

Atypical facets of brain tumors: glioblastoma in schizophrenia and state after ablation of meningiomas in Parkinson's disease

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Abstract

Decades ago, an issue concerning the association between schizophrenia and glioblastoma multiforme was raised. Despite some conflicting evidence, there seemed to be a reduced propensity for glioblastoma incidence in schizophrenic patients. Moreover, the widespread use of antipsychotic medications in these patients appears to have affected the course of glioblastoma. In any case, the psychiatric medical treatment may have precedence over a putative molecular mechanism concerning the effect on glioblastoma. Independently, isolated Parkinson's patients, notably, those affected by hemi-Parkinson's disease, when they displayed a meningioma on top of their basic neurological disorder, and had the tumor removed surgically, they may tend to witness a remission in the neurologic disease. The causes of the aberrant interactions between psychiatric or neurodegenerative diseases and the associated tumors will be explored. The analysis may reveal unexpected and significant associations. Evidence of these atypical features and associations in primary brain tumors appear to have been ignored so far by most physicians concerned.

Keywords: Schizophrenia, glioblastoma, Parkinson disease, Meningioma, Ablation, Remission

Introduction and Review

Glioblastoma multiforme (GBM) is probably the most prevalent of primary neoplasms of the central nervous system. It is mostly resistant to treatment, and therefore usually fatal. The carcinogenesis concerned apparently involves mitochondria [1].

Many years ago, an issue was raised, consequent to conflicting observations [2]: was glioblastoma multiforme (GBM) less frequent in schizophrenic (SCZ) patients? Or else this psychiatric disorder had no impact on the evolution of the most aggressive brain cancer [3,4].

Though the reports on this topic are far from common, there seems to be a predilection for an association between SCZ and a resistance to the development of GBM [5,6]. It has been assumed that the reduced incidence of GBM in SCZ may be due in part to tumor suppressor genes, equivalent in both diseases. While these genes are part of the genetic structure in most patients suffering from SCZ, they are considered, in contrast, to be acquired genes during the evolution of the GBM. The Disrupted in Schizophrenia 1 (DISC1) gene was primarily related to schizophrenia, and the t(1;11)(q42;q14.3) of the DISC1 was associated with features of schizophrenia. The DISC1 gene has been classified as an element of neurodevelopment. Moreover, the gene was identified in mitochondria of cortical neurons [1,2,7].

It is of note, that several antipsychotic drugs have been identified as exhibiting a level of anti-GBM therapeutic efficiency. Others seem to display a full-blown therapeutic effect, several of these medications have disclosed a revision of antipsychotic drugs into anti-cancer medications [8].

The medications of concern encompass first-generation antipsychotic drugs: chlorpromazine and haloperidol; second-generation antipsychotic medicines: aripiprazole and olanzapine. In addition, antidepressants: fluoxetine, escitalopram oxalate and miscellaneous: a mood stabilizer-valproic acid [6,9] [Table 1].

A distinct relationship between a brain lesion and a brain tumor, especially with the neoplasm ablation, has rarely been reported. This phenomenon may be of concern with Parkinson's disease (PD), and more specifically with the hemi-Parkinson subset thereof. In this context, meningioma, if exhibited by imaging, and later resected, may have as consequence the remission of the primary disorder (PD).

A crude evaluation of the awareness on both above phenomena, among the physicians of our (Tertiary) Medical Center, including neurosurgeons, psychiatrists, neurologists, and pathologists as controls, was performed. Not a single physician, nor clinical

pharmacologist, had been aware of the phenomenon, as described above.

Discussion

A study of two atypical occurrences, both concerning the interactions between a diffuse brain neurological disorder and the development of a brain tumor in the same patient, did suggest an independent correlation between condition as disparate, on the one hand as SCZ and GBM, and on the other, between PD and the resection of a meningioma, and a PD patient thereof.

A rare incidence of the above occurrences may be sufficient to reckon the ignorance of the corps medical about them. However, more earthy explanations may be in order. Thus, a limited incidence of GBM may be observed in SCZ and may be due to a parallel distribution of tumor suppressor genes in both SCZ and the GBM. Moreover, a critical role is played by antipsychotic and anti-depressive drugs, as they take over anti-cancerous functions. It is not totally excluded that the correlation cited in this paper are not completely founded on hard data, thus sustaining the general knowledge displayed by the several physicians interviewed by the authors.

The resolution of the Parkinson's disease, consequent to the resection of a large meningioma in a near typical PD patient, is somewhat divergent: from the origin, we are not dealing with a classic PD. The incipient meningioma, usually of large size, often localized in the frontal lobe, initiates an increasing pressure in the basal ganglia area. Mostly, the PD symptoms are incomplete, and they will recess soon after the ablation of the meningioma.

A series of reports predominantly compiled by neurological and internal medicine reviews, comment about an unusual concept. The cases described in this study, will be often displayed briefly

as follows: the patient of any gender showed at first parkinsonian symptoms of partial or one-sided nature. The clinical features are termed parkinsonism traits. The trigger, bringing out the changes, is often in the form of a meningioma, although it may encompass other tumors, AVCs, or an intoxication. Such cases will be described as secondary PD. The striking event at this stage will be the resolution of the parkinsonism, which evolved after the resection of the meningioma.

Before an attempt at deciphering the mode of disappearance of the parkinsonism, one should attempt to explain its original appearance. The theory concerning its evolution is often presented in the reports. Probably, the preliminary step consists in the appearance and the growth of the meningioma. A significant number of tumors may be large, and their growth vector may affect mainly to be directed to the base of the skull. The pressure inflicted on the basal ganglia will initiate the ensuing Parkinson's symptoms, detectable at this stage [10-14].

This instance is one of the very few presenting an association between brain neoplasms and a movement disorder [10]. A role is probably played by the dopamine D2 receptor and by the p53 protein in the evolution of the meningioma and of the above interactions [15].

To sustain the correlation, a case is presented, displaying total resolution of the parkinsonism after the tumor resection. A later recurrence of the cerebral meningioma has highlighted the return of the PD symptoms [16].

It is suggested that the occurrence described above is, to a high degree, consistent with a iatrogenic illness, and that, in both instances.

Table 1: Molecular mechanisms as the basis of the anticancer effect of antipsychotic drugs in the brain [6].

Molecular mechan.	Psychiatric drugs	Type of tumor	Primary use
Dopamine receptors	Olanzapine	GBM	Cognition,motivation, memory
Epigenetic (modif)	Vorinostat	GBM & else	Histone acetylation, most important
Src oncogene	Tyros. Kinase, ARP	Glioma cells	SCZ, sc-affective
Wnt/beta catenin	VPA	GBM	Self-renewal,prolifer
Autophagy	SSRI, clozapine	GBM	Efficient cell death

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Conflicts of Interest

The authors declare 'No conflicts of interest exist'.

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