(البحث السادس)

The Clinical Utility of Tissue Factor Level as a Biomarker in Multiple Myeloma

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Tissue factor is a key component in the initiation of coagulation and may play a role in cancer-related processes such as hypercoagulability, tumor growth, angiogenesis, and metastasis. An early study showed an increased expression of TF in haematologic malignancies as AML, polycythemia vera and essential thrombocythemia. However, the role of TF in MM has not been studied in detail. Aim of the work: is to assess the clinical utility of tissue factor level as a biomarker for prediction of risk of thromboembolism and its relation to type،stage and duration of disease in multiple myeloma patients. Subjects & Methods: This study included 75 MM patients (group I) 52 males and 23 females with a mean age of 56.40 ± 5.75 years and 20 age and sex- matched healthy subjects served as controls (group II). All patients were subjected to detailed clinical examination and investigations which included CBC, liver & kidney functions tests, uric acid, serum calcium, CRP, serum protein electrophoresis, immunofixation, bone marrow aspirate and biopsy, B2 microglobulin, serum albumin, PT, aPTT, D dimmer،FDPS, fibrinogen, tissue factor levels, skeletal survey and bilateral lower limb venous duplex. Results tissue factor was significantly higher in MM patients than controls (p-value 0.0001). There is no statistically significant difference between MM patients when classified according to sex (P= 0.3), type of myeloma wither IgG or IgA (P = 0.7) and wither were recently diagnosed or already on treatment (P=0.7).TF levels were significantly higher in patients expressing Lambda compared with those expressing Kappa chain (P= 0.04). IT was higher in patients complicated with DVT than those without DVT (P= 0.0001). No difference was reported in patients with or without ischemic CVS (P= 0.8). TF levels were higher in patients with positive markers of activated coagulation (D-dimer and FDPs) when compared to those with negative markers (P= 0.0001 & 0.002 respectively). TF was positively correlated with D-dimer and FDP (r 0.4&0.3, P= 0.001&0.004 respectively), while negatively correlated with fibrinogen (r -0.3 & P= 0.01). According to therapeutic regimens, TF level showed no statistically significant difference between patients received VAD-based regimen and those who did not (P= 0.9), it was lower in patients received brotezomib-based regimen compared to those who did not (P= 0.01) while it was higher in patients received thalidomide-based regimen than those who did not (P= 0.004). TF levels were positively correlated with duration of treatment with thalidomide (r 0.4, P =0.001). The sensitivity and specificity of the TF level as a marker of thrombosis in MM patients (as determined by the ROC Curve) were found to be 77.3% & 90% respectively. Positive predictive value of 96.7 and negative predictive value of 51.4 and area under the curve of 0.88 were detected. Tissue factor was found to be significantly higher in stage III patients when compared with stage I & stage II (P= 0.0001.(Also we reported that TF is positively correlated with stage and duration of the disease (r 0.4, P= 0.0001 & r 0.5& P= 0.007 respectively) and B2microglubulines (r 0.4, P= 0.001), but negatively correlated with albumin (r -0.4, P= 0.001), Conclusion Multiple myeloma patients express high level of tissue factor especially in cases complicated with thromboembolism, those who have positive markers of activated coagulation and those receiving thalidomide.So TF level can be used as a predictor for risk of thrombosis in multiple myeloma patients, its sensitivity, specificity PPV&NPV are for further evaluation on wider scales. The correlations of TF with stage and duration of disease، albumin & B2microglubulines are finding that necessitate further work to determine the extent to which targeting and monitoring TF expression may be useful, from a diagnostic, prognostic, and therapeutic standpoint.

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