flow cytometry for central nervous system lymphoma characterization: advantages and pitfalls.

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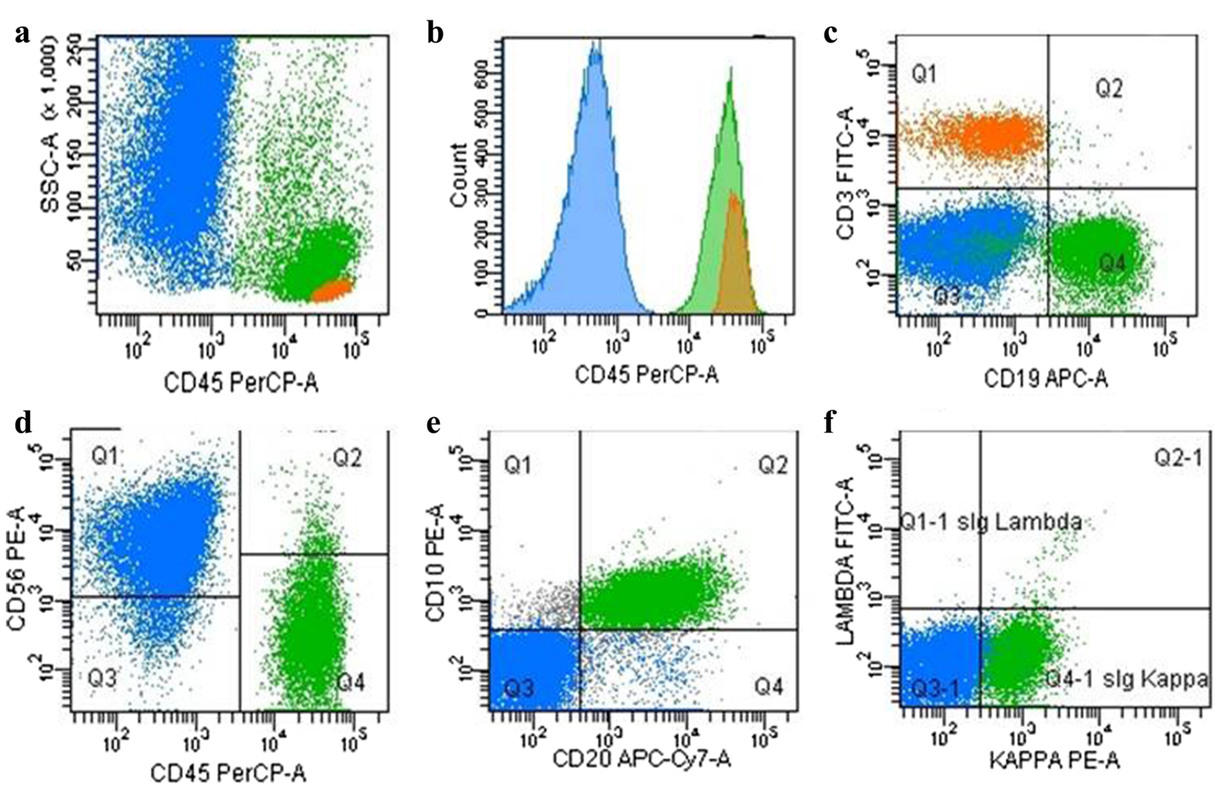
Iole Cordone,[1] Serena Masi,[1] Mariantonia Carosi,[2] Antonello Vidiri,[3] Francesco Marchesi,[4] Mirella Marino,[2] Stefano Telera,[5] Alessia Pasquale,[1] Andrea Mengarelli,[4] Laura Conti,[1] Edoardo Pescarmona,[2] Andrea Pace[6] and Carmine M. Carapella[5], R Boccaletti[5]
IRCCS Regina Elena National Cancer Institute, Rome (Italy)
[1]Clinical Pathology, [2]Pathology, [3]Radiology, [4]Hematology and Stem Cell Transplant, [5]Neurosurgery, [6]Neuroncology.

Background

Brain stereotactic biopsy (SB) followed by conventional histopathology and immunohistochemistry (IHC) is the gold standard approach for primary central nervous system lymphoma (PCNSL) diagnosis. Flow cytometry (FCM) characterization of fine-needle aspiration cytology and core needle biopsies are increasingly utilized to diagnose lymphomas however, no biological data have been published on FCM characterization of fresh single cell suspension from PCNSL SB. The aim of this study was to establish the feasibility and utility of FCM for the diagnosis and characterization of brain lymphomas from a tissue samples obtained by a single SB disaggregation.

Flow cytometry analysis of cell suspension from one brain stereotactic needle biopsy of PCNSL. Blue color has been utilized to mark CD56 positive/CD45 negative brain cells (a, b, d), green for CD10 CD19 CD20 sIg-Kappa light chain positive large lymphoma cells (c, e, f), orange for the side population of CD3 positive T lymphocytes (a, b, c).

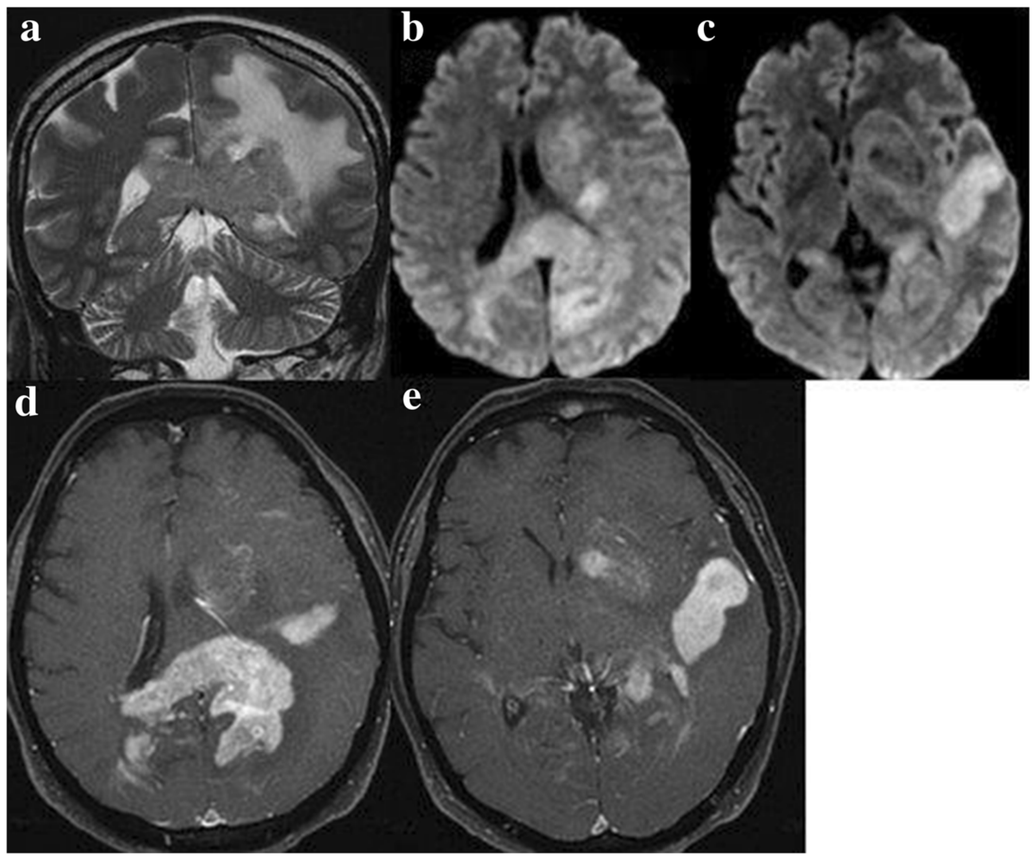


Methods

Twenty-nine patients with a magnetic resonance suggestive for PCNSL entered the study. A median of 6 SB were performed for each patient. A cell suspension generated from manual tissue disaggregation of a single, unfixed, brain SB, was characterized by FCM. The FCM versus standard approach was prospectively compared.

Results

FCM and IHC showed an high degree of agreement (89%) in brain lymphoma identification. By FCM, 16 out of 18 PCNSL were identified within 2 hours from biopsy. All were of B cell type, with a heterogeneous CD20 mean fluorescence intensity (MFI), CD10 positive in 3 cases (19%) with surface Ig light chain restriction documented in 11 cases (69%). No false positive lymphomas cases were observed. Up to 40% of the brain leukocyte population consisted of CD8 reactive T cells, in contrast with the CD4 positive lymphocytes of the peripheral blood samples ($P<0.001$). By histopathology, 18 B-PCNSL, only one CD10 positive (5%), 1 primitive neuroectodermal tumor (PNET) and 10 gliomas were diagnosed. A median of 6 days was required for IHC diagnosis.



MRI findings strongly suggestive for brain lymphoma: SE T2 sequences in coronal plane (a), diffusion in axial plane (b, c) and fat-suppressed T1
after contrast medium infusion in axial plane (d, e). MRI shows multiple bilateral, periventricula sites with low signal intensity on T2, with oedema, hyperintensity signal on DWI and homogensously enhancement after contrast medium infusion

Conclusions

Complementary to histopathology FCM can contribute to a better characterization of PCNSL, although necrosis and previous steroid treatment can represent a pitfall of this approach. A single brain SB is a valid source for accurate FCM characterization of both lymphoma and reactive lymphocyte population, routinely applicable for antigen intensity quantification and consistently documenting an active mechanism of reactive CD8 T-lymphocytes migration in brain lymphomas. Moreover, FCM confirmed to be more sensitive than IHC for the identification of selected markers.