I CONGRESSO INTERNACIONAL
MULTIDISCIPLINAR

GLIOBLASTOMAS AND THE DILEMMA OF ITS TREATMENT: A PHILOSOPHICAL PERSPECTIVE

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ABSTRACT
Glioblastomas (GBs) are aggressive brain tumors with limited treatment options, where surgery, radiotherapy (RXT), and chemotherapy (CMT) offer marginal survival benefits. The economic and healthcare system's role in GB treatment, particularly in developing countries, highlights disparities in patient outcomes and challenges in providing appropriate care.

Keywords: Glioblastomas, Healthcare Disparities.

INTRODUCTION

Glioblastomas (GBs) are the most common and malign tumor of the central nervous system(1). The standard treatment for GBs is based upon surgery, radiotherapy (RXT) and chemotherapy (CMT)(2-4). Although many clinical trials have addressed its treatment over the last years, it remains an incurable and fatal disease, with the best series describing an overall survival of only 12-15 months after the diagnosis(3,4). The provision of CMT, still not available everywhere, may improve the patient's outcome(2-4). However, what looks like a lack of appropriate care might hide a more complex problem, made of insufficient support of care such as psychological aid, palliative care and families' support. What is more, when compared to the series of patients from developed countries, patients from developing ones perform worse since the standard therapies very often lack. Even though the benefit from the standard treatment for those patients remains marginal, one

observes that the additional survival for those patients may represent a cost for the health care system. Nevertheless, the marginal benefits promoted by the standard therapy may suffice for solving particular and social problems (often neglected) before passing. The minor benefit from the therapy according to the health care providers may represent the last chance for a farewell among patients and their relatives.

So, the question that arises is: what does it mean cost in health system? Until when and for how long one will continue to use only cost analyses as a driven force to dictate health policies worldwide? Not to mention, when one sees the country's expenses and the budget allocated for war and "defense" seems like counterintuitive waste of money with guns to support a death culture instead of using this same money with health and research aiming cure and relief for a given disease. Just to exemplify, the US spends 3.45% of its gross domestic product (GDP) annually with the industry of war, comparing with 16.6% with healthcare[(5)]. So, in this short essay one is going to address some of the dilemmas regarding GBs and its impact for both the families and the health system.

GLIOBLASTOMAS – THE BURDEN OF A FATAL DISEASE

GBs were first described in 1926 with a name of Spongioblastoma Multiforme. Back then there were no sophisticated image tools such as computerized tomography scan (CAT scan) and magnetic resonance. The diagnosis were made exclusively by histopathological samples (although still are the final diagnosis by this mean) taken out from the patients' brains. Over the years, many different classifications were made to characterize GBs as a malign tumor and today its diagnosis is based not only on histopathologic findings, but also on molecular ones such as IDH and p53[(6)].

Nevertheless, the medicine itself has evolved and many diseases until then incurable had its course interrupted with the patients' cure. Unfortunately, that was not the case of GBs that since its description, too little has changed in terms of cure and survival. Nowadays the pillar of GBs treatment consists in surgery, with maximal possible resection when feasible. In addition, RXT and CMT might add some months in terms of survival. The QT is based on the usage of an alkylant agent called Themodal, which was already proved in some clinical trials to prolong the patient's survival in at least 3 months. In addition, both QT and RXT may prolong the time free of progression and improve the patient's quality of life[(2-4,7)].

WHEN DOCTORS ARE POWERLESS

When one sees medicine as a rule, it is obvious that many diseases are nowadays curable and easily manageable compared to the recent past. Though, that is not the case of GBs, which imposes a great challenge for doctors and patients. In this regard, sometimes doctors are inquired about the

value of a surgery, RXT and CMT, since the tumor will not be curable by any means. Those moments are important for doctors to reflect upon, recognizing how little they can contribute. At the same time it becomes clear the limitation of medicine per se, where one can influence only an infinitesimal part of the variables that very often one faces.

THE SURGERY IN GB´S - WHEN, HOW AND WHAT FOR?

If the surgery itself has been done for decades and very little has changed ever since regarding the technique, what is its real role in GB´s nowadays? Like in many situations in medicine, it depends on the clinical and neurological conditions. For example, if both (or any of it) clinical and neurological status is poor, the only option available is a simple biopsy by a craniotomy or burr hole. Even though the biopsy is not enough to decrease a hypothetical intracranial hypertension or to promote an improvement in the neurological condition, it may be necessary for the correct diagnosis (remind you that MRI is not sufficient for giving the diagnosis).

On the other hand, if the patient is alert, responsive or functionally independent, craniotomy with maximal safe resection is the golden standard and already proved as a way of improving a patient's survival. However, the question that often arises is: if this more radical form of surgery is not enough for curing the patient, is it worth the risk? Technically speaking, the surgery is always worthwhile, since it allows the diagnosis, may alleviate the intracranial pressure and along with RXT and CMT, improve the patient prognosis.

THE ROLE OF THE ECONOMY IN GBS TREATMENT: DEVELOPED X DEVELOPING COUNTRIES

Even though the natural course of GBs has changed little over the years, when one faces the reality in developing countries, things are still worse. Many times, the patients have his or her surgeries done, but even before they get access to the RXT and CMT, the tumor grows all over again, given the time between the referral for those treatments and the beginning of the therapy itself. Frequently, many patients die before getting the chance of undergoing the RXT and CMT. In addition, many centers in developing countries lack CMT and RXT as an adjuvant treatment, imposing still worse figures. Sadly, there are no papers that might prove this point, giving us the right records for the undertreated patients. Besides, due to the patients' worsening, many times the relatives claim for a new surgery "in order to try something", which is contrary to the right medical conduct. So, one wonders why those patients do not receive the right standard treatment despite it being relatively inexpensive. Until when the health policies regarding GBs are going to keep the same in developing countries? To accept a deplorable scenario concerning GBs treatment in those countries is to agree that, as a doctor, you are at least complicit in this colossal health care failure.

THE FLIP SIDE OF THE COIN: THE CASE OF THE STATE AND HEALTH CARE PROVIDERS

While seen from an economic perspective, the treatment of GBs is debatable, with figures not favoring a great cost benefit rate. There is a lack of papers that analyze the costs of treating GBs (see references). However, one thing that is clear is that both state agencies and health insurance make all their efforts to postpone the treatment. Even though one cannot prove the nature of this accusation, it seems clear to any doctor that is involved in GBs' treatment. Apparently, the amount of time that they "gain" is enough to contraindicate a certain treatment, since the worsening of the symptoms that naturally happen are a contraindication to a surgery, for example. Doing so, less money is spent on the treatment itself.

THE DIFFERENCE BETWEEN THE PRIVATE MEDICINE AND THE PUBLIC ONE: THE CASE OF BRAZIL (AND POSSIBLY MANY OTHER COUNTRIES):

When observed from the diverse health care systems around the world, the kind of hospital the patient has been treated in, things might be even worse. The impact of being treated in a private hospital plays a significant role in patients' outcome. The lack of standard treatment in public hospitals imposes to the doctors a self-limited care. In other words, not having CMT and RXT is the hallmark of the catastrophe that became treating patients with GBs in the developing world. However, when the patients from the developing countries get access to the standard treatment, their outcomes are about the same as in the developed countries. Consequently, the lack of resources seems more influential than the country or any other epidemiological variable.

THE PATIENT AND HIS OR HER FAMILIES' OPINION:

When one sees the GB´s from the viewpoint of the sufferers, it is easy to understand how desperate it should be. It seems like a death sentence that you get once received the final diagnosis. The feeling and sensation of impotence, frustration and loss of all relatives is something that, as a doctor, you never want to see. Not to mention, for those who have not lived "enough" their lives it's still worse, adding a worse ingredient when he or she has young children to take care of. In a world where references, as fathers and mothers are missing, GB´s might look like a curse for the patients and his or her families. However, the question that often arises is: is it possible in the middle of this turmoil to learn something from your own life? Not rarely the answer is "yes, indeed!" Even though the obvious consequences are death and suffering, the whole process according to the patients and his or her relatives imposes reflections, judgment and self-analyses of their lives. Sometimes, according to them, a slow death creates opportunities that they would have never experienced if they

had had a sudden death, for example. Finally, chances to apologize and reestablish relations are invaluable according to them.

SHOULD ONE INSIST ON THE SAME THERAPIES AND EXPECT DIFFERENT RESULTS?

Even with the advent of new technologies in oncology and in neurosurgery, the only option of treatment still is what one named standard treatment, which has marginal benefits, as mentioned. However, the question that always arises is: why are we still expecting different results and outcomes if one does almost the same thing over the past 20 years? Although immunotherapy has been used with significant results in melanoma and non-small lung cancer, its benefits for GBM are still limited[8, 9]. Therefore, up to now, one cannot expect different results from what one has been doing.

THE BENEFITS OF INVESTING IN AN INCURABLE DISEASE IN A DEVELOPING COUNTRY AND NEGLECT THE MOST COMMON DISEASES

One lives in a world with 85,5% of developing countries, with more than 700 million people living in extreme poverty[10, 11]. In addition, according to WHO, more than x people still die from curable and avoidable diseases such as diarrhea and infectious diseases. Considering the nature of GB's, committing age people, with short life expectancy and taking into account that infectious diseases are a leading cause of death in infants, may raise the question: Is investing in a CT for an incurable disease detrimental to curable ones in infants? The limit of financial resources imposes those tough questions in developing countries. This may be unthinkable for doctors living and working in a developed country, although it is a routine fact in developing countries, where prioritization of resources is mandatory.

THE (MANY) UNANSWERED QUESTIONS:

There are no answers for most topics here exposed. Given the differences not only in cultural aspects but also in social ones, the right approach should be individualized according to each culture. The way each culture faces death and grief is very peculiar. Should one treat a patient in his or her 80's or 90's with a potential morbid surgery, even though they are in a great clinical shape? Alternatively, is the best conduct to deny a treatment to a given patient who still has faith and hope about what the future holds? In addition, in a developing country is fair to leave a patient with a treatable and "simpler" disease without access to his or her therapy since this country decided to invest only in more "complex" diseases such as GB´s? Those and many other questions explain well our human nature, with all our limitations, uncertainties and frustrations. However, one should keep in mind that one can still make a difference in our patient and relative´s lives by comforting,

explaining and trying to be in somebody else's shoes. In the end, that makes us human beings, being able to feel sorry for someone and at the same time saying: “I am here! You can count on me”.

FINAL REMARKS

Although one seems to be far from GBs cure, some advance was seen in its treatment over the last years. Even though this advance has not been significant, it could provide patients and their families with the opportunity to solve many problems and conflicts until then unsolved. However, one should keep in mind that so much is necessary to implement decent centers in developing countries as well as in public hospitals. While one should consider the costs of the whole treatment as required for the State and health insurances, one ought to keep in mind the main interest in this process: the patient. His or her own fears, feelings, frustrations and one single certainty: the natural evolution of his or her tumor, which means death in its indelible path.

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