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Blood 142 (2023) 6083–6084

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

621.LYMPHOMAS: TRANSLATIONAL-MOLECULAR AND GENETIC

Significance of the Rhoa G17V Mutation Detected By Ddpcr in Diagnostic and Monitor of Angioimmunoblastic T-Cell Lymphoma

Yi Miao, MD[1], *Siqi Qian*[1], *Xiao Lu*[2], *Tonglu Qiu*[1], *Shuchao Qin*[1], *Yi Xia, MDPhD*[1], *Lei Fan, MD*[1], *Jianyong Li, MD*[1], *Huayuan Zhu*[1]

[1] Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China
[2] Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China

Introduction
Angioimmunoblastic T-cell lymphoma (AITL) is a subtype of peripheral T-cell lymphoma (PTCL) that originates from T follicular helper cells (TFH). RHOA G17V mutation is the most common hotspot locus which could be detected in 50%-70% of cases, showing its potential value for the diagnosis and clinical monitor of this disease.

Methods
RHOA G17V mutation were detected by Droplet digital PCR (ddPCR) in available samples from PTCL patients, at baseline and before every cycle. Response assessments were done by PET/CT and evaluated according to Lugano criteria after 3 cycles and end of first line chemotherapy(EOT), or at suspicious of disease progression. All data analyses were performed using SPSS 20.0 software (SPSS, Inc.) and GraphPad Prism 9.0 software (GraphPad software). p-Value < 0.05 was considered statistically significant.

Results
30 patients with PTCL were included in our center from 2021-01-01 to 2023-07-01,21 were confirmed as AITL and 9 were PTCL-NOS by pathologist review. In whole cohort, RHOA G17V mutation could be detected in 46.7%(14/30) of all patients, also was positive in 61.9%(13/21) and negative in 38.1% (9/21) of patients with AITL. The sensitivity and specificity of RHOA G17V mutation in AITL by ddPCR is 61.9% and 88.9%, with a positive predictive value of 92.9%, and a negative predictive value of 50%. Hyperglobulinemia, positive direct Coombs test, elevated LDH, elevated β2-MG were founded in 76.9%(10/13),61.5%(8/13) ,61.5%(8/13) and 76.9% (10/13) of AITL patients with RHOA G17V mutation, which were significantly higher than those without RHOA G17V mutation(P=0.002,0.019,0.019,0.026). Furthermore, all of the of RHOA G17V mutated AITL patients were in clinical stage III or IV(100%, 13/13), 76.9%(10/13) of them with detectable whole-blood EBV-DNA(≥500 copies/mL) and all have three or more TFH markers(100%,13/13).
We next evaluated the baseline and dynamical changes in RHOA G17V VAF-positive patients with AITL. Pretreatment VAF was significantly lower for patients who achieved complete remission or partial remission at EOT compared with that of patients with progressive disease or stable disease (mean VAF, 20.75% vs. 4.31%, $p = 0.0028$). (Figure 1). In addition, the median PFS in AITL patients with and without RHOA G17V mutation was 9.157 months and 15.154 months respectively(P=0.32).Finally, in 10 AITL patients with dynamic results of RHOA G17V mutation (Figure 2) , a good correlation was found in between dynamic changes of VAF of RHOA G17V mutation and response assessment by PET/CT, rerise of RHOA G17V mutation VAF could be detected prior to clinical progression in two patients,showing for the its protentional value for disease monitor.

Conclusions
Our study first reported the diagnostic value of single hotspot detection of G17V RHOA mutation by ddPCR in PTCL. Monitoring of G17V RHOA mutation in AITL has predictive value of assess tumor burden and response, also can complement the longitudinal supervise of disease.

Disclosures No relevant conflicts of interest to declare.

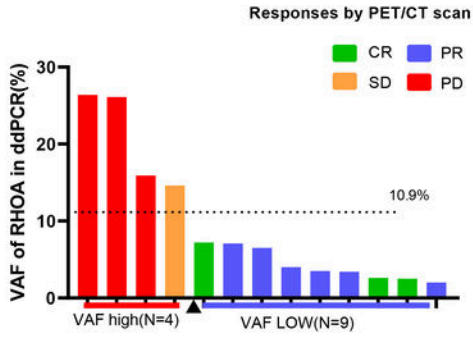

Figure 1: VAF of Patients with RHOA positive in AITL at the end of the first line treatment

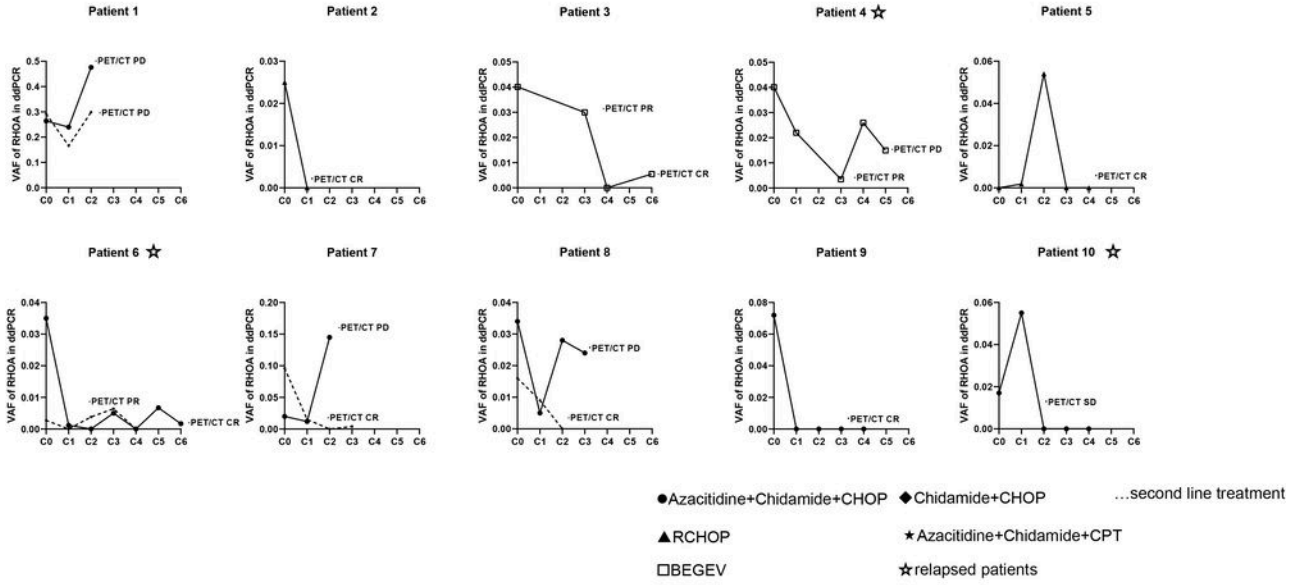

Figure 2: the dynamic changes of RHOA G17V mutation in patients with AITL

Figure 1

https://doi.org/10.1182/blood-2023-182617