

LETTER TO THE EDITOR

A CLINICAL LESSON: GLIOBLASTOMA MULTIFORME MASQUERADING AS DEPRESSION IN A CHRONIC ALCOHOLIC

BENEDIKT HABERMEYER^{1*}, MARCUS WEILAND¹, RALF MAGER¹, GERHARD A. WIESBECK¹ and
FRIEDRICH M. WURST^{1,2}

¹Psychiatric University Clinic, University of Basel, Switzerland

²Department of Psychiatry and Psychotherapy II/Addiction Medicine, Christian Doppler Clinic, Paracelsus Medical University, Salzburg, Austria

(Received 25 June 2007; first review notified 07 September 2007; in revised form 11 September 2007;
advance access publication 13 October 2007)

Abstract — Aims: To highlight the need to consider other medical conditions when the presentation initially appears to be alcohol-related. **Method:** We report the case of a 34-year-old male alcoholic, who presented with clinical depression and later a delirious state, and was subsequently diagnosed to have a right frontal glioblastoma multiforme. **Conclusions:** Psychiatric patients, especially alcoholics, may present with physical and neurological symptoms in the emergency department, which are linked by the examiner to the toxic effects of alcohol. However, consideration should be given to the possibility that the symptoms are due to other severe medical conditions.

INTRODUCTION

Alcohol-related conditions represent a major psychiatric problem in emergency departments (ED). Cases associated with alcohol abuse represent the most common diagnosis (30.7%) in patients with psychiatric problems presenting to the ED (te Wildt *et al.*, 2006). Within this group, alcohol intoxication was the most frequent diagnosis (71.4%). The case report of Yaldizli *et al.* (2006) emphasizes that all psychiatric symptoms can be potentially due to medical conditions, such as brain tumors or metabolic disorders. In recent studies, the role of routine brain imaging in psychiatric patients has become a focus of controversy, as some reports conclude that no clinical benefit is derived from this expensive diagnostic procedure (Agzarian *et al.*, 2006). However, in some cases when brain imaging is not performed, an underlying medical problem may be missed and patients are inadvertently assigned with a psychiatric diagnosis. In patients with a pre-existing psychiatric condition, this risk is potentially even higher. We present the case of a chronic alcoholic patient presented to the ED with symptoms of depression, who after transfer to the psychiatric ward was subsequently diagnosed with a glioblastoma multiforme (GBM) of the right frontal lobe.

CASE DESCRIPTION

The patient was a 34-year-old male with a medical history significant to alcoholism for more than 10 years. Previously, he never had severe withdrawal states or seizures. Six months prior to hospitalization, secondary to deterioration in his ability to live independently, he moved back in with

his parents. On the day of admission, he was brought to the ED by his mother for depressed mood and neglect of personal hygiene. The patient stated that he had performed a self-initiated alcohol withdrawal program and had not consumed alcohol for the past 21 days. He admitted having suicidal ideation. He also complained of intermittent diffuse headaches, without an aura or triggering factors, which developed in the preceding 7 days and improved with aspirin. In the ED, the general medical examination was unremarkable and there was no evidence of any physical or neurological abnormality—specifically he did not exhibit any clinical signs of alcohol withdrawal, such as tremor, sweating, confusion or agitation. Serum alcohol was zero, and gamma-glutamyl transferase (GGT) and mean corpuscular volume (MCV) were within normal limits. Based on the present history and the past medical history of chronic alcoholism, a diagnosis of a severe depression was made in the ED and the patient was referred to the psychiatric department for inpatient treatment.

Upon admission to our psychiatric ward, the patient showed classic features of depression with depressed mood, anhedonia, reduced energy, increased fatigability, reduced concentration and attention, as well as suicidal ideation. After a few days he developed intermittent signs of delirium with a fluctuating level of alertness, disorientation and impaired memory. He scored 24/30 points in the Mini Mental State (MMS) examination (Folstein *et al.*, 1975).

In order to treat a possible Wernicke's encephalopathy, thiamine was prescribed immediately. Although he did not have hand tremor or sweating, a symptomatic treatment of the delirious state with oral haloperidol (4 mg/d) and clomethiazole (768 mg/d) was initiated. Because the symptoms worsened, electroencephalography (EEG) was performed, which could be compared with an EEG performed 4 years earlier and which showed continuous and localized delta-activity (partly irregular in waveform) with suppression of background activity in the right fronto-temporal regions (Figure 1). Magnetic resonance imaging (MRI) of the brain revealed a 5 × 4 cm right frontal heterogeneous brain tumor with compression of

*Author to whom correspondence should be addressed at: Department of Psychiatry, University of Basel, Wilhelm Klein-Strasse 27, CH-4056 Basel, Switzerland. Tel: +41 (0) 61 325 5402; Fax: +41 (0) 61 325 5405; E-mail: benedikt.habermeyer@upkbs.ch

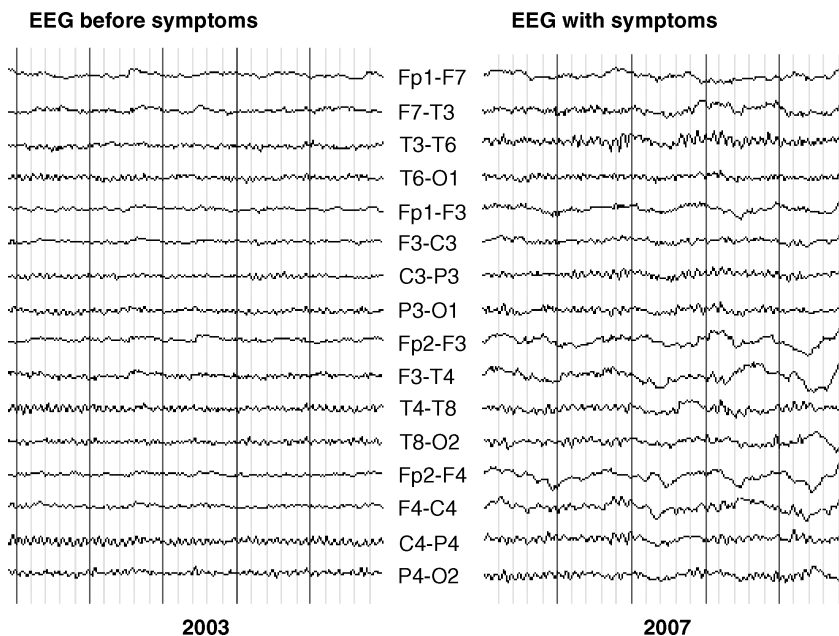


Fig. 1. The EEG reveals a right-sided fronto-temporal delta focus with suppression of background activity (2007). For comparison a former EEG (2003) is shown on the left side.

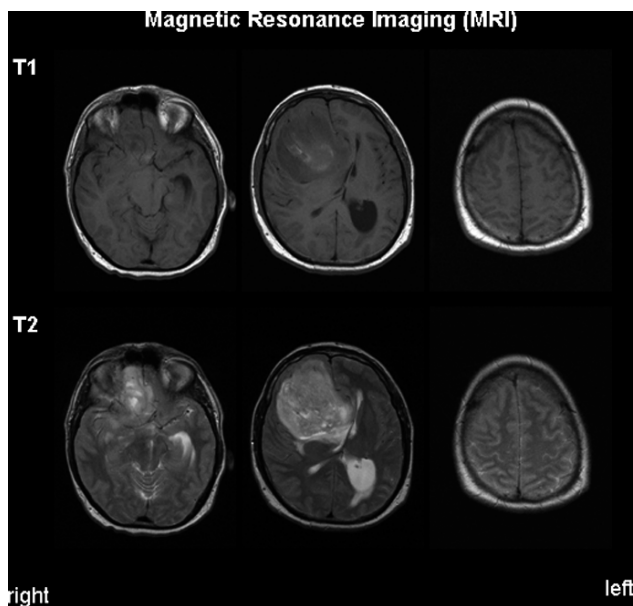


Fig. 2. MRI showed a large infiltrative orbito-frontal brain tumor in the right hemisphere with midline shift to the left, compression of the right lateral ventricle and early signs of herniation. The right motor cortex is not involved.

the right lateral ventricle and a midline shift of 0.5 cm to the left (Figure 2). The tumor was resected and a histological examination confirmed a GBM grade IV. He was treated with radiotherapy (60 Gy) and was given chemotherapy with temozolomide (75 mg/m²).

Although his psychiatric symptoms resolved after resection of the tumor, he was transferred back to our department for inpatient psychiatric treatment to further stabilize his alcohol

abstinence and to ensure adherence to the chemotherapeutic regimen. After 5 months he was discharged to outpatient therapy in our alcohol-treatment ambulatory clinic and he currently remains abstinent from alcohol with good quality of life.

DISCUSSION

People with substance abuse disorders have higher comorbid rates of mental disorders than vice versa. While causal pathways differ across substances and disorders, there is evidence that alcohol is a precipitating factor in up to 10% of male depression (Jane-Llopis and Matytsina, 2006). There is some evidence suggesting that symptomatology decreases spontaneously with prolonged abstinence. In fact, much of the psychopathology described by alcoholics decreases within 2–3 weeks of withdrawal without specific treatment for the psychiatric disorder (Wetterling *et al.*, 2006). Our patient already completed a self-initiated withdrawal from alcohol when he presented himself to the ED, corroborated by serum alcohol, GGT and MCV. When he later developed fluctuations in cognition, the differential diagnosis included delirium tremens, Korsakoff's syndrome and Wernicke's encephalopathy. Despite the lack of clear evidence for one of the above mentioned diseases, treatment options, including substitution of thiamine, treatment with antipsychotics and benzodiazepines, were immediately initiated on grounds of suspicion, as clinical guidelines recommend urgent action in order to prevent further deterioration (Thomson and Marshall, 2006).

Due to the attribution of the clinical picture to complications or consequences of chronic alcoholism, 10 days elapsed between the first presentation in the ED and the diagnosis of a malignant brain tumor, which put the patient at a considerable

risk for rapid and unpredictable deterioration of his clinical state.

Upon presentation to the ED, the patient complained of diffused headache. In up to 40% of patients diagnosed with a GBM, headache is the initial presenting symptom (Yuile *et al.*, 2006). However, brain tumors may potentially present only with psychiatric symptoms, such as mood changes (depression or mania), psychotic symptoms, panic attacks, changes in personality or memory difficulties (Moise and Madhusoodanan, 2006). If a right-sided frontal structural lesion, as in our case, does not affect the motor cortex, focal neurological signs are unlikely to be detected on routine examination, unless special effort and neurological expertise is used to screen the patient. As MMS is more sensitive to left hemispheric pathology, a seemingly unspecific result, as in our case of 24/30 points, should not be taken as excluding organic pathology of the right hemisphere. Karl Bonhoeffer described a syndrome of irritable weakness calling it 'emotional-hyperaesthetic weakness state' (Bonhoeffer, 1912). The gradual development of a depressive and delirious picture due to a general medical condition is described in detail. This historical concept, however, is not stressed in either the DSM IV or ICD 10.

Reeves *et al.* (2000) reviewed 64 cases of unrecognized medical emergencies, which were admitted to psychiatric units. About 5% suffered from a central nervous disorder, such as stroke, subdural hematoma or infectious encephalitis, which could have been diagnosed on the basis on brain imaging. In other studies, it has been reported that the incidence of medical findings in acutely ill psychiatric patients ranges from 24 to 80% (Tintinalli *et al.*, 1994). However, some authors argue that the lack of specific medical complaints in combination with negative physical findings and stable vital signs in the setting of an established psychiatric diagnosis identifies a subgroup of patients in which further diagnostic efforts are not necessary (Korn *et al.*, 2000). In 2006, two studies concluded that in the absence of neurological signs on clinical examination, the use of brain imaging should be restricted (Agzarian *et al.*, 2006; Mueller *et al.*, 2006).

Within this context, the case we described demonstrated that even in the absence of clear focal neurological signs a significant brain pathology may be present. The presence of a slowly progressive brain tumor presenting with only gradual changes of mood and behaviour may remain undetected in patients in whom we expect these symptoms as a part of the pre-existing psychiatric diagnosis. Furthermore, organic central nervous system comorbidities should be considered, especially in alcoholics, as it is well known that chronic alcoholics have a high incidence of subdural hematomas (Sonne and Tonnesen, 1992), intracerebral hemorrhage (Peng *et al.*, 2007) and infections of the central nervous system (Scheld, 1984), such as pneumococcal meningitis.

REFERENCES

- Agzarian, M. J., Chryssidis, S., Davies, R. P. *et al.* (2006) Use of routine computed tomography brain scanning of psychiatry patients. *Australasian Radiology* **50**, 27–28.
- Bonhoeffer, K. (1912) Die Psychosen im Gefolge von akuten Infektionen, allgemeinen Erkrankungen und inneren Erkrankungen. In *Handbuch der Psychiatrie. Spezieller Teil*, Aschaffenburg, G., and Deuticke, F. eds, Leipzig, pp. 1–120.
- Folstein, M. F., Folstein, S. E. and McHugh, P. R. (1975) Mini-Mental-State: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* **12**, 189–198.
- Jane-Llopis, E. and Matytsina, I. (2006) Mental health and alcohol, drugs and tobacco: a review of the comorbidity between mental disorders and the use of alcohol, tobacco and illicit drugs. *Drug and Alcohol Review* **25**, 515–536.
- Korn, C. S., Currier, G. W. and Henderson, S. O. (2000) "Medical clearance" of psychiatric patients without medical complaints in the Emergency Department. *Journal of Emergency Medicine* **18**, 173–176.
- Moise, D. and Madhusoodanan, S. (2006) Psychiatric symptoms associated with brain tumors: a clinical enigma. *CNS Spectrums* **11**, 28–31.
- Mueller, C., Rufer, M., Moergeli, H. *et al.* (2006) Brain imaging in psychiatry—a study of 435 psychiatric in-patients at a university clinic. *Acta Psychiatrica Scandinavica* **114**, 91–100.
- Peng, G. S., Yin, S. J., Cheng, C. A. *et al.* (2007) Increased risk of cerebral hemorrhage in Chinese male heavy drinkers with mild liver disorder. *Cerebrovascular Diseases* **23**, 309–314.
- Reeves, R. R., Pendarvis, E. J. and Kimble, R. (2000) Unrecognized medical emergencies admitted to psychiatric units. *American Journal of Emergency Medicine* **18**, 390–393.
- Scheld, W. M. (1984) Bacterial meningitis in the patient at risk: intrinsic risk factors and host defense mechanisms. *American Journal of Medicine* **76**, 193–207.
- Sonne, N. M. and Tonnesen, H. (1992) The influence of alcoholism on outcome after evacuation of subdural haematoma. *British Journal of Neurosurgery* **6**, 125–130.
- te Wildt, B. T., Andreis, C., Auffahrt, I. *et al.* (2006) Alcohol related conditions represent a major psychiatric problem in emergency departments. *Emergency Medicine Journal* **23**, 428–430.
- Thomson, A. D. and Marshall, E. J. (2006) The treatment of patients at risk of developing Wernicke's encephalopathy in the community. *Alcohol and Alcoholism* **41**, 159–167.
- Tintinalli, J. E., Peacock, F. Wt. and Wright, M. A. (1994) Emergency medical evaluation of psychiatric patients. *Annals of Emergency Medicine* **23**, 859–862.
- Wetterling, T., Weber, B., Depfenhart, M. *et al.* (2006) Development of a rating scale to predict the severity of alcohol withdrawal syndrome. *Alcohol and Alcoholism* **41**, 611–615.
- Yaldizli, O., Wurst, F. M., Euler, S. *et al.* (2006) Multiple cerebral metastases mimicking Wernicke's encephalopathy in a chronic alcoholic. *Alcohol and Alcoholism* **41**, 678–680.
- Yuile, P., Dent, O., Cook, R. *et al.* (2006) Survival of glioblastoma patients related to presenting symptoms, brain site and treatment variables. *Journal of Clinical Neuroscience* **13**, 747–751.