### LETTER TO THE EDITOR

# Late Onset of Schizophrenia and Temporal Lobe Epilepsy: Coincidence or Causal?

Dear Editor

We report the case of a female patient with chronic schizophrenia who developed right-sided temporal lobe epilepsy for the first time at the age of 73. When unusual behaviour was noted by her brother, it was initially attributed to a deterioration in her psychosis. When the behavioural symptoms persisted despite increased doses of neuroleptic, further investigations revealed right-sided temporal lobe epilepsy. Anticonvulsant treatment was effective in controlling her behaviour. Evidence for an association between psychotic symptomatology and the lateralization of temporal lobe epileptic foci is discussed.

#### CASE REPORT

Presenting history

The patient, who has given consent for this case report, is a right-handed 74-year-old woman with an 11-year history of chronic schizophrenia, who had remained free of positive symptoms for 3 years on regular depot neuroleptic (flupenthixol 30 mg 4-weekly) and was maintained in her home with a visiting CPN. In October 1995 her brother described an episode of sudden onset mutism, disorientation and clouding of consciousness in which she appeared alert but was unresponsive to her environment or relatives. These symptoms persisted for 12 hours before she was referred by her GP to her local general hospital where she was found to be pyrexial, as a presumed consequence of a urinary tract infection. She responded to treatment with oral antibiotics and was discharged 4 days later with a normal mental state. Three months later there was another episode of bizarre behaviour during which she became disoriented and took freshly ironed laundry back to the Laundromat to wash. She was again taken to casualty, where a low-grade pyrexia was noted and she was given haloperidol 2 mg intramuscularly and admitted to a psychiatric ward for further assessment.

When interviewed by a psychiatrist the next morning, she was oriented with no evidence of any psychotic symptoms. A routine blood screen was unremarkable. Four weeks later, she suffered a relapse of her psychotic symptoms with second person auditory hallucinations and difficulty in sleeping because she said she could feel electricity running through her bed. After review, she agreed to a 10 mg increase in the dose of her flupenthixol. After receiving the new dose of depot, she refused any further injections. At this time, her brother reported three episodes of bizarre behaviour which occurred while she was in bed. Typically, these would begin with a weak screaming sound after which she would be found on the floor with her legs shaking for 10–15 minutes with open eyes but unresponsive to questions. Following these episodes, the patient agreed to resume the depot. When reviewed in outpatients 2 weeks later, her mental state was normal and there had been no further unusual episodes. As there appeared to be a link between the disappearance of her behavioural symptoms and recommencement of depot medication, her episodes of bizarre behaviour were initially considered a manifestation of her psychosis. She remained well for the next 6 weeks before another episode of strange behaviour. On this occasion, she complained of a headache and took two coproxamol tablets before retiring to bed. The following morning, when she was woken for breakfast by her brother, she initially behaved normally, but at nine o'clock, while sitting in the lounge, she began to lipsmack and became 'glassy-eyed', disoriented, unresponsive and repeatedly tried to open her wardrobe using her front door keys. Her brother noted that her right arm shook for 15 minutes during the attack. Her mental state remained abnormal until 6 pm, when she became communicative and was able to cook the evening meal, which she ate before retiring to bed. The next

morning, she was reported to be completely back to her normal self but had no recollection of the events of the previous day.

The persistence of the unexplained bizarre behaviour despite regular antipsychotic medication and the prolonged nature of the most recent episodes prompted her admission into hospital for observation and further investigations.

#### Personal history

The patient was the eldest child of five siblings, one of whom died of a stomach malignancy. There is no known family history of epilepsy or psychiatric disorder. She was born following a normal delivery and her childhood development was normal. She left school at age 14 with no qualifications and worked for 8 years at a manufacturing chemist. During World War II she worked in the Women's Land Army. When the war ended, she joined a steel factory, but left after 6 months so she could remain at home to look after her mother, who had 'stomach trouble', and her younger brothers. She never married and lives with her unmarried brother in what was the parental home. In her medical history, she had suffered a head injury when hit by a piece of steel on the left side of her head. This had not resulted in a loss of consciousness and a skull X-ray taken at that time showed no fracture. She was first diagnosed with schizophrenia in 1985, at the age of 63 years, and had been maintained on a once-monthly depot of flupenthixol decanoate 15 mg which she received at a depot clinic. In May 1994, after she had defaulted from her clinic appointments, a CPN was assigned to administer the depot. In January 1995, she refused any further depot injections, but her CPN continued to visit weekly. She remained well until May 1995, when her psychotic symptoms returned, at which time she agreed to recommence the depot injections. The symptoms responded and she was well until the emergence of bizarre behaviour in October 1995.

## INPATIENT EXAMINATION AND INVESTIGATIONS

On mental state examination, there was no evidence of any psychotic symptoms. The Mini-Mental State score was 24.5/30. On physical examination, the only neurological abnormality was bilateral extensor plantar response. A full

blood screen revealed no abnormalities. Culture of a mid-stream urine specimen indicated a urinary tract infection due to E. Coli, which was treated with a 1-week course of Cefadroxil. An EEG revealed repeated generalized bursts of sharp and slow activity against a normal background and runs of sharp waves in the right temporal region. Although in this age group such EEG findings may not indicate specific pathology, the consultant neurophysiologist who reported the EEG thought that the recording suggested epilepsy of right temporal origin. An MRI head scan was performed to provide further structural detail of the temporal lobe and, in particular, the hippocampal region. Discrete small high-signal lesions were visible in the left frontoparietal and in the right frontal white matter. There was moderate enlargement of the right lateral ventricle, widening of the sylvian fissures and mild to moderate widening of cortical sulci, particularly in the right occipital region. The hippocampi appeared within normal limits bilaterally. The appearances suggested patchy infarcts, particularly affecting the right occipital region, associated with patchy mild cerebral atrophy in keeping with vascular disease. (See Fig. 1.)

#### **WORKING DIAGNOSIS**

The recurrent brief episodes of bizarre behaviour and abnormal movements together with neurophysiological and imaging evidence suggested that the patient's late onset schizophrenia was complicated by complex partial seizures of temporal lobe origin.

#### TREATMENT AND PROGRESS

While on the ward, no further episodes of bizarre behaviour were observed. Carbamazepine was started at a dose of 100 mg nocte and blood levels taken 1 week later were within therapeutic range. She was discharged home. Five days after discharge (14 days on carbamazepine), she developed an itchy erythematous macular skin rash over her face, upper torso and arms. This was thought to be a drug reaction to carbamazepine, which was stopped and the rash subsided. The anticonvulsant was changed to sodium valproate CR at a starting dose of 200 mg daily. While the sodium valproate dose was being increased, another seizure occurred. She was admitted the following day and at interview was still confused and unable to follow questions. She

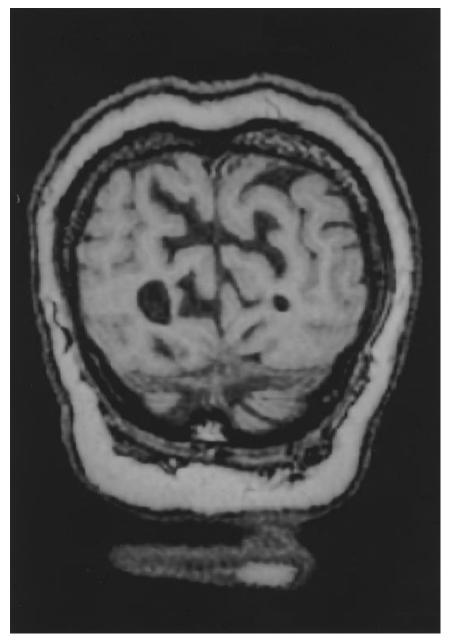


Fig. 1. Coronal MRI through posterior temporal region shows right (on left of image) temporal lobe atrophy

perserverated, repeatedly mentioned 'tablets' and wandered into other patients' bedrooms looking for her medication. Episodes of lip-smacking and fluttering of her eyes were noted. Physical examination was unremarkable. A blood screen revealed a neutrophilic leucocytosis and subtherapeutic valproate levels.

After increasing the sodium valproate by 100 mg per week to 400 mg daily, the blood levels improved and no further seizures were observed over the next 2 weeks. She was discharged home and has since been reviewed in outpatients on two occasions when her mental state was stable. No further seizures have been reported.

#### NEUROPSYCHOLOGICAL TESTING

Neuropsychological testing was carried out while she was seizure-free. She was assessed for premorbid intellectual functioning using the National Adult Reading Test (NART; Nelson, 1982) and the Schonell Graded Reading Test (Schonell and Goodacre, 1974), current intellectual functioning using the Wechsler Adult Intelligence Scale Revised (WAIS-R; Wechsler, 1982), memory functioning using the Middlesex Elderly Assessment of Mental State (MEAMS; Golding, 1991) and the Rivermead Behavioural Memory Test: Supplement Elderly People (RBMT; Wilson et al., 1991) and visual reproduction of the Wechsler Memory Scale (WMS-R; Wechsler, 1987), for copying skills using the Rey-Osterreith Complex Figure Test (Rey, 1941), for perceptual processing using the Visual Object and Space Perception Battery (VOSP; Warrington and James, 1991) and for verbal fluency using the Controlled Word Association Test (CWAT; Lezak, 1983). Table 1 provides details of the results of the neuropsychological assessment.

The patient's premorbid level of intellectual functioning lies in the borderline range. Concomitant with this, her current intellectual functioning lies in the borderline range. On the MEAMS testing, there was some difficulty with comprehension. She was oriented for name, date of birth, date and place. On memory testing, she demonstrated a significant impairment of verbal memory for both immediate and delayed memory. Such

verbal memory deficits are suggestive of left temporal lobe pathology. On a test of verbal fluency, there revealed a marked impairment. This result may be indicative of difficulty with retrieving information from semantic memory. Impaired verbal fluency is associated with left frontal lobe damage. The patient revealed intact visual memory, good object and facial recognition memory and name learning. She demonstrated a deficit of perceptual processing for both early spatial processing, where she had difficulty with position discrimination, and higher-level apperceptive processing, where she showed difficulties with identifying silhouettes. Her copying skills, however, were intact. Perceptual processing deficits are associated with right hemisphere damage. Overall, she presents a mixed neuropsychological profile suggestive of left temporal, frontal and right hemisphere damage.

#### DISCUSSION

The association between epilepsy and psychosis was first recognized by Pond (1957), Hill (1953) and Slater and Beard (1963), who noted that the form of psychosis was schizophrenia-like, often with prominent first-rank symptoms, and that the epilepsy predominantly originated from the temporal lobes. In 1969, Flor-Henry studied epileptic patients referred for temporal lobectomy and found that those presenting with schizophrenia-like psychosis

Table 1. Results of neuropsychological assessment

Predicted full-scale IQ	NART Schonell Graded Reading Test	77
Current intellectual functioning	WAIS-R full scale IQ WAIS-R verbal IQ WAIS-R performance IQ	78 76 80
Memory	WMS-R visual reproduction Immediate Delayed MEAMS (borderline range, failed comprehension, usual views and verbal fluency) RBMT (normal range, failed orientation, verbal recall of stories, immediate and de	46th centile 22nd centile 9/12 subtests passed 7/11 subtests passed layed)
Perceptual processing	VOSP (failed object decision, progressive silhouette and position discrimination)	6/9 subtests passed
Copying skills	Rey-Osterreith Complex Figure	10-25th centile
Verbal fluency	CWAT	5/10 for category animals

were more likely to have a focus in the dominant hemisphere. Subsequent studies by Gregoriadis et al. (1971), Taylor (1975), Hara et al. (1980), Sherwin (1981, 1982), Toone (1982), Perez et al. (1984) and Ounsted and Lindsay (1981) supported the idea that temporal lobe foci associated with psychosis are lateralized to the dominant hemisphere. Trimble (1990) reviewed these reports and found that out of the 180 patients with a schizophreniform psychosis of epilepsy, 112 had leftsided, 27 right-sided and 41 bilateral temporal lobe lesions. Most recently, imaging studies have also indicated an association between interictal psychosis and left-sided temporal lobe abnormality. Gallhofer et al. (1985) compared a small group of patients with epilepsy and interictal psychosis to epileptic patients without a history of psychosis using positron emission tomography (PET). The psychotic group had significant hypometabolism in several left-sided temporal lobe areas. Similarly, Conlon et al. (1990) found that psychotic patients who had experienced first-rank auditory hallucinations had longer TI relaxation times in left temporal white matter than those without hallucinations.

On close examination of the relationship between schizophrenia-like psychosis and left-sided temporal epilepsy, Trimble (1990) found that the association held true particularly for cases presenting with Schneiderian first-rank symptoms. Indeed, studies which had failed to detect a laterality relationship had not used Schneiderian concepts in diagnosis. For example, Jensen and Larsen (1979) found no laterality effect in patients referred to as having 'chronic paranoid states', while Kristensen and Sindrup (1978) found no laterality in patients with paranoid ideas and/or hallucinations. HM's interictal phenomenology which is not Schneiderian in nature and arose from a right-sided focus is, however, consistent with the less restrictive criteria used in these two studies. Although a psychosis associated with temporal lobe epilepsy is traditionally considered in the differential diagnosis of schizophrenic and schizophrenia-like psychoses, particularly when cases are atypical as in the late onset of psychosis in the patient described, the late emergence of clearly epileptic phenomena in an 11-year history of psychosis might suggest that their association in her was coincidental. Her excellent previous symptomatic response to antipsychotic medication would also support this view. MRI evidence of both focal and generalized right-sided pathological change indicates that the underlying cause for her epilepsy may be longstanding, but without previous EEG examinations it is impossible to determine whether or not subclinical epileptic activity was present prior to her latest presentations.

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