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ATTI

PATOLOGIA SPERIMENTALE

THE CLINICOPATHOLOGICAL AND PROGNOSTIC SIGNIFICANCES OF C1Q EXPRESSION IN GLIOMAS: A BIOINFORMATICS ANALYSIS

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Introduction. The complement system represents an important component of the inflammatory response and acts as a functional bridge between the innate and adaptive immune response. The contribution of the complement component C1q in the pathophysiology of brain cancers has been recently considered in light of its well-known involvement in carcinogenesis. Brain malignancies arise from cells of the CNS and are classified according to the tissue of phylogenetic origin. Gliomas represent the most common and aggressive form of brain tumours in adults. They derive from glial cells that help to support the functions of the other main brain cells type, the neurons (1). These are a heterogeneous group of diseases with multiple subtypes (1, 2). Glioblastoma multiforme (GBM) is the most common and fatal form of a primary brain tumour, accounting for approximately 60% of all glioma cases (3), whereas grade-II and -III gliomas are the second most common type of glioma in adults (~30%) (3). C1q molecule, together with other complement components, can be locally produced within the CNS by microglia and astrocytes, rendering it an attractive player in primary brain tumour development (4). The role of C1q in gliomas microenvironment is still poorly characterized and it is still quite puzzling whether it exerts a beneficial or a harmful activity for cancer progression. In the present study we performed a bioinformatics analysis aimed at investigating if C1q can serve as a potential prognostic marker for gliomas.

Methods. The expression levels of *C1qA*, *C1qB* and *C1qC* genes in gliomas were analysed using Oncomine analysis. Available genomics data from The Cancer Genome Atlas project was used for Kaplan–Meier survival analysis to generate survival probability plots, using UALCAN analysis.

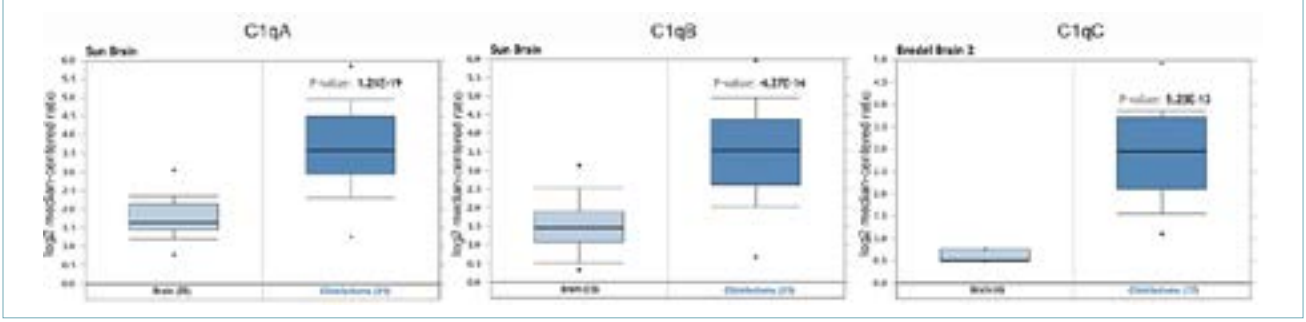

Fig. 1.

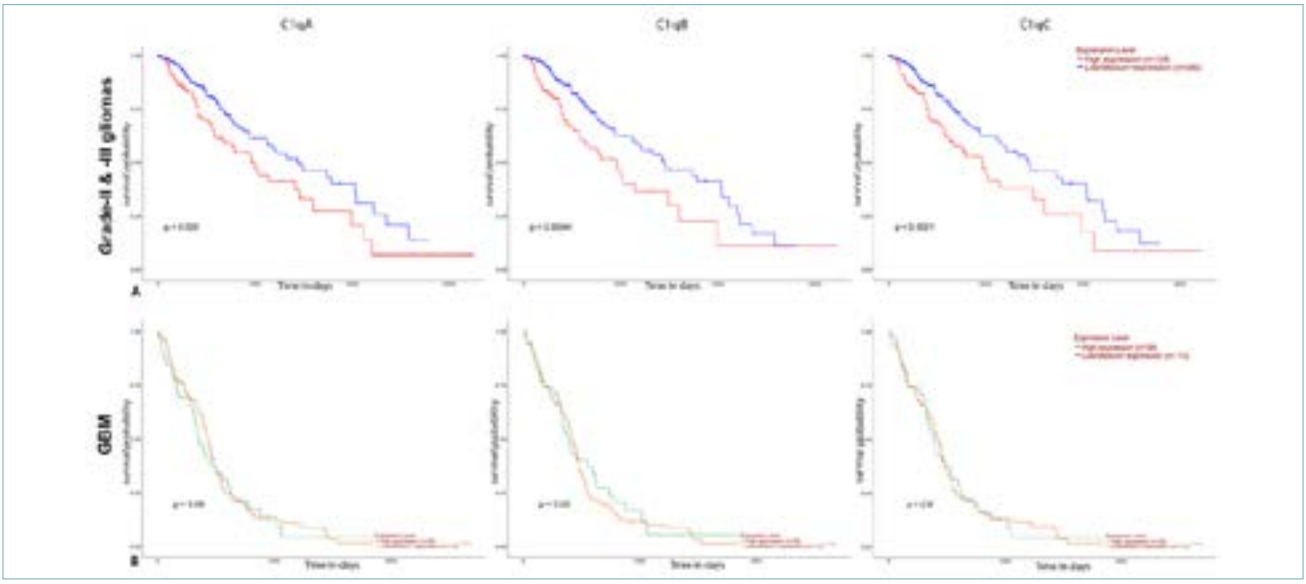

Fig. 2.

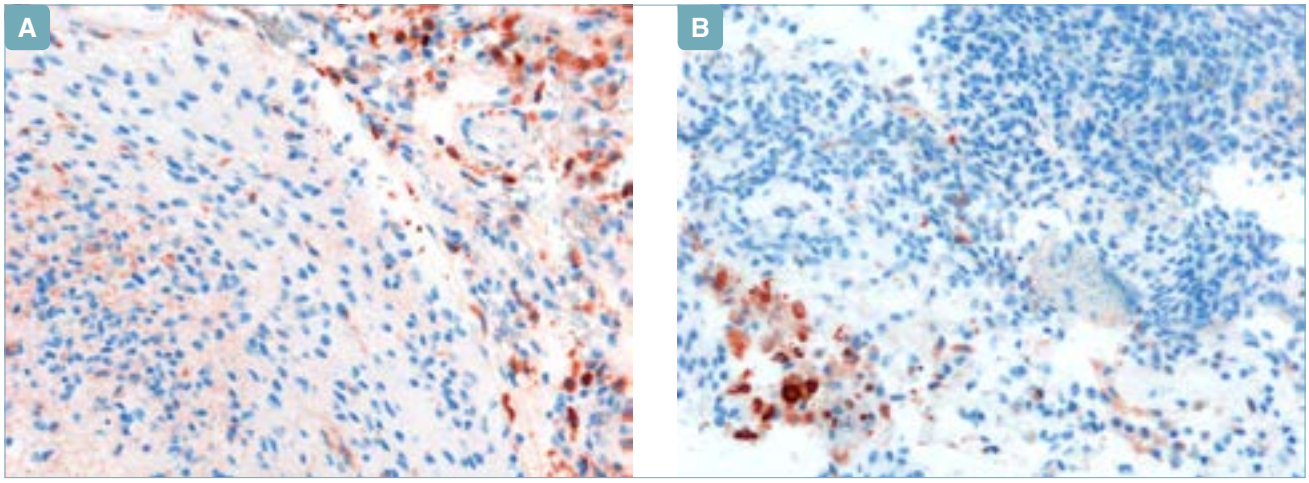

Fig. 3.

Results. From the analysis performed on several datasets using Oncomine, we showed a significantly higher mRNA expression levels for *C1qA*, *C1qB* and *C1qC* chains were detected in gliomas (different histotypes and grades) as compared to normal brain tissue (Fig. 1). We observed a positive correlation between the mRNA expression of *C1qA*, *C1qB* and *C1qC* mRNA polypeptide chains and the unfavorable prognosis only in gliomas grade-II and -III, where the survival probability is indeed reduced (P <0.05) (Fig. 2). No correlation was observed in glioblastoma multiforme (Fig. 2). By immunohistochemical approaches we detected a high deposition of C1q in the tumor microenvironment of both in grade-II and -III gliomas and in GBMs examined (Fig. 3a glioma, 3b glioblastoma multiforme; 20x Magnification). Moreover, in double immunocytochemical experiments we demonstrated that CD68 positive infiltrating cells are actively synthesizing C1q in the tumor micro-environment. CD68 expression is characteristic of tumor-associated macrophages, whose enrichment in glioma has been associated with poor prognosis (5).

Conclusion. In our study C1q expression was significantly correlated with poor survival probability in gliomas grade-II and -III while this is not the case for GBM. These data altogether underline how complex, multifaceted and still poorly understood is the role C1q can exert on tumor progression, and how the very same molecule can differentially affect the outcome depending on the biological context it comes to act.

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PATOLOGIA TESTA COLLO

MIXED ODONTOGENIC TUMORS: A CASE REPORT

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Background. Odontogenic tumors (OT) represent a heterogeneous group of lesions ranging from hamartomas to benign and malignant tumors. They arise from ectomesenchymal and/or epithelial tissues involved in odontogenesis [(1)] and depending on the tooth germ tissue of origin, they are classified as epithelial, ectomesenchymal or mixed tumors [(2,3)]. The latest (4th) edition of the WHO Classification of Odontogenic and maxillofacial bone lesions, introduced significant changes in the classification of these lesions, particularly in the chapter of mixed odontogenic tumors, adding a new entity (the *primordial odontogenic tumor*) and removing four other ones including the odontoameloblastoma and ameloblastic fibro-odontoma (AFO).

Case presentation. We report a case of a 14-years-old male patient, with a lesion in the left mandibular angle, clinically compatible with odontoma. Histopathological examination of the incisional biopsy revealed proliferating odontogenic epithelium arranged in islands, cords, follicles and interconnecting strands in a highly hypercellular myxoid stroma (ameloblastoma-like) and odontoma-like elements: dentin containing dentinal tubules, enamel space and tissue resembling pulp. This morphological features are compatible with a mixed odontogenic tumor with areas consistent with ameloblastic fibro-odontoma associated with complex odontoma, formerly called odontoameloblastoma/ameloblastic odontoma.

Discussion. Odontoameloblastoma was introduced in the 1971 WHO classification and described as a mixed