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PSYCHIATRIC MANIFESTATIONS OF BRAIN TUMOURS: A REVIEW

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ABSTRACT

Objective: To carry out a current review of psychiatric manifestations of brain tumours

Data Source: To carry out a review of psychiatric manifestations of brain tumours utilizing electronic databases in the internet including Google Scholar, PubMed, Medline, MedScape and Psych Info Searches.

Data Extraction: Abstracts of relevant articles identified were assessed, read, and analysed to determine their eligibility and relevance to the subject under review

Data Synthesis: After establishing eligibility and relevance from abstracts, the entire article was read and the significant points incorporated in the subject under review

Conclusion: Tumours of the brain can present clinically with neurological or psychiatric symptoms or a combination of both. Rarely patients present with psychiatric symptoms without physical or neurological localizing symptoms frequently leading to misdiagnosis and mistreatment with psychotropic drugs. Clinicians must have high index of suspicion when managing psychiatric symptoms that are atypical, new-onset, anxiety, or with poor response and resistance to known and efficacious psychopharmaco-therapy treatment regimes, as there may be an underlying brain tumour responsible for the symptomatology. This must be ruled out through effective neuro-imaging techniques including Computerized Tomography (CT) scan and Magnetic Resonance Imaging (MRI), and if diagnosis confirmed, treated definitively by surgical excision, radiotherapy and chemotherapy alone or in combination.

INTRODUCTION

Brain tumours are either primary or secondary from other common primary sites

such as urinary bladder, breast, lungs, kidney and melanoma. Prostate and colon cancer rarely metastasize to the brain. Brain tumours are relatively common with an

annual incidence of 9 per 100,000 for primary brain tumours and 8.3 per 100,000 for metastatic brain tumours, and may be classified on the basis of anatomical location or histopathologic characteristics. The most common primary brain tumours are gliomas which arise from glial tissue and account for 40%-55% of all brain tumours. Secondary tumours metastasizing to the brain represent 15%-25% of all brain tumours (1-4). A great majority of brain tumours present with specific neurologic symptoms and signs due to mass effect. However a few number of patients present primarily with psychiatric symptoms only as the first clinical manifestation of brain tumour. They are considered as secondary causes of psychiatric symptoms alongside drugs, infection and metabolic disturbances (4-6).

Whether an intracranial mass develops in the presence of psychosis, or the psychosis develops as a result of it, the psychiatric symptom may effectively clinically mask the presence of a brain tumour due to the complete absence of neurological localizing symptoms and focal neurological deficits (7-9). Symptoms of brain tumours depends on the functions of the anatomical location of the brain affected. For example anorexia symptoms are associated with pituitary tumours, mood symptoms with frontal lobe tumours, and memory symptoms with thalamic tumours (10, 11). Approximately three percent of institutionalized psychiatric patients also present with brain tumours, this being a very uncommon phenomenon (7,12).

The prevalence of major depressive disorder (MDD), utilizing DSM IV criteria in patients who were treated for primary malignant brain disease is at 28%. In-patient psychiatric consultations in a sample of brain tumour patients showed that 41% were diagnosed with organic brain disorders (13). This only goes to an extent to show that cases of misdiagnosis are high, which can be attributed to some extent to

the natural presentation and progression of the disease process (14-16). This review summarizes psychiatric manifestations associated with brain tumours, their clinical presentation, diagnosis, and management including treatment and prognosis including historical and African perspectives.

HISTORICAL PERSPECTIVE

During the first century, there were reports of the 'madness' of Emperor Titus, in the Talmudic tradition, being associated with an object that looked like a sparrow, "two selas in weight " after physicians opened his skull upon his demise (12). Beliefs in the middle ages and the renaissance depict psychiatric symptoms being associated with a 'stone' in the brain (12). During the 16th and 17th centuries, as the practice of performing autopsies picked up, links were established between brain tumours and mental symptoms.

Clinically, Giovanni Battista Morgagni (1682-1771) was the first physician to describe a patient with psychiatric symptoms and what seemed like a brain tumour (12). Further, connections were recognized as the scientific practice of empirical data gathering took root.

Fast tracking to the late 20th century there are cases of brain tumours being diagnosed very late- referred to as neurologically silent tumours. Diagnosis of these tumours was made using imaging modalities, and some at necropsy (7,17). Currently, the availability of newer neuro-imaging techniques has made it easier to rule out brain neoplasms in patients who present with atypical psychiatric symptoms.

AFRICAN PERSPECTIVE

There is paucity of data on neuropsychiatry of brain tumours within the African region. Studies conducted in Africa show that the extent of mental illness in Africa is at least as

substantial as the rest of the world and evidence suggests that morbidity rates due to mental illness may even be greater in Africa (18). Despite this phenomenon, the continent is burdened with several other issues such as communicable diseases, malnutrition and low life expectancies, thus making mental illness among the last on the list of the policy makers. This is further compounded by poor funding of health activities, and lack of mental health policies, programs and action plans in a number of African countries (19). The burden of mental health is expected to get worse, and the proportion represented by Africa is bound to get higher.

There is also a high prevalence of superstitious beliefs in Africa and mental illness is associated with supernatural phenomena. This causes patients to present late at health facilities as a considerable amount of time is spent at traditional healers prior to presentation. Depression and anxiety appear to be omnipresent as is similar elsewhere (18). Psychosis presents frequently acutely or sub-acutely. It is sometimes associated with other diseases such as malaria and HIV/AIDS that are prevalent in this region.

The use of drugs is also on the rise as young Africans attempt to emulate lifestyle choices promoted on media. The presence of conflict and strife in several African countries is a cause for concern. On the other hand, African societies have a generally strong family bond which increases the ability of an individual to deal with mental illness due to the support available. Other efforts made include; collecting information about mental health programs, supporting training activities, and creating networks for collecting and disseminating relevant information in the fields of psychiatry and mental illness (19). The problems above further compound the diagnosis of neuropsychiatric disease within this continent.

In Kenya, a mental health report by Kenya National Commission on Human Rights titled silenced minds: the systemic neglect of the mental health system in Kenya published in 2011 (20) brought to attention the marginalization of mental illness which has consequently led to the discrimination of persons suffering from mental disorders. It further indicated that mental health conditions contribute significantly to the disease burden in Kenya and that there is a low clinician detection rate for mental disorders. This is corroborated by Ndetei et al who put the clinician detection rate at 4.1% (21).

The above can be in one way extrapolated to mean that most psychiatric illnesses remain undiagnosed or misdiagnosed and untreated or mistreated. In connection to this review it is imperative to also note that some brain neoplasms may present with psychiatric symptoms which may contribute to misdiagnosis. Thus a holistic approach in history taking, examination and diagnosis is mandatory.

Another report by Kiima et al titled Mental health policy in Kenya concluded and demonstrated the use of a multi-faceted and comprehensive program to promote sustainable system change in light of an integrated approach to scaling up equitable care for poor populations (22). Although most donor and development agency attention is focussed on communicable diseases in Kenya, the importance of non-communicable diseases including mental health and mental illness is increasingly apparent, both in their own right and because of their influence on health, education and social goals. Mental illness is common but the specialist service is extremely sparse and primary care is struggling to cope with major health demands. Non health sectors e.g. education, prisons, police, community development, gender and children, regional administration and local government have

significant concerns about mental health, but general health programmes have been surprisingly slow to appreciate the significance of mental health for physical health targets. Despite a people centred post-colonial health delivery system, poverty and global social changes have seriously undermined equity. This project sought to meet these challenges, aiming to introduce sustainable mental health policy and implementation across the country, within the context of extremely scarce resources. Of note, there are two major elements amongst others in the report which in one way or another touch on neuropsychiatry and the need for its emphasis. These are one, advocacy and public education which can go ahead to look at the neuropsychiatric manifestations of brain tumours and the need to increase the clinician's diagnostic acuity. Two is the use of rapid appropriate treatment at the primary care level which can point out at the use of neuroimaging for all patients who present with alterations in mental status and/or psychiatric symptoms.

From the rest of Africa, an overview in 2005 by Oosthuizen from South Africa discussed the factors likely to affect the clinical presentation of brain tumours, clinical clues that a brain tumour may be present and possible localizing features of brain tumours (23). The paper concluded that neuro-imaging is not necessary in all patients, however clinicians have to be vigilant in patients older than 45 years with new onset, sudden onset symptoms or sudden changes in personality and behaviour (23).

Ouma reported 2 cases of adult patients in South Africa who were diagnosed with psychosis and later found to have intraventricular tumours (24). In both patients, the psychotic manifestations disappeared following surgical removal of the tumours (24). A 3 year necropsy based study by Cole revealed that 5 out of 6

cerebral neoplasms in psychiatric patients were undiagnosed. The psychiatric symptoms that were prominent included: dementia, psychotic symptoms, and confusional states. Thus, a higher index of suspicion among the clinicians would have led to earlier detection and possibly prevention of death (7). Only 3 studies identified in the literature on neuropsychiatry were from South Africa and they point overall to the paucity of data from the African region on neuropsychiatric manifestations of brain tumours.

DIAGNOSIS

Brain tumours are only rarely responsible as the primary cause of psychiatric symptoms in patients. There are very serious diagnostic challenges as a result of this rarity, coupled with the vague symptomatology, and the insidiousness of the disease process. Diagnosis must therefore commence with a high index of clinical suspicion which may result in early diagnosis, treatment and better quality of life for the patient. A complete medical history and physical examination is mandatory to exclude psychiatric symptoms such as personality and mood change, anxiety, anorexia, atypical or new-onset symptoms that are refractory to treatment (3,16). Abnormalities in Vitamin B12 and folate levels, thyroid function tests, liver function tests, full blood count and serological tests for syphilis can cause a patient to present with psychiatric symptomatology similar to those which may be seen in patients with brain tumours. These are some of the medical causes of psychiatric symptoms that have to be ruled out in a patient suspected to have a brain tumour. It is necessary to rule out brain tumours using neuroimaging techniques especially in patients who present with atypical, new-onset, and symptoms resistant to treatment. Neuroimaging, being the primary diagnostic modality utilized to

investigate brain tumours is carried out through computerized tomography (CT) scanning, and magnetic resonance imaging (MRI). Magnetic resonance spectroscopy is used for the relative quantification of various metabolites in different parts of the brain. MRI is more efficient compared to CT scanning and is the procedure of choice when available. MRI offers higher resolution and is useful in evaluating brain tumours, necrosis, haemorrhage, cysts and white matter changes (3,4,16). It is currently recommended that any patient above the age of 40 years with a change in mental status, cognitive or emotional, should have neuroimaging of the brain especially if there is no other clear alternative aetiology. Neuroimaging is also necessary in psychiatric patients with specific neurobehavioral or neurologic findings or a poor response to psychopharmaco-therapy or those with apparently 'functional' affective illness (1,4).

TREATMENT

The standard therapy for treatment of brain tumours is surgical resection followed by a combination of chemotherapy and radiotherapy. This may completely resolve the psychiatric symptoms, as most of the cases point towards the neoplasm being the underlying cause of the symptoms. Additionally, the treatment of acute mass effects such as increased intracranial pressure or hydrocephalus may improve cognitive functioning and reduce psychiatric and behavioural symptoms. Excision of the neoplasm is usually followed by considerable improvement in psychiatric symptomatology. However in some few cases, neuropsychiatric and behavioural symptoms persist or even worsen after surgical excision. Under these circumstances, psychotherapeutic measures are instituted in order to improve the clinical

state and quality of life of the patient (2,3,13).

Pharmacological management follows general therapeutic principles of tumour free patients with similar psychiatric symptoms. However, patients with brain tumours may have increased susceptibility for delirium, seizures and side effects of treatment. Antidepressants are efficacious in patients presenting primarily with depressive symptoms, while mood stabilizers are useful in the treatment of manic symptoms. Antipsychotics treat psychosis with hallucinations, delusions and disturbances in thought content and processes. Patients who after surgical resection and radiotherapy still have symptoms of depression that are not responsive to medication can be treated with electro-convulsive therapy (ECT) with good outcomes. Psychotherapy is also an important treatment modality which assists in improving overall functional status, functional and psychological stressors and functional cognitive status (3,5,25).

PROGNOSIS

Patients treated with surgical resection of the tumour improve the neuropsychiatric symptoms; and the cognitive function deterioration is completely eliminated or reduced following surgical intervention. Patients are also able to discontinue their psychotropic medication due to significant improvement of symptoms (25).

DISCUSSION

Patients with brain tumours clinically present with signs and symptoms ranging from physical to psychological: These may occur either concurrently or one group of symptoms pre-dominates over another. In some cases psychiatric symptoms may precede neurological symptoms. In patients presenting with psychological symptoms

alone, it is imperative that clinicians have a high index of suspicion to suspect brain tumours and order for neuro-imaging studies. This is especially important in patients with new-onset symptoms, atypical psychiatric symptoms or symptoms resistant to psychotropic medication (16).

Psychiatric symptoms that may be present include: mood changes (depression or mania), dementia, psychotic symptoms, anxiety, personality changes, catatonia, anorexia nervosa or memory difficulties in the absence of neurological symptoms (1,4,26–28).

Younger patients may also manifest these symptoms as anxiety, school phobia, psychomotor delay and mood changes (29–31). Patients with existing brain tumours can also be diagnosed with psychiatric symptoms such as depression due to the diagnosis, poor prognosis of some brain tumours and the long term rehabilitation that is required for this condition (32). Adjustment disorders are more frequent than organic mental disorders but this can be reversed in primary brain tumour patients (13). Patients with lesions of the ventral frontal cortex or lesions of the temporo-parietal cortex reported post-operatively significantly worse mood states than patients with lesions elsewhere (33).

Several attempts have been made to correlate psychiatric symptoms with brain tumours that occur in particular locations. Frontal lobe tumours have been reported to commonly be associated with abulia, personality changes or depression; temporolimbic tumours associated with auditory and visual hallucinations, mania, panic attacks or amnesia; and tumours in silent regions of the brain such as the occipital lobe, corpus callosum and intraventricular areas to present with transitory psychiatric symptoms (2,4,23,34,35).

The frontal lobes can be divided into the orbitofrontal area, frontal convexity, and

medial aspects of frontal lobes that cause three different symptom complexes. The orbitofrontal area lesions are associated with 'pseudopsychopathic' features such as disinhibition, impulsivity, inappropriate jocular effect, euphoria and emotional lability, whereas the frontal convexity tumours present with apathy, indifference, psychomotor retardation and occasional sudden, aggressive outbursts with no or minimal provocation (23). The clinical picture of medial aspects of frontal lobe lesions is profound reduction in spontaneous movements, speech, poor response to commands and episodes of incontinence (23). However, despite these attempts at correlating psychiatric symptoms with particular locations of brain tumours, the clinical picture still remains non-specific and unreliable (4,11).

The commonest tumour diagnosed histologically was a glioma. These patients were mostly female and their ages ranged from 24 to 79 years. The symptomatology included; depressed mood, insomnia, anhedonia, hopelessness/helplessness, poor appetite, poor general function, weight loss, and suicidal ideation and attempts. The patients may also manifest with seizure like symptoms. Other patients with a diagnosis of glioblastoma multiforme (a grade IV glioma) presented with auditory hallucinations, visual memory deficits and dissociative symptoms (36).

Posterior fossa and pineal meningiomas present with peduncular hallucinosis (37,38). This refers to a psychosensorial disorder consisting of multiple visual coloured images of brief duration which occur in the dark, and the patient is aware that the images are not real (38). Middle and superior frontal meningiomas present with depression, apathy, incontinence, dementia and fits whereas basal frontal meningiomas are associated with hypomania and hallucinosis (39,40). Olfactory fossa

meningiomas may also present as a depressive disorder (41).

Paediatric germ cell tumours may have atypical presentations consisting of psychomotor delay, as well as behavioural and mood changes (30). These presentations may delay diagnosis and treatment and may be secondary to atypical locations as well as endocrine dysfunction manifesting as psychiatric symptoms (30). Pituitary adenoma may present with refractory depression and psychotic features with Cushing disease (42). Craniopharyngiomas may exhibit recurrent depressive illness or mania (31,43). Colloid cysts, which account for approximately 2% of primary brain tumours, and usually develop in the rostral aspect of the third ventricle in the foramen of Monroe, have a high prevalence of psychiatric symptoms. The psychiatric symptoms occur as frequently as the classical neurological symptoms and range from anterograde amnesia to gustatory hallucinations (44). These gelatinous neoplasms lined by a single layer of mucin-secreting columnar epithelium that are thought to arise from errors in folding of the primitive neuroepithelium. They develop in the rostral aspect of the third ventricle in the foramen of Monroe in 99% of cases and despite their benign histology carry a poor prognosis, with mortality greater than 10% in symptomatic cases. The location of colloid cysts within the ventricular system results in obstruction of the foramen of Monroe as the cyst grows, disrupting the circulation of cerebrospinal fluid (CSF). Lesions of the corpus callosum that are growing such as a haemorrhagic cavernous haemangioma can presumably cause acute psychotic attacks (45). Temporal cavernous haemangiomas clinically also present with recurrent panic attacks mimicking panic disorder (46).

A review of 8 patients by Filley et. al revealed that benign transitional-type meningioma manifested with progressive apathy, social withdrawal, and poor self-

care; malignant immunoblastic lymphoma manifested with personality changes, and irritability; metastatic squamous cell carcinoma showed profound depression, oligoastrocytoma manifested auditory hallucinations, memory and word finding problems, oligodendroglioma manifested auditory and visual hallucinations, glioblastoma multiforme manifested intermittent depression, flight of ideas, and pressured speech; and pituitary adenomas manifested panic attacks and depression (2). Arachnoid cysts may present with obsessive compulsive behaviour associated with psychosis (47). These reveal that there is a wide band of brain tumours that may manifest with psychiatric symptoms.

The past medical and psychiatric history is important in these patients. Prior admissions in psychiatric facilities, the duration of admission, the diagnosis during each admission (as these might change over time due to the prevailing symptoms), and medications prescribed, the patient's response and compliance should be clearly captured during history taking in these patients.

Some patients may also have a prior history of another tumour or a familial history of cancer (4). The drug history of the patients, especially marijuana and alcohol use are important as they may significantly contribute to the psychiatric manifestations. Sexual and physical abuse should be directly questioned as the patient may have symptoms suggestive of post-traumatic stress disorder. HIV positive patients with primary CNS lymphomas (PCNSL) may present with neuropsychiatric symptoms (48). Notably, the psychiatric symptoms may manifest for a period of between months up to 4 years before the patient shows any indication of tumour on imaging (2,4).

The Folstein Mini Mental State Exam (MMSE) is important in systematically assessing and documenting findings in patients with psychiatric symptoms (49,50).

The score of the exam will be based on the prevailing diagnosis of the patient. Supplementary rating scales such as Beck Depression Inventory (BDI) and Hamilton Rating Scale for Depression (HRSD) help to further strengthen the diagnosis. Patients will score variably on the Glasgow Coma Scale (GCS) depending on the extent of the tumour and its mass effect, and the time of presentation of the neurological symptoms (51).

Neoplasms destroy particular regions of the brain and these then have an effect on the person's functioning, depending on whether the area involved is motor, sensory or for behavioural function(2). Notably, the tumours are generally not discretely located in one area as is seen in cerebrovascular lesions and thus it is difficult to pinpoint an explicit psychiatric symptom that is associated with the neoplasm (2,11). However, general conclusions on the possible location of the tumour can be drawn from the symptomatology and guiding principles that state the functions of a lobe(52). By way of illustration, a tumour in the frontal lobe may likely result in 'frontal lobe syndrome' that includes disinhibition, apathy, abulia, and deficits in executive function (2). For instance, a patient with a hemangiopericytoma involving the orbitofrontal cortex exhibited impulsive sexual behaviour with acquired paedophilia, marked constructional apraxia, and agraphia as reported by Burns et.al (53) altered sexual behaviour, and sociopathy. The patient displayed impulsive sexual behaviour with paedophilia, marked constructional apraxia, and agraphia. The behavioural symptoms and constructional deficits, including agraphia, resolved following tumour resection. For patients with acquired sociopathy and paraphilia, an orbitofrontal localization requires consideration. This case further illustrates that constructional apraxia can arise from right prefrontal lobe dysfunction. Agraphia

may represent a manifestation of constructional apraxia in the absence of aphasia and ideomotor apraxia. On the other hand, patients with existing known cancers are at risk of depression and mood-related disorders which can be attributed to known morbidity and mortality of disease. The negative consequences of these disorders are suicidal ideation, increased physical complications and somatic symptoms which have a negative influence on overall prognosis (54,55). Thus, routine screening and adequate assessment of depressive spectrum disorders is necessary in these patients (54). Fatigue, emotional distress, and existential issues may exist; however, the presence of depressive symptoms is the single most important predictor of quality of life in these patients (56).

CONCLUSION

Psychiatric symptoms may be the only clinical presentation in a few patients with brain tumours. Clinicians must therefore have a very high index of suspicion when managing patients presenting with psychiatric symptoms that are atypical, new-onset, psychosis, anxiety, mood or memory changes, anorexia, or resistance to treatment. This is due to the fact that there could be an underlying brain tumour causing the symptomatology. This should be followed by a thorough history coupled with comprehensive physical examination mandatory for early diagnosis which is critical to prognosis and improved quality of life of patients.

Neuroimaging with computer tomography (CT) scan and magnetic resonance imaging (MRI) must be effected in all patients presenting with psychotic symptoms without physical or neurological localizing symptoms. Definitive management should focus on the treatment of the tumour, its complications, and the persistent psychiatric symptoms.

Management of brain tumours consists of surgical resection of the tumour, stereotactic radiosurgery, radiotherapy and chemotherapy. Treatment of the psychiatric symptoms caused by brain tumours depends on the presenting symptoms and includes antidepressants, antipsychotics and anxiolytics among others. Any patient diagnosed with brain tumour should also be assessed for psychiatric symptoms using the Mini -Mental State Exam (MMSE) in order to rule out psychiatric disorders.

FOOTNOTES

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