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Glycemia and coagulation in patients with glioblastomas

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Abstract

Glioblastomas are among the most malignant tumors which, despite aggressive treatment, currently have an abysmal prognosis. These lesions are known to cause local and systemic perturbations in the coagulation system, leading to neo-angiogenesis and a high risk of venous thromboembolism. Indeed, there have been multiple proposals of the coagulation system being a possible target for future treatment of these patients. However, non-selective anticoagulant therapy has proven suboptimal and leads to a significant increase of intracranial hemorrhage. Thus, recognizing factors which lead to hyper-coagulation is considered paramount. Hyperglycemia is a well-known pro-thrombotic factor, a fact which has received little attention in neuro-oncology so-far. We previously hypothesized that patients with brain tumors could be highly susceptible to iatrogenic glycemia dysregulation. Here, we analyzed the connection between glycated hemoglobin (HbA1c) and the routine coagulation markers (D-dimers, prothrombin time (PT) and activated partial thromboplastin time (aPTT)) in patients with de novo intracranial glioblastomas. Included in this study were 74 patients, operated on in three hospitals, Clinical Hospital Dubrava, Zagreb, Croatia; University Hospital Center Split, Split, Croatia and University Hospital de la Princesa, Madrid, Spain. We found a significant inverse correlation between HbA1c and aPTT (ρ=-0.379; P=0.0009). We also found a significant inverse correlation between Ki67 immunoreactivity and aPTT (ρ=-0.211; P=0.0082). No connection was found between HbA1c and D-dimers or PT. Our results suggest that hyperglycemic patients, with a more proliferative glioblastoma, could in fact have their coagulation profile significantly disrupted, primarily through the intrinsic coagulation pathway. Such findings could have great clinical importance. Further research in this area could help elucidate the vicious connection between glioblastomas and coagulation, and help combat the deadly disease.

Keywords: aPTT; coagulation; glioblastoma; glycated hemoglobin; venous thromboembolism.