IJAE
Vol. 123, n. 1 (Supplement): 130, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

The clinic-pathological meaning of MCT1, MCT4, and GLUT1 in testicular germ cell tumors

Rocco Malivindi, Vittoria Rago, Marta Santoro, Saveria Aquila

Department of Pharmacy and Sciences of Health and Nutrition, University of Calabria, Cosenza, Italia

Testicular germ cell tumors (TGCTs) are the most frequent malignant tumors in male patients aged 15–45 years, their incidence is increasing in recent years. There are two main subclasses of TGCTs: seminomas (SE) and non-seminomatous germ cell tumors (NSGCTs). NSGCTs have varying degrees of differentiation such as embryonal carcinoma (EC) which tends to be metastatic at presentation and a worse prognosis than SE. Although the majority of patients with TGCTs have good responses to treatment, some of them resist to therapy presenting disease progression. Thus, it is important to better understand the biological heterogeneity of TGCTs to optimize treatments by exploring new pathways involved in tumor development and progression. Alterations in cellular metabolism are among the most consistent hallmarks of cancer. Depending on cellular context, cancers manifest an array of metabolic phenotypes. Here, aimed to identify immunohistochemistry (IHC) prognostic markers which could be used to the TGCTs management, we investigated the relevance of some metabolic target in TGCTs and normal testicular tissue (NT). Further, we evaluated the region adjacent to TGCTs (40% of samples) showing the presence of abnormal seminiferous tubules with decreased tubular diameters, identified as intratubular germ cell neoplasia (IGCNU) and representing testicular carcinoma in situ. There is evidence that these tumors are highly glycolytic, although just one study evaluated the monocarboxylate transporters MCT1 and MCT4 expression, while findings on GLUT1 in TGCTs are lacking. The glycolytic phenotype, a metabolic reprogramming in which cancer cells produce energy through glycolysis, leads to a greater glucose consumption and lactate production than normal metabolic profile. To avoid intracellular acidification some proteins are upregulated, including MCT1 and 4 mainly associated with lactate efflux. Glucose uptake is higher in some tumors by an increase of glucose transporters (GLUTs) and GLUT1 usually correlates with cancer malignancy. Interestingly, from our IHC data it emerged that: MCT1 was higher expressed in EC with respect SE and IGCNU, although there were no significant differences with respect NT; MCT4 expression increased in EC with respect SE, IGCNU and NT; GLUT1 levels augmented in EC and in a lesser extent in SE with respect IGCNU and NT where it is absent. The association of MCT1, MCT4 and GLUT1 expression with characteristics of worse prognosis, such as nonseminomatous histology, higher stages, metastasis occurrence, vascular invasion, reflect the function of these proteins in lactate efflux, thus maintaining an extracellular acid pH, and a greater influx of glucose, corroborating the glycolytic phenotype of these tumors.

This study discovered that GLUT1 may be considered of clinic-pathological significance in TGCTs and as an IHC prognostic marker in the differentiation of these tumors.