

Insulinoma Presenting as Epilepsia Partialis Continua

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Abstract

Insulinoma is a rare tumour which is commonly misdiagnosed initially as a primary neurological or psychiatric disease. Here we describe the case of an insulinoma which presented with left sided focal motor seizures and progressed to epilepsy partialis continua. Continuous clinical left sided epileptic activity (epilepsia partialis continua) was confirmed on EEG with focal epileptic activity in the right F4 C4 P4 region. Insulinoma was confirmed biochemically, radiologically and subsequently histologically. Seizures were not responsive to antiepileptic agents but ceased after management of the hypoglycaemia. To our knowledge epilepsy partialis continua has not been reported to be caused by an insulinoma. This case reminds us that alternate diagnoses should always be considered where seizures or seizure-like episodes are refractory to traditional management.

Case report

A 71-year-old lady had a 3-year history of focal seizures. Her husband described periods of left sided jerking, without loss of consciousness but with associated confusion and agitation. These episodes progressed from brief sporadic episodes by day or night to episodes occurring nightly, which could last several hours. Over this period her husband also reported that between attacks she had become intellectually less alert. Approximately three years after her first episode she was admitted with sustained left sided jerking. Medication included Phenytoin 400mg once nightly and Topiramate 100mg twice per day. Other antiepileptic drugs tried previously included Carbamazepine and Lamotrigine. Examination revealed no focal neurological deficit but continuous jerking of the left arm and leg, which persisted during sleep. The patient was drowsy due to administration of benzodiazepines prior to admission to hospital and she had developed an aspiration pneumonia.

Previous investigations had shown the following: MRI; mild vasculopathic changes but no structural lesion. Multiple EEGs had shown widespread slow activity and or occasional sharp waves in the temporal lobes. EEG telemetry had not recorded any episodes. Investigations on admission revealed normal haematology and biochemistry including baseline glucose of 3.7. The CRP was elevated, consistent with the aspiration pneumonia. A CSF examination revealed normal pressure and constituents. An 'ictal' EEG was performed with ongoing left leg twitching. This revealed focal epileptic activity in the right

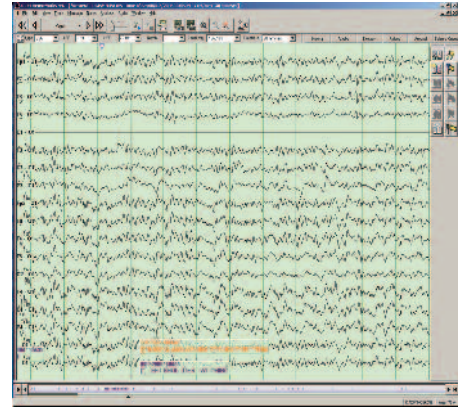


Figure 1: EEG showing waxing and waning abnormal activity over right F4/C4/P4 electrodes.

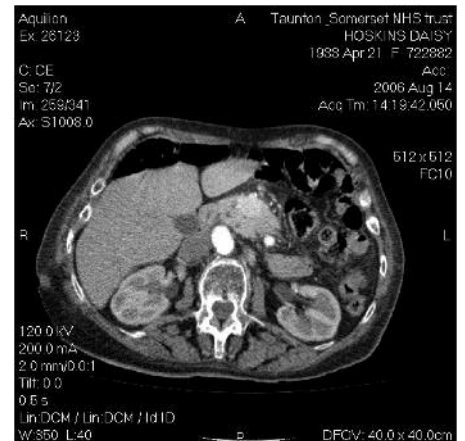


Figure 2 - CT abdomen showing the lesion in the head of pancreas.

F4 C4 P4 region (Figure 1).

Although her left sided twitching was constant as an inpatient she was noted to have episodes of increased confusion and drowsiness. During these episodes she was found to be hypoglycaemic. Glucose of 1.1 was recorded and coincided with an insulin of 6.3 ($n < 2$) and c-peptide of 1162 ($n < 600$) UNIT?? consistent with an insulinoma. Pituitary function tests were normal and sulphonylurea screen was negative. Computed Tomography revealed a 2-3 cm lesion in the head of the pancreas again consistent with an insulinoma (Figure 2).

Blood glucose was maintained in the normal range initially with a dextrose infusion and subsequently with diazoxide. This led to a termination of the left sided twitching. The tumour was resected. Histological examination showed a well-differentiated neuroendocrine neoplasm

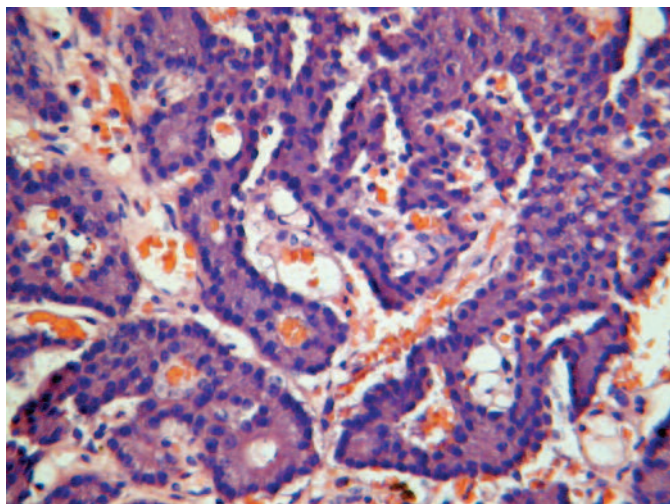


Figure 3a: Lesion in head of pancreas is composed of cells closely resembling neuroendocrine cells in normal pancreatic islets - haematoxylin and eosin, original magnification x 200.

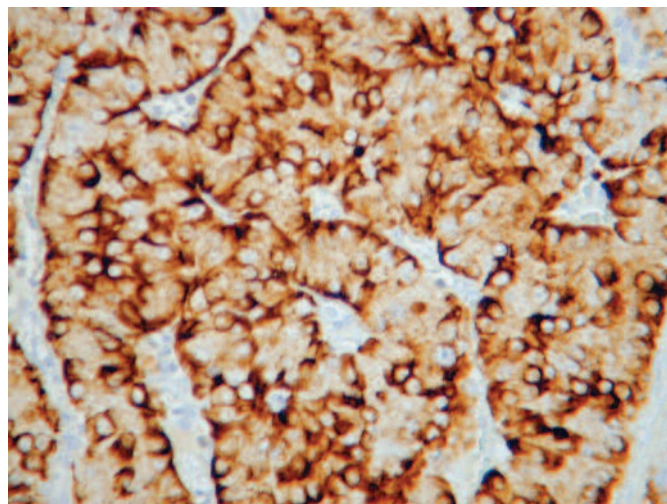


Figure 3b: Histology - Tumour cells are diffusely immunoreactive for insulin - immunoperoxidase, original magnification x 200.

(Figure 3a). Tumour cells were diffusely immunoreactive for insulin, supporting a diagnosis of an insulinoma (Figure 3b). She has remained seizure free since this time.

We report the case of an insulinoma presenting with simple focal seizures and progressing to *epilepsia partialis continua*.

Insulinomas are rare tumours of pancreatic islet cells with an incidence of between 1 and 5 per million per year. They are typically small (0.5-5 mm diameter) solitary and benign and are found throughout the pancreas. Diagnosis is based upon the finding of an elevated insulin and c-peptide in the presence of hypoglycaemia. A 72 hour fast has a 95% sensitivity for detecting such lesions. Radiological localisation is often difficult due to the small tumour size.¹

Typical neuroglycopenic symptoms include: confusion, cognitive decline, personality change, bizarre behaviour, coma, blurred vision, diplopia and transient neurological deficits including seizures. Associated autonomic activation usually results in sweating, palpitations, anxiety and tremor (although this may be habituate).

In one retrospective series of 59 patients with insulinoma 39% were initially diagnosed with a primary seizure disorder. In this same series delay from symptom onset to diagnosis ranged from 1 month to 30 years, with a mean delay of 24 months. Insulinoma has also been reported in a patient previously thought to have pseudoseizures.²

Epilepsia partialis continua (EPC) is a partial somatomotor status characterised by clonic muscular twitching in one part of the body for a period of days or longer.³ EPC is rare with a prevalence rate of less than one per million per year. Its aetiology is most commonly Rasmussen's encephalitis or vascular disease but it has been reported to occur in CJD, brain neoplasms, mitochondrial disease and interestingly with hyperglycaemia of diabetic ketoacidosis.⁴ It has not however been previously reported to occur with hypoglycaemia.

Insulinomas may produce diagnostic difficulties in two ways. Firstly, neuroglycopenic symptoms may be mistaken for epileptic seizures, and secondly, hypoglycaemic seizures may be mistaken for primary epilepsy. In a

small prospective study of 25 patients presenting to a neurology outpatient clinic with 'funny turns', two patients (8%) were subsequently found to have insulinomas.⁵ Despite this interesting observation the literature on seizures due to insulinoma is small.

Here we have presented the first reported case of *epilepsia partialis continua* caused by neuroglycopenia from an insulinoma. We are reminded that neuroglycopenia caused by insulinoma (a potentially curable disorder) should be considered in all unusual cases of epilepsy, or indeed funny turns in general, especially if they do not respond to standard treatments.

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