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***Corresponding author:** Kayode AA Abolanle, Department of Biochemistry, Babcock University, Ilishan-Remo, Ogun State, Nigeria, Tel: +234-8038272670; E-mail: bolakayot@gmail.com; kayodeab@babcock.edu.ng

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ORCID: <https://orcid.org/0000-0002-7101-9177>

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Review article

Brain Tumor: An overview of the basic clinical manifestations and treatment

Abolanle AA Kayode^{1*}, Amina Shahzadi², Muhammad Akram³, Hina Anwar³, Omowumi T Kayode⁴, Omowumi O Akinnawo¹ and Sunday O Okoh⁵

¹Department of Biochemistry, Babcock University, Ilishan-Remo, Ogun State, Nigeria

²Department of Eastern Medicine, University of Poonch, Rawalakot Azad Jammu and Kashmir, Pakistan

³Department of Eastern Medicine, Government College University Faisalabad-Pakistan

⁴Department of Biochemistry, Landmark University, Omu-Aran, Kwara State, Nigeria

⁵Department of Chemical Sciences, Faculty of Science and Science Education, Anchor University, Lagos, Nigeria

Abstract

We review the basic clinical manifestation, diagnosis and management of brain tumor.

Google search was done by using different terms associated with brain tumor and different databases were used, such as Google Scholar, Cochrane Database, and Science Direct etc.

In spite of the fact that clinical manifestations fluctuate on the basis of category, magnitude and site of tumor, the most common clinical features reported are persistent headache, seizures, nausea and vomiting, loss of consciousness, dizziness, mood fluctuation, cognitive problems, visual defects, weakness of body parts, difficulty with speech and language, and hearing impairment. Apart from neurologic examination, diagnostic approaches include Computed Tomography (CT) scan, MRI and biopsy.

Treatment strategies, determined by a variety of factors, include surgery, radiotherapy, chemotherapy and indicative therapy. This mini-review summarizes brain tumor biology as regards its classification, grading, risk factors, clinical presentation, diagnostic tools and treatment modalities.

Background

Brain tumor constitutes 2–3% of all malignant neoplasms and nearly 85–90% of all primary CNS tumors, with an estimated five-year survival rate of up to 35% for malignant tumors and about 90% for benign tumors [1]. Studies put brain tumors in the list of most common malignancy after leukemia in children with an incidence of up to 25% [2,3]. Growing prevalence rate in developed countries may be attributed to availability of advanced techniques for detection and diagnosis when compared to that of developing countries where most

people have limited access to equipment for early detection. This results in undiagnosed and unregistered cases, thereby, decreasing the level of incidence and prevalence reported [4]. Brain tumors are diagnosed at the age of 3–12 years in children and 40 – 70 years in adults. Brain tumors range from benign to malignant and eventually to metastatic tumors. Metastatic brain tumors are more prevalent in adults [5]. Carcinomas metastasizing to brain include lung, breast, skin (melanoma), kidney and colon with predominant contribution made by lung cancer (small cell lung cancer), accounting for about one half of all disseminated cases, according to reports from various



studies [6-9]. Brain tumors are graded from I-IV by World Health Organization (WHO) on the basis of their catastrophic potentials [10]. The tittle, low grade tumor (I & II) is appropriate for tumors with excellent and good prognosis in contrast to high grade tumors (III & IV) which tend to be malignant, thereby, leading to serious complications [11]. Primary brain tumor categories owing to cell type from which they originate are: gliomas; having their association with glial cells, meningiomas; abnormal growth of meninges, ependymomas; originate from cells (ependymocytes) lining the CSF filled ventricles, astrocytomas; developing from star-shaped glial cells (astrocytes) and so on. The majority of primary brain tumors are gliomas, a class of tumors evolving from supporting cells of the nervous system (glial cells/ neuroglia), with an integer of nearly 33% [12]. Gliomas have various histological subtypes grading from pilocytic astrocytoma (innocent and least offensive) to glioblastoma (drastic and terminal illness) [13]. Normally, gliomas are tumors of adults with their optimal presentation beyond 45 years of age, although it can come up at any other period in a lifetime. Susceptibility of men to gliomas has been reported as well as other brain tumors except meningiomas which are more frequent among females [14].

Main text

Risk factors

Etiology of primary brain tumors is still obscure, however, there are some risk factors ascribed for population susceptibility to tumors (Table 1). Besides its reliance upon cellular origin and location of tumor, probability of brain tumors increases with age, with the utmost frequency between 55 and 64 years of life. Brain tumors incidence is distributed between the two genders in a male to female ratio of 1.5:1, excluding meningioma which are virtually customary to the female folks only [15]. Literature shows propensity of white population in the US to gliomas as well. There have been some inconsistencies regarding the risk factors of brain tumors compared to other body tumors. Despite the controversy surrounding the risk factors, prior subjection of the head to high dose of ionizing radiations such as X- rays, CT scans [16] and MRI, especially for therapeutic purpose are some of the risk factors implicated in the development of brain tumors [17-19]. It is has been reported that children exposed to radiotherapy for the treatment of various diseases are vulnerable

to brain tumors within an interval of practically 15 years after exposure. Radiation-induced brain tumors development are relatively common among young ones experiencing leukemia. Although genetics plays part, there are some inherited cancerous conditions such as neurofibromatosis types I & II, Von Hippel- Lindau disease , Tuberous sclerosis, Li-Fraumeni syndrome, Coden disease, Gorlin syndrome, Turcot syndrome making a contribution of up to 2% to brain tumor [20,21]. Publications proposing contribution of other risk factors i.e. cell phones, viruses, allergens, alcohol, N-nitroso compounds, infections, chemicals and smoking on subject of establishment of brain tumors have been conflicting. Although no specific statement regarding cell phone as a risk factor is available [22], the World Health Organization (WHO) suggests restricted usage of mobile phones considering them feasibly noxious.

Clinical presentation

Clinical manifestations of brain tumors are baffling and fluctuate substantially depending upon the category, locality, bulk & rate of growth of tumor [23]. With respect to pathogenesis, clinical features can be graded into raised intracranial pressure and focal, a characteristic of indigenous tissue destruction [19,24]. To date, the most reported symptom experienced by patients have been headache [25]. Headache being categorized as a general feature is one of the ordinary complaints experienced by nearly one half of victims. Headache presents itself as an inceptive symptom in most of cases. Besides headache and seizures other manifestations include nausea and emesis, ataxia, visual disturbances, personality and behavior changes, speech difficulties, altered consciousness, sleep disturbances, drowsiness, fatigue, memory problems, tingling sensations in some body parts [25,26]. Focal symptoms in the areas of brain involved include:

Frontal lobe

Personality and behavior changes, Cognitive dysfunction, Memory loss, Contralateral motor loss.

Parietal lobe

Spatial disorientation, Writing, naming and drawing difficulties, Aphasia, Recognition problems.

Occipital lobe

Unilateral/ bilateral vision loss, Visual field defects, Illusions, Hallucinations, Blurred vision.

Temporal lobe

Short and long-term memory problems, Speech and language deficits, Emotional changes e.g. aggressiveness, Difficulty in understanding words.

Cerebellum

Ataxia, Difficulty with fine motor skills.

Brainstem

Difficulty in swallowing, Facial paresis/ tingling, Double vision.

Table 1: Risk Factors associated with brain tumor.

Validated Risk Factors	Unverified Risk Factors
Environmental	Environmental
Prior exposure to high-dose ionizing radiations	Cell phones
Genetic	Alcohol
Neurofibromatosis types 1 & 2	Virus- induced
Li-Fraumeni syndrome	Infections
Von Hippel-Lindau disease	Smoking
Tuberous sclerosis	Exposure to Vinyl chloride, Pesticides, Rubber etc.
Turcot syndrome	Dietary N-nitroso compounds
Cowden disease	Exposure to Aspartame
Gorlin syndrome	Exposure to Electromagnetic fields
	Genetic
	Genetic polymorphisms (e.g. XRCC1)



Diagnosis

Comprehensive medical history combined with thorough general physical examination, coupled with neurologic examination, relevant imaging modalities and histopathological assay are very crucial in the establishment of the diagnosis. While performing neurologic examination, the neurosurgeon assesses vision, coordination, reflexes, hearing, orientation, muscle tone etc. Aside from regular MRI which is a primary tool, other imaging modalities of note include gadolinium enhanced-MRI, functional MRI, perfusion MRI, CT scan, PET-CT scan [27]. Depending upon the requirements, further diagnostic tools can be lumbar puncture/spinal tap, stereotactic biopsy, angiogram, molecular assay, myelogram and craniotomy. MRI which uses strong magnetic fields rather than X-rays/ ionizing radiations to produce transparent depiction, is a desired imaging technique followed by other diagnostic tools [10]. Although MRI is a central imaging tool in patients, where MRI is not a desirable due to any reason (obesity, indwelling implants, catheters, fear of close spaces), CT scan can be used as an option. Besides radiology (MRI / PET-CT scan etc.) that boasts striking worth in diagnosis, histopathology is imperative for evaluation of variety of tumor making the diagnosis certain.

Treatment

Elements that determine therapeutic approaches can be grouped into tumor's extent, category, grade, site coupled with patient's age, general fitness, comorbidity and their choice of treatment [28]. A multidisciplinary team consisting of neurosurgeon, medical specialist, medical oncologist, neurosurgeon, radiation oncologist and nutritionist design the schedule of treatment. Regular remedial plans include scrutiny, symptomatic treatment, surgery, radiotherapy, chemotherapy, targeted therapy, physiotherapy exclusively/or in combination. Surgical removal being typically the major one is the mainstay of treatment in most of the cases, frequently required solely in benign ones [29,30]. The added advantage of surgery is the provision of tissue for histopathology thereby serving in the determination of further treatment. Also in cases, where patient cannot be cured by surgery, excision of tumor assuages the burden of symptoms ascribed to pressure of growth. Inoperable growths because of location/or other factors, restricts the application of surgery. High-grade tumors often entail a combination of surgery, radiotherapy and chemotherapy [30,31]. Radiotherapy (treatment with radiations (high-energy beams)) generally accompanied by surgery is classified into external-beam radiotherapy, internal radiotherapy/or brachytherapy, conventional radiotherapy, 3-D conformal radiotherapy, intensity modulated radiotherapy, proton therapy and stereotactic radiosurgery, of which the common one is external- beam radiotherapy. Often accompanied by surgery, regular chemotherapy (a form of systemic therapy) can be directed singly/concomitantly with targeted therapy by medical oncologist. Contemporary therapy comprise of radiotherapy and chemotherapy as the standard way of treating inoperable cases as well as in cases of primary malignant tumors accompanied by surgery. In recurrent cases, it is also known for its relevant worth. Chemotherapy regimens

regularly divided in cycles given over a scheduled interval of time can be taken intravenously or orally. Targeted therapy, another type of systemic therapy, categorized into two main types, basically attacks the tumor's specific proteins, genes and the habitat that facilitates tumor's growth and survival without causing damage to normal cells. Alternating electric field therapy carried out by Optune (a noninvasive portable gadget) is also brought into consideration as a therapeutic tool for glioblastomas. Besides the afore mentioned treatment strategies, the patient is also subjected to other treatment protocols i.e. regular follow up, rehabilitation therapy in addition to palliative/ supportive care [32].

Conclusion

Brain tumor, a subject matter bearing a lot of disharmony and hesitancy, calls for further epidemiological exploration to be carried out and elucidated conservatively. Though brain tumors are not frequent among adults, their frequency is growing possibly due to advanced diagnostic techniques available in developed countries.

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