Clinical Report

Levetiracetam-induced severe acute granulomatous interstitial nephritis

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Abstract
Granulomatous interstitial nephritis (GIN) is an uncommon cause of renal failure, which may be caused by drugs. Levetiracetam is an increasingly used anti-epileptic medication that is not known to cause renal toxicity in adults. To our knowledge, levetiracetam has not previously been reported as a cause of GIN. We report the case of a 69-year-old woman who developed haemodialysis-requiring acute renal failure after commencement of treatment with levetiracetam, which was shown to be GIN by renal biopsy. She made a complete recovery with cessation of levetiracetam and treatment with steroids.

Keywords: acute renal failure; granulomatous interstitial nephritis; levetiracetam

Introduction
Levetiracetam is an anti-epileptic drug used for the treatment of partial and generalized seizures. We report the case of a 69-year-old woman with previously normal renal function who developed acute granulomatous interstitial nephritis (GIN) requiring dialysis following levetiracetam consumption.

Case report
A 69-year-old woman with a background of early stage chronic lymphocytic leukaemia (CLL) was noted to have episodes of phrase repetition and instances of memory loss over 1 year. An electroencephalogram showed changes consistent with temporal lobe epilepsy. A magnetic resonance imaging showed mild deep white matter small vessel ischaemic changes with a small old infarct of the right caudate nucleus. She was commenced on carbamazepine. Six weeks later, she developed generalized erythematous macular rash (Figure 1A) and was admitted to hospital for fever and worsening azotaemia. A skin biopsy confirmed a lichenoid drug reaction and a widespread erythematous rash with areas of desquamation. Urinalysis demonstrated +1 protein and +1 blood. She had severe mucosal ulceration affecting the tongue and mouth but sparing the conjunctiva. She had a widespread rash with areas of desquamation. Urinalysis demonstrated +1 protein and +1 blood. She had severe mucosal ulceration affecting the tongue and mouth but sparing the conjunctiva. She had a widespread rash with areas of desquamation. Urinalysis demonstrated +1 protein and +1 blood.

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Fourteen days following commencement of levetiracetam, she presented with a 2-day history of severe oral mucositis and feeling generally unwell. On examination, she was afebrile and her blood pressure was 120/65 mmHg. She had severe mucosal ulceration affecting the tongue and mouth but sparing the conjunctiva. She had a widespread rash with areas of desquamation. Urinalysis demonstrated +1 protein and +1 blood.

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glomerulonephritis by routine light microscopic, immuno-
fluorescence or electron microscopic examination.

She was initially treated with intravenous methylpredni-
solone daily (500 mg for 3 days) and the levetiracetam was
replaced by sodium valproate 500 mg twice a day. Other
more common causes of granulomatous interstitial disease
were considered including tuberculosis, which was excluded
with a negative urine culture and polymerase chain reaction
(PCR). Sarcoidosis was also excluded with a CT scan of the
chest and abdomen that did not reveal hilar lymphadenop-
athy or other features suggestive of sarcoidosis and a normal
serum angiotensin-converting enzyme 35 U/L (8–52).

The oral mucositis was secondary to Herpes simplex virus
as demonstrated on PCR of a swab of an oral lesion and was
treated with acyclovir (dose adjusted for renal impairment,
250 mg intravenously for 3 days). She had panhypogamma-
globulinaemia \(\text{IgG} = 5.4 \text{ g/L} (540 \text{ mg/dL}), \text{IgM} < 10 \text{ mg/L}
(10 \text{ mg/dL}), \text{IgA} = 480 \text{ mg/L} (48 \text{ mg/dL})\) secondary to CLL
and was given intravenous gammaglobulin (24 g daily over
3 days). Her hospital stay was further complicated by delir-
ium and valproate was discontinued.

She had three haemodialysis treatments over 6 days and
rapidly recovered renal function with increasing urine output
and improved biochemistry (Figure 2). She had a course of oral
prednisone commencing at 50 mg daily (1 mg/kg/day) that
was withdrawn gradually over 3 months. Her renal function
normalized and her current serum creatinine is 70 mmol/L
(0.80 mg/dL).

**Discussion**

Renal toxicity secondary to levetiracetam has not previously
been reported in adults although there is a single paediatric
case report [1]. The most common side effects of levetirace-
tam in adults are somnolence, asthenia and dizziness [2].
Other side effects include depression and anxiety. It has high
oral bioavailability and is excreted predominantly in the urine
(93% after 48 h). Adjustment of the dose is required in renal
impairment as its elimination is directly dependent on crea-
tinine clearance [3].

Although tubulointerstitial nephritis is relatively common,
GIN is rare, accounting for ~1% of diagnoses in native renal
biopsies [4, 5]. The most common causes of GIN are sarcoido-
sis, drugs and infection, particularly tuberculosis [6]. Drugs
implicated in cases of GIN are varied and include non-steroidal
anti-inflammatory drugs, phenytoin, nitrofurantoin and van-
comycin. GIN is also part of the tubulointerstitial nephritis and
uveitis syndrome. GIN has been seen as a consequence of CLL
with one case reporting leukaemic cells infiltrating the renal
 tissue with surrounding T cells and granuloma formation [6].
Our patient did not have leukaemic cells identified on renal
biopsy.

This patient had renal failure requiring haemodialysis and a
diagnosis of GIN confirmed by renal biopsy. She made a rapid
recovery with withdrawal of levetiracetam and treatment
with steroids. The outcome of patients with GIN is generally
favourable [5] but some patients with an insidious

![Skin rash and renal histopathology.](https://example.com/skin_rash.png)

**Fig. 1.** Skin rash and renal histopathology. (A) Rash representative of that affecting the entire body after commencement of carbamazepine. (B) Renal biopsy (haematoxylin and eosin (H&E) stain \(\times 250\)) showing diffuse active non-caseating granulomatous tubulointerstitial nephritis. (C) H&E stain \(\times 400\) demonstrating areas of GIN with lymphohistiocytic infiltrate and giant cells.

![Graph representing creatinine during course of disease.](https://example.com/creatinine_graph.png)

**Fig. 2.** Graph representing creatinine during course of disease. Timing of haemodialysis and commencement and cessation of all medications during disease course noted.
presentation may progress to end-stage renal failure. Steroids have been used at varying dosages but due to the infrequency of the disease, there are no defined treatment guidelines.

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References


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