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Neutrophil extracellular traps predict disease condition in complement-mediated thrombotic microangiopathy patients

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Objectives : We explored the level of neutrophil extracellular traps and its relationship with TMA condition in CM-TMA patients.
Methods : The study enrolled 107 CM-TMA patients, explored the plasma and renal level of NETs, compared the plasma level of NETs (cfDNA、CitH3-DNA、MPO-DNA、S100A8/A9) and renal NETs formation (NE-DNA area/tissue area ratio) in CM-TMA patients with normal control (NC), analyzed the relationship between NETs and the clinicopathological index in CM-TMA patients.
Results : The plasma NETs were increased in CM-TMA patients, including cfDNA (P <0.001, Figure 2A), MPO-DNA complex (P <0.001, Figure 2B), CitH3-DNA complex (P <0.001, Figure 2C), S100A8/A9 (P <0.001, Figure 2D). The formation of NETs also significantly increased in the glomeruli (Figure 2E and 2G) and interstitial (Figure 2F and 2G) of CM-TMA patients. Plasma cfDNA levels was significantly negatively correlated with PLT in CM-TMA patients (P = 0.013), Hb (P = 0.032) and eGFR (P = 0.031) (Figure 2H), was significantly positively correlated with LDH levels (P = 0.041), PT (P = 0.027). Glomerular NE-DNA area/tissue area ratio was significantly positively associated with glomerular thrombi (P = 0.012), and endothelial hyperplasia and sclerosis (P = 0.034) (Figure 2I). The levels of plasma NETs marker cfDNA (P = 0.004, Figure 3A), CitH3-DNA (P = 0.007, Figure 3B), MPO-DNA (P = 0.009, Figure 3C), and S100A8/A9 (P <0.001, Figure 3D) in TMA acute phase were all significantly higher than those in the TMA remission phase of 17 CM-TMA patients. Renal NETs deposition showed significant positive associations with MAC deposition in glomeruli (r = 0.637, P <0.001, Figures 3E and 3F) and tubulointerstitium (r = 0.394, P <0.001, Figures 3G and 3H).
Conclusions : NETs are associated with clinicopathological changes, disease activity, organ damage, and complement activation, which can be used as a biological marker of disease activity in CM-TMA patients.

Fig 2_画板 1.png

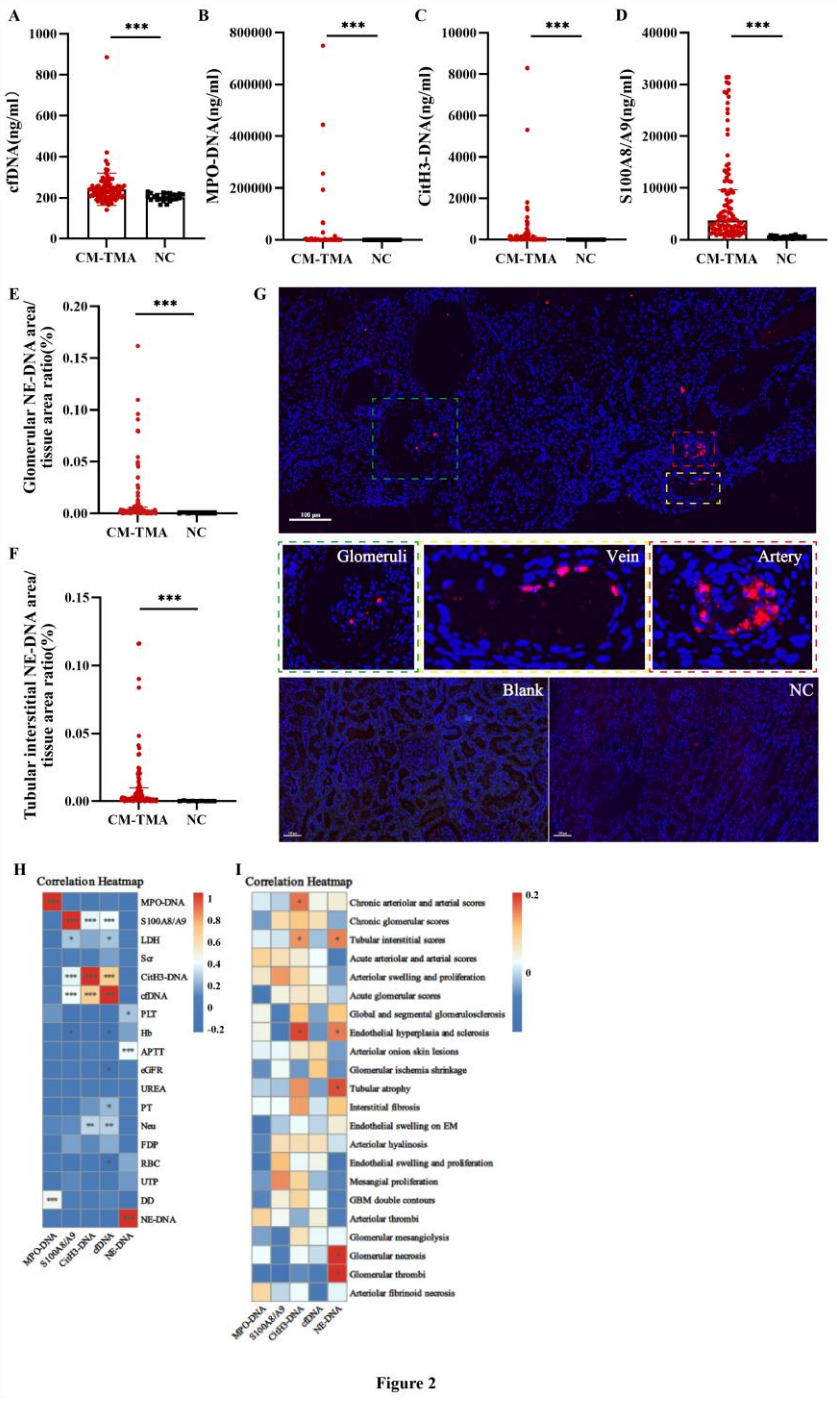

Figure 2

Fig 2_画板 1.png

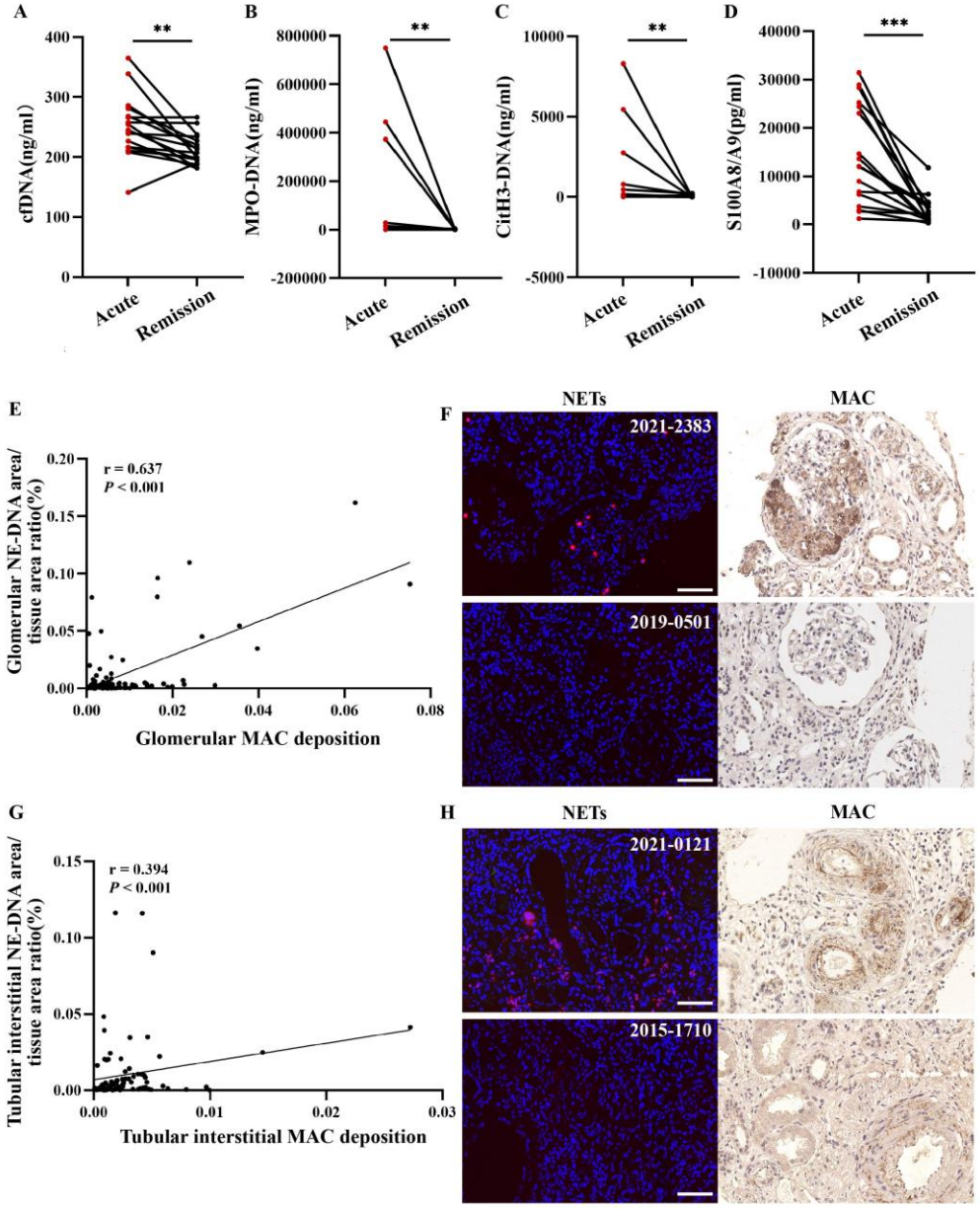
A
cfDNA(ng/ml)
**
Acute
Remission
B
MPO-DNA(ng/ml)
**
C
CitH3-DNA(ng/ml)
**
D
S100A8/A9(pg/ml)
***
E
Glomerular NE-DNA area/ tissue area ratio(%)
r = 0.637
P < 0.001
Glomerular MAC deposition
F
NETs
MAC
2021-2383
2019-0501
G
Tubular interstitial NE-DNA area/ tissue area ratio(%)
r = 0.394
P < 0.001
Tubular interstitial MAC deposition
H
NETs
MAC
2021-0121
2015-1710

Figure 3