Enterovirus encephalitis presenting with acute psychosis

Dr Thomas Gubbin, Dr Sarah Rose
Salford Royal NHS Foundation Trust

ABSTRACT
In the UK, viral encephalitis is most commonly caused by central nervous system (CNS) infection with herpes simplex virus 1, but can rarely be associated with Enteroviruses[1,2]. This generally presents with fever, headache, reduced consciousness level and sometimes seizures[3]. This case describes an unusual presentation of Enterovirus encephalitis in a thirty-four-year-old man. He was brought to the emergency department (ED) acutely agitated and voicing suicidal thoughts. Further history revealed a two-day history of auditory hallucinations and bizarre delusional beliefs, and he displayed evidence of formal thought disorder. He had no previous psychiatric history but was known to abuse alcohol and the benzodiazepine analogue, etizolam, from which he had abstained for the last fourteen days and twenty-one days respectively. Initial examination in ED was unremarkable, other than low-grade pyrexia, but he then had a self terminating generalised seizure. Bloods tests revealed leukocytosis with neutrophilia. Cerebrospinal fluid (CSF) analysis showed pleocytosis and raised protein levels. No organisms were identified on microscopy or culture and a sample was sent for viral polymerase chain reactions (PCR). Imaging of the brain showed non specific changes. Due to diagnostic uncertainty, immediate management included seizure prophylaxis and antimicrobial cover for infective encephalitis, as well as treating possible withdrawal syndrome. Olanzapine was also given in light of the psychiatric features at presentation. PCR of the CSF detected Enterovirus RNA and supportive treatment was continued. His psychiatric symptoms resolved and he remained seizure-free after the initial event. This case raises several important points for clinical practice. Patients presenting with acute psychosis must have organic causes comprehensively excluded before a functional diagnosis is made, and a high index of suspicion for infective encephalitis should be maintained until virology and culture results are known. Furthermore, substance withdrawal may be causing or contributing to symptoms, necessitating a thorough drug history in such cases.

INTRODUCTION
Viral encephalitis classically presents acutely with fever, headache and progression to cerebral dysfunction. This dysfunction usually manifests as impaired consciousness with or without seizures and focal neurology, whilst neuropsychiatric features are uncommon[4]. Acute viral encephalitis is predominantly caused by members of the Herpesvirus family, in particular herpes simplex virus 1, but other causes are uncommonly seen[5-8]. In a recent Finnish study, using CSF PCR to identify the aetiology of CNS infection in over 3,000 patients, Enteroviruses were responsible for 11% of cases[9]. Enteroviruses are a group of single-stranded RNA viruses of the family Picornaviridae, which includes polioviruses, coxsackieviruses and echoviruses. They predominantly cause clinically evident disease in children, with few cases reported in immunocompetent adults[10].

CASE
Police were called to the home of thirty-four-year-old man, who’s concerned family reported him to be voicing suicidal thoughts on a background of change in behaviour and rambling speech over the last two days. He reported a running inner monologue ‘punctuating the world’, which was interrupted by having to communicate with others. The police found him acutely agitated and confused, and he was brought to ED by ambulance. He had no previous medical or psychiatric history but admitted to drinking 24 units of alcohol per week, although reported no symptoms of withdrawal. He had not consumed alcohol in the preceding fourteen days. He had also been taking the long-acting benzodiazepine analogue etizolam, which he had purchased on the internet for anxiety, but abruptly stopped this twenty-one days previously. On assessment in ED he appeared flushed with a low-grade pyrexia of 37.7 ºC, but initial observations showed he was haemodynamically stable with a regular pulse and no respiratory distress. Physical examination of the chest and abdomen were unremarkable and revealed no rashes. His Glasgow Coma Score was 16 in light of his ongoing confusion, but no focal neurology was found. His capillary blood glucose was 9.7 mmol/L. On mental state examination in ED he appeared unkempt and displayed bouts of laughter that were incongruous to his subjectively low mood. His speech was pressured and nonsensical with evidence of flight-of-ideas and parallaxa. He described bizarre delusions of mirrors being inserted into the lights in the ED, which were triggered by doors opening and closing. He also admitted to auditory hallucinations, hearing a distorting and distracting “white noise” in addition to the inner monologue that had persisted for the last few days. He had fixed delusional beliefs, with very little insight. Shortly after initial assessment, ED staff observed a generalised tonic-clonic seizure, which self terminated within three minutes.

Initial investigations included blood tests and cultures, lumbar puncture and computed tomography (CT) imaging of the brain (see Table 1). The diagnosis remained unclear and so immediate management covered a broad range of differentials. Intravenous aciclovir and ceftriaxone was started empirically to cover CNS infection, pending CSF culture and PCR results. Levetiracetam was commenced for seizure prophylaxis, as well as olanzapine due to the presence psychotic features on admission. The recent cessation of alcohol and etizolam raised the possibility of withdrawal syndrome and chloralhydrate and thiamine were also started. Magnetic resonance (MR) imaging of the brain showed mild, generalised leptomeningeal enhancement and T2 signal abnormalities within the insular cortices bilaterally, which would be consistent with a viral or autoimmune encephalitis. PCR testing revealed the presence of Enterovirus RNA in the CSF, whilst screening for panenzylopleptics and coagulative disease and bone-born viruses were negative. Supportive management was continued for viral encephalitis and his psychiatric symptoms resolved. He remained seizure free after the initial event and after further negative electroencephalogram results and outpatient clinic review, his antiepileptic medications were stopped and he was discharged from follow-up.

DISCUSSION
This unusual presentation of viral encephalitis raises several important learning points. Firstly, a high suspicion for CNS infection must be maintained until culture and viral PCR results are known. In this case, the initial CSF results were equivocal and definitive microbiology results were not available during the acute stages of the illness. This stresses the importance of empirical antimicrobial therapy if there is diagnostic doubt, as CNS infection can carry a high risk of morbidity and mortality[5-8]. The clinical uncertainty was further fuelled by the dominance of psychiatric features in this presentation. This demonstrates the importance of comprehensive investigation of organic causes in acutely psychotic patients. This is especially pertinent in a first presentation, but we must always be wary of cognitive bias when assessing patients with a previous psychiatric history. This case was complicated by the recent withdrawal of the benzodiazepine analogue etizolam. Newer analogues of more traditional drugs of abuse, as well as increasing access to these online, has created a class of medications that are not prescribed, but neither are they necessarily viewed as recreational drugs. This, therefore, presents a clinical problem in that use of such drugs can be missed when taking a history, but clinicians can overcome this with an increased awareness and a comprehensive drug history. Although an alternate diagnosis was eventually found, acute withdrawal symptoms may have contributed to the unusual presentation in this case. The management of this 34-year-old man, presenting with acute psychotic features, relied upon consideration of several differentials, which is evidenced by the thorough investigation and broad cover of the initial management. This approach ultimately led to a positive patient outcome.

REFERENCES

Table 1: Initial Investigations

| Bloods | WCC 13.1x10^9 cells/L; Neutrophils 8.6x10^9 cells/L; CRP <4 mg/L. |
| Peripheral blood culture | No growth. |
| CSF analysis | Clear, colourless. WCC 6 cells; Protein 0.49 mg/dL. |
| CT Brain | No acute change. |

No acute change.