

Psychotic manifestations in brain tumour patients: 2 case reports from South Africa

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ABSTRACT

Two cases are presented of adult males diagnosed with psychosis who were found to have intraventricular tumours (central neurocytomas). In both cases the psychotic manifestations disappeared following surgical removal of the tumours. The relationship between structural brain lesions and psychotic manifestations is discussed.

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INTRODUCTION AND OBJECTIVES

Brain tumour patients usually manifest with features of raised intracranial pressure, focal neurological deficits and seizures. Psychotic manifestations are not usually seen. It must be recognized however that though rare, these can be the presenting features of intra-cranial tumours. Patients presenting with psychosis associated with atypical manifestations such as advanced age, resistance to treatment or focal neurological deficits and papillo-oedema should warrant a full workup to exclude structural intra-cranial mass lesions.

The main objective of this report is to highlight this population of patients who can be helped if properly diagnosed.

CASE NUMBER 1:

A 26-year-old black African male was admitted to the Johannesburg Hospital with an eight-month history of auditory hallucinations (mainly of command), delusions of grandeur and non-purposive violent outbursts with no clouding of consciousness. He complained of headaches occasionally. He had had no prior history of psychosis.

There was no history of substance abuse, febrile illness or any other significant medical complaints. He was placed on anti-psychotic medication by the psychiatric service but consistently defaulted on his treatment so that he was eventually admitted to the medical floor and a CT scan obtained on the basis of concern about the reported headaches. Prior to this, he had not been formally investigated.

Clinically he was in good general condition. He had bilateral papillo-oedema and no other focal neurological deficits, and was fully conscious. Mental status testing revealed disturbances in memory and higher cognitive functions especially calculations and proverb interpretation. The remainder of the parameters were within normal limits.

A CT scan of the brain (Figure 1) showed a homogeneously enhancing mass lesion in the left lateral ventricle associated with ventriculomegaly of that ventricle mass effect and midline shift.

He underwent a craniotomy at which the tumour was approached via the corpus callosum. It was pinkish-grey, moderately vascular and soft in nature. It was completely removed and histological examination showed it to be a central neurocytoma.

There was immediate resolution of all his psychotic symptoms following the operation.

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Figure 1:



Case Number 2:

A 43-year-old black African male presented with a 1½-year history of being extremely psychotic characterized by non-specific auditory hallucinations, persecutory delusions and episodes of non-directed violence. Unfortunately there was no family available to give history regarding substance abuse or any significant past medical events. He had been committed to a psychiatric institution in Johannesburg where the control of his condition was difficult even on multi-drug therapy. There was no record of any previous investigations having been done specifically with regard to his psychosis, nor any details regarding the treatment he had been on prior to admission to the psychiatric hospital.

On the basis of this difficulty in treatment, a CT scan of the brain was obtained (Figure 2). Clinically, he tended to be aggressive and uncooperative. He had no focal neurological signs. It was not possible to obtain formal mental status or neuropsychological testing owing to his state. There was no papillo-oedema on fundoscopy.

The CT scan demonstrated a predominantly solid enhancing mass in the left lateral ventricle and attached to the septum pellucidum. There were multiple cystic areas in the lesion. In addition, there was moderate hydrocephalus of both lateral

ventricles.

He too underwent a craniotomy with approach through the corpus callosum and complete removal of the tumour, which, as in the previous case, was also demonstrated to be a central neurocytoma.

Post-operatively, he was aphasic and had a right hemi paresis. These deficits improved to total recovery over a period of two weeks at which point he was found to have no residual psychotic manifestations.

Figure 2



DISCUSSION

Psychotic manifestations are not uncommon in clinical practice in South Africa, and the presentation of these two patients is likely to be repeated several times in any year in our hospitals.

Frequently, one finds that functional causes such as schizophrenia and manic-depressive psychosis as well as substance abuse of various types are the issues underlying most patients presenting in this manner.

The exact degree to which organic causes are responsible, and specifically space occupying mass lesions, is difficult to determine. Much of the wider population depend on community clinics and small, far flung peripheral hospitals for their primary care, and it is here that decisions are made which determine the course of their management. Access to more sophisticated secondary and tertiary hospitals with experienced clinicians and facilities such as CAT and MRI scans are not a luxury enjoyed by the majority of these patients.

Hence one can only speculate and extrapolate as to the size of the problem, on the basis of those patients who do end up at tertiary units such as ours, usually with long histories of being “known schizophrenics”, in whom alternative diagnoses are eventually made. We do see quite a few annually. When one reviews these patients, there are usually “red flags” present in either the history or the physical examination that could have alerted the original clinician as to the diagnosis of something more sinister than just another psychotic patient.

Among these are late onset psychosis, resistance to treatment in a compliant patient, headaches associated with the symptoms of psychosis, a history of seizures and any focal neurological deficit including, for this purpose, papilloedema. The mental status examination, where this can be done, can be quite helpful at alerting one to the possibility of lateralizing intracranial disease.

Tumours occurring in various parts of the brain have been associated with the presence of psychotic illness in the literature and in several instances resolution of psychotic symptoms has been documented after surgical treatment for these tumours.

A suprasellar germinoma involving bilaterally the basal ganglia has been associated with psychotic and obsessive-compulsive symptoms in a 13-year-old boy ¹.

A 26-year-old lady presenting with psychosis and found to have a meningioma in the right lateral ventricle with extension into the corpus callosum and periventricular white matter is discussed.² The symptoms completely resolved after surgical excision of the tumour and she remained in remission at the 2½-year follow-up point on no medications.

A 9-year-old boy is reported presenting with psychosis and found on MRI to have a tumour in the anterior third ventricle associated with mild to moderate hydrocephalus. On resection the tumour turned out to be a choroid plexus papilloma and the patient remained free of psychosis or mood disorder at one-year follow-up.³

Even more intriguing has been the reported association of posterior fossa structural abnormalities with neuropsychiatric symptoms ⁴. It is hypothesized that in these cases disruption of the cerebellar output to mesiodopaminergic areas, locus coeruleus and raphe nuclei or deafferentation of the

thalamolimbic circuits by cerebellar lesions may lead to these behavioural and psychiatric changes.

A 55-year-old woman with a six year history of uncontrollable complex partial seizures and severe delusions is reported to have improved following removal of a right frontal lobe mixed oligoastrocytoma or dysembryoplastic neuroepithelial tumour ⁵.

A case is reported of a 19-year-old female who had undergone resection of an astrocytoma of the left basal temporal lobe which had initially presented with psychomotor and grand mal seizures and who presented 30 months later with acute onset of paranoid psychosis including delusions and various hallucinations and on repeat MR scanning was found to have a small relapse of the tumour. Her psychotic symptoms responded to neuroleptic therapy and after surgical removal of the relapsed tumour there was a lasting remission of the psychotic symptoms with discontinuation of the neuroleptics ⁶.

Going against the grain of the previous reports in which psychosis improves after resection of a brain tumour, is a report ⁷ of psychosis developing after resection of a ganglioma or DNET (dysembryoplastic neuroepithelial tumour) for treatment of intractable epilepsy.

The two cases presented in this report had central neurocytomas proximal to elements of the limbic system and presumably developed psychosis on this basis, as rapid relief followed surgery.

Why psychosis does not complicate other cases with similarly located tumours, though, remains to be explained.

The concept of psychosis surgery is helpful to understand the possible structural aetiology of mental illness⁸. Disruption of the interconnections between the frontal and temporal lobes, the anterior insula, the mediodorsal thalamic nucleus and the corpus callosum may result in a hypothesized disconnection syndrome and manifest as psychosis including schizophrenia.

Papez ^{9,10} was the first to suggest the concept that a circuit of specific brain structures could be responsible for human emotion. Observing that the hypothalamus played a significant role in the expression of emotion and that higher cognitive function and thought arose from activity in the cortical areas, specifically the frontal lobes, Papez subjectively reasoned that because emotion could be influenced by thought and thought could be influenced by emotion the hypothalamus (emotion) must reciprocally connect with higher cortical areas (thought). He proposed a circuit in which the cortex connects to the cingulate gyrus, which connects to the hippocampus, which in turn connects to the mamillary bodies (hypothalamus)

through the fornix. The mamillary bodies then project to the anterior thalamic nuclei, which project back to the cingulate gyrus and then to wide areas of the cortex. The higher cortical regions could thus influence the hypothalamus and vice versa. Later ¹¹ the limbic system was expanded to include the septal area, the nucleus accumbens, the orbitofrontal and anterior temporal cortex, the dorsomedial thalamic nuclei and the amigdala. The structures of the limbic system are ideally located to regulate the impact of primary sensory processing in one brain area on the construction of higher order mental processes in other areas. ¹⁰

Goldenburg ¹² proposed dividing the limbic system into three subcircuits; 1) a medial limbic circuit, which includes the classic circuit of Papez; 2) a basolateral circuit, which includes the orbitofrontal and anterior temporal cortex, amygdala, and magnocellular division of the dorsomedial nucleus of the thalamus (frontothalamic pathway); and 3) a defense reaction circuit, which includes portions of the hypothalamus, stria terminalis and amygdala.

The circuits of the limbic system and the interactions with the basal ganglia are believed to be the anatomic substrate for human emotion and behaviour ¹⁰ and perturbations in these systems are thought to be responsible for various components of psychiatric illness. ¹¹

The positive correlation between structural brain abnormalities and mental illness has been borne out by several studies. These include ventriculomegaly and smaller temporal lobes, frontal parietal and superior temporal gyrus grey matter ¹³. Hippocampal volume reduction has been reported in schizophrenia ^{14,15} as well as volume reduction in the parahippocampal and fusiform gyri on the left side in another study on schizophrenics ¹⁶.

Left subgenual cingulate abnormalities have been found in patients hospitalized for psychotic affective disorder ¹⁷. Agenesis of the septum pellucidum has been identified in a patient suffering from schizophrenic psychosis ¹⁸. Yet another study ¹⁹ has demonstrated lateral and third ventricular enlargement as well as preferential abnormalities of medial temporal lobe structures including the amygdala, hippocampus, and the parahippocampal gyrus and neocortical temporal lobe regions in patients with schizophrenia. In addition, abnormalities of the frontal and parietal lobes as

well as sub cortical structures such as the cavum septum pellucidum, abnormalities of the basal ganglia, the corpus callosum and thalamus were identified in this study.

Midline abnormalities such as cavum septum pellucidum and cavum vergi as well as agenesis of the corpus callosum have also been found to be significantly present in patients with psychotic disorders ²⁰.

Furthermore, ²¹ patients suffering from schizotypal personality disorder have also been shown to have brain abnormalities in the superior temporal gyrus, the parahippocampus, the temporal horn region of the lateral ventricles, the corpus callosum, thalamus and septum pellucidum as well as in total CSF (cerebrospinal fluid) volume similar to those seen in persons with schizophrenia. The foregoing references firmly cement the relationship between mental illness and structural brain abnormalities.

CONCLUSION

The foregoing discussion establishes clearly the relationship between structural brain abnormalities and mental illness. The neurosurgeon, therefore, must be wary not be caught off guard in dismissing psychotic manifestations as purely the preserve of the psychiatrist.

Equally the psychiatrists must constantly be on the lookout for patients in their care who may harbour serious and potentially treatable intracranial structural lesions.

However, most importantly, every effort must be made to increase the awareness of the rural, primary doctors and community nurses about these issues if anything is to be achieved.

The two case reports presented in this paper as well as the several examples quoted from the literature illustrate that this can be a worthwhile undertaking.

REFERENCES

1. Mordecai D, Shaw RJ, Fischer PG, Mittelstadt PA, Cuterman T, Donaldson SS. Case study: suprasellar germinoma presenting with psychotic and obsessive-compulsive symptoms. *J Am Acad Child Adolesc Psychiatry* 2000 Jan; 39(1): 116-9.
2. Lisanby SH, Kohler C, Swanson CL, Gur RE. Psychosis secondary to brain tumour. *Semin Clin Neuropsychiatry* 1998 Jan; 3(1): 12-22.
3. Carson BS, Weingart JD, Guarnieri M, Fisher PG. Third ventricular choroids plexus papilloma with psychosis. Case report. *J Neurosurg* 1997 Jul; 87(1): 103-8.
4. Pollak L, Klein C, Rabey JM, Schiffer J. Posterior fossa lesions associated with neuropsychiatric symptomatology. *Int J Neurosci* 1996 Nov; 87(3-4): 119-26.
5. Sato T, Takeichi M, Abe M, Tabuchi K, Hara T. Frontal lobe tumour associated with late-onset seizure and psychosis: a

- case report. *Jpn J Psychiatry Neurol* 1993 Sept; 47(3): 541-4.
6. Struck M, Becker T, Dittman W, Hofmann E, Laux G. Remission of schizophreniform psychosis after brain tumour surgery. *Zentralbl Neurochir* 1992; 53(3): 156-62.
 7. Andermann LF, Sarard G, Meencke HJ, McLachlan R, Moshe S, Andermann F. Psychosis after resection of ganglioma or DNET: evidence for an association. *Epilepsia* 1999 Jan; 40(1): 83-7.
 8. Bunney BG, Potkin SG, Bunney WE Jr. New morphological and neuropathological findings in schizophrenia: a neurodevelopmental perspective. *Clin Neurosci* 1995; 3(2): 81-8.
 9. Papes JW. A proposed mechanism of emotion. *Arch Neurol Psychiatry* 1937; 38: 725-743.
 10. Feldman RP, Alterman RL, Goodrich JT. Contemporary psychosurgery and a look to the future. *J Neurosurg* 2001; 95: 944-956.
 11. MacLean PD. The limbic system ("visceral brain") and emotional behaviour. *Arch Neurol Psychiatry* 1955; 73: 130-134.
 12. Goldenburg PL. Functional neurosurgery, in Schmidek HH, and Sweet WH (eds). Operative neurosurgical techniques: Indications, methods and results, ed 2. *Orlando: Grune and Stratton* 1998, Vol 2 pp 1035-1068.
 13. Marsh L, Sullivan EV, Morrell M, Lim Ko Pfefferbaum A. Structural brain abnormalities in patients with schizophrenia, epilepsy and epilepsy with chronic interictal psychosis. *Psychiatry Res* 2001 Nov 5; 108(1): 1-15.
 14. Matsumoto H, Simmons A, Williams S, Pipe R, Murray R, Frangou S. Structural magnetic imaging of the hippocampus in early onset schizophrenia. *Biol Psychiatry* 2001 May 15; 49(10): 824-31.
 15. Velakoulis D, Wood SJ, McGorry PD, Pantelis C. Evidence for progression for brain structural abnormalities in schizophrenia: beyond the neurodevelopmental model. *Aust N Z J Psychiatry* 2000 Nov; 34 Suppl: S113-26.
 16. McDonald B, Highley JR, Walker MA, Herron BM, Cooper SJ, Esiri MM, Crow TJ. Anomalous asymmetry of fusiform and parahippocampal gyrus gray matter in schizophrenia: A postmortem study. *Am J Psychiatry* 2000 Jan; 159(1): 40-7.
 17. Hirayasu Y, Shenton ME, Salisbury DF, Kuron JS, Wible CG, Fischer IA, et al. Subgenual cingulate cortex volume in first episode psychosis. *Am J Psychiatry* 1999 Jul; 156(7): 1091-3.
 18. Supprian T, Heils A, Hofmann E, Warmuth-Metz M, Stober G, Franzek E. Agenesis septum pellucidum in a schizophrenic patient. *Nervenarzt* 1999 Mar; 70(3): 269-75.
 19. Shenton ME, Dickey CC, Frumin M, McCorley RW. A review of MRI findings in schizophrenia. *Schizophr Res* 2001 Apr 15; 49(1-2): 1-52.
 20. Scott TF, Price TR, George MS, Brillman J, Rothfus W. Midline cerebral malformations and schizophrenia. *J Neuropsychiatry Clin Neurosci* 1993 Summer; 5(3): 287-93.
 21. Dickey CC, McCarley RW, Shenton ME. The brain in schizotypal personality disorder: a review of structural MRI and CT findings. *Han Rev Psychiatry* 2002 Jan-Feb; 10(1): 1-15.

ERRATUM

The lead article of *African Health Sciences* of August 2004, by Karunakara and colleagues has one main error as follows:

Karunakara UK, Neuner F, Schauer M, Singh K, Hill K, Elbert T, Burnha G. Traumatic events and symptoms of post-traumatic stress disorder amongst Sudanese nationals, refugees and Ugandans in the West Nile. *Afr Health Sci.* 2004 Aug;4(2):83-93.

This has now been corrected to read as:

Karunakara UK, Neuner F, Schauer M, Singh K, Hill K, Elbert T, Burnham G. Traumatic events and symptoms of post-traumatic stress disorder amongst Sudanese nationals, refugees and Ugandans in the West Nile. *Afr Health Sci.* 2004 Aug;4(2):83-93.

The error is regretted. Editor.