BMC Musculoskeletal Disorders

CASE REPORT Open Access

A rare cause for osteonecrosis of femoral head and peripheral nerve damage of a child with depression

Ke Wang[1], Yun Chen[2] and Hao Zhou[3*]

Abstract

Background Avascular necrosis of the femoral head (ANFH) that is due to the use of carbamazepine (CBZ) in children whose condition requires long-term oral CBZ is relatively rare, and there are no clinical reports on this topic. Herein, we present a rare case of femoral head necrosis and peripheral nerve damage due to long-term use of CBZ in a child with depression.

Patient presentation A 12-year-old boy who was taking oral CBZ for depression presented to the hospital with a sudden onset of impaired consciousness. On admission, the blood CBZ concentration was 32.6 μg/mL, an electromyogram (EMG) revealed severe partial injury to the left common peroneal and tibial nerves, and magnetic resonance imaging (MRI) of the hip revealed necrosis of the left femoral head. On predischarge evaluation, the CBZ blood level was < 0.2 μg/mL. The long-term use of CBZ is thought to have resulted in femoral head necrosis and peripheral nerve damage.

Conclusions To our knowledge, this is the first literature report of femoral head necrosis with peripheral nerve damage due to long-term CBZ use. For patients receiving long-term treatment with CBZ, careful monitoring for osteoarthritis, bone pain, and decreased sensation and range of motion of the extremities, as well as detailed medical history-taking and complete imaging, electromyography, and neurosonography of the hip joint, are needed.

Keywords Avascular necrosis of the femoral head, Peripheral nerve damage, Carbamazepine, Case report

Background

ANFH is a common disorder characterized by abnormal bone metabolism in the femoral head. ANFH is caused by various factors that lead to imbalances in lipid metabolism and disturbances in blood microcirculation. Common causes of ANFH include trauma, corticosteroid use, excessive alcohol consumption, hypercholesterolemia, smoking, and some inflammatory diseases [1, 2]. An imbalance between bone resorption and bone formation can lead to diseases such as osteoporosis, osteonecrosis, and fractures that heal abnormally [3]. Previous studies have shown that long-term CBZ administration can increase the metabolism of vitamin D and convert

*Correspondence:
Hao Zhou
zhouhaogz@sina.com
[1]Zhejiang Provincial People's Hospital Bijie Hospital, Bijie, Guizhou Province 551700, China
[2]Shanghai Children's Medical Center Guizhou Hospital, Guiyang, Guizhou Province 550002, China
[3]Department of Rehabilitation, Children's Hospital of Fudan University, Shanghai 201102, China

it to inactivated forms, which may negatively affect bone health [4, 5]. CBZ is a common antiepileptic drug that also acts as a mood stabilizer in patients with bipolar disorder [6–8]. The side effects of CBZ include rash, toxic epidermal necrolysis and peeling, drug-induced liver injury, leukopenia, hyponatremia, vitamin D metabolism disorders, aplastic anemia, hepatitis, sleep disturbances and depression [9]. Severe toxicity occurs when the blood concentration of CBZ exceeds 40 μg/mL, and side effects are more likely to occur at these high concentrations [10]. Previous studies have shown that CBZ affects bone metabolism [11], which may be related to the induction of the cytochrome P450 enzyme system by CBZ. CBZ use can lead to vitamin D deficiency, hypocalcemia, hypophosphatemia, and elevated parathyroid hormone levels [5, 12–14], and prolonged use of CBZ can result in nontraumatic fractures [15, 16]. CBZ can relieve peripheral nerve neuropathic pain resulting from various causes by decreasing the excitability of peripheral and central connections [17]. Peripheral neuralgia or peripheral neuropathic pain may be caused by nerve damage of various etiologies, including medical conditions such as diabetes, infections, kidney disease, nerve compression, trauma, cancer, or a combination of these conditions [18]. Studies have also shown that long-term administration of CBZ can lead to peripheral nerve damage, which may be related to the antidiuretic effect of CBZ; in this case, water intoxication reduces sodium levels in the blood, increases pressure in the nerve lumen, and damages axons, which can lead to a slowing of conduction [19, 20]. To our knowledge, there have been no reports to date of ANFH with peripheral nerve injury in children due to CBZ use.

Case presentation

A 12-year-old male child was referred to our pediatric emergency department because of 10 h of unconsciousness. He was unable to respond to calls and had generalized paralysis. The patient treatment timeline is shown in Fig. 1. After a series of treatments, the child regained consciousness. However, the patient reported significant pain in the left lower extremity, which was intolerable and affected his ability to sleep at night. Upon examination, both active and passive movements were painful for the patient, but the hip range of motion was normal, with Grade 4 muscle strength. The child also experienced the loss of proprioception and abnormal sensations, such as tingling, electric shock-like pain, numbness, and burning sensations in the distal part of the left lower extremity, as shown in Fig. 2. In addition, the patient showed weakness in dorsiflexion and plantar flexion of the left toe, along with hyperreflexia of the Achilles tendon and knee tendon.

Upon reviewing the child's personal history, it was discovered that he had been taking oral CBZ (800 mg per day in divided doses) for depression for the past year. Owing to a lack of attention from the family, the child was not monitored for drug dosage for the last six months. The child and his family denied his taking large amounts of the medication over short periods. Prior to the onset of the disease, the child was in good general condition with normal sensation and movement of the lower extremities. No history of traumatic surgery, smoking, drug allergies, or any other pertinent medical conditions was reported. The child's birth weight was 4.0 kg. At presentation, he was 170 cm tall and weighed 62 kg.

Upon admission, the patient's blood CBZ concentration was 32.60 μg/mL. The blood concentrations of coagulation factors were as follows: D-dimer, 1.66 μg/mL; and fibrin degradation products, 3.90 μg/mL. The other blood parameters were as follows: 25-hydroxyvitamin D, 14.1 ng/mL; C-reactive protein, 14.29 mg/L; creatinine, 181 μmol/L; alanine aminotransferase, 71.00 U/L; aspartate aminotransferase, 26471.00 U/L; creatine kinase isoenzyme, 396.74 U/L; myoglobin, > 3000.00 μg/mL; and creatine kinase, 43953.00 U/L. Urinalysis revealed that the urine was positive for occult blood (++++) and weakly positive for protein (±). Tests for blood cell counts; electrolyte, blood glucose, and lipid levels; the blood sedimentation rate; blood ammonia, lactate, amylase, and cholinesterase levels; and the urine amylase level, as well as 3P tests, revealed no significant abnormalities (partial test results are detailed in Table 1). Electrocardiography (EKG) revealed sinus arrhythmia, whereas electromyography (EMG) revealed severe partial damage to the left common peroneal and tibial nerves. Repeat EMG after one month revealed persistent and severe partial damage to the left common peroneal and tibial nerves, and potential damage to the cauda equina could not be ruled out. Nerve ultrasound revealed injury to the left common peroneal and tibial nerves (popliteal segment), as illustrated in Fig. 3. Additionally, hip magnetic resonance imaging (MRI) revealed necrosis of the left femoral head (Fig. 4). Evaluation before discharge showed that the CBZ blood concentration was < 0.2 μg/mL.

The Neuropathic Pain Assessment Scale (Douleur Neuropathique 4 questionnaire; DN4) and the I-DN4 scale were used for scoring neuropathic pain. The scores were 8 (such as burning pain, electric shock-like pain, numbness and tingling, pin-and-needle-like pain, numbness, decreased tactile sensation, decreased tingling sensation, and increased pain due to friction in the area of pain) and 5 (including burning pain, electric shock-like pain, tingling, pin-and-needle-like pain, and numbness), respectively.

After admission, the patient was immediately transferred to the pediatric intensive care unit for

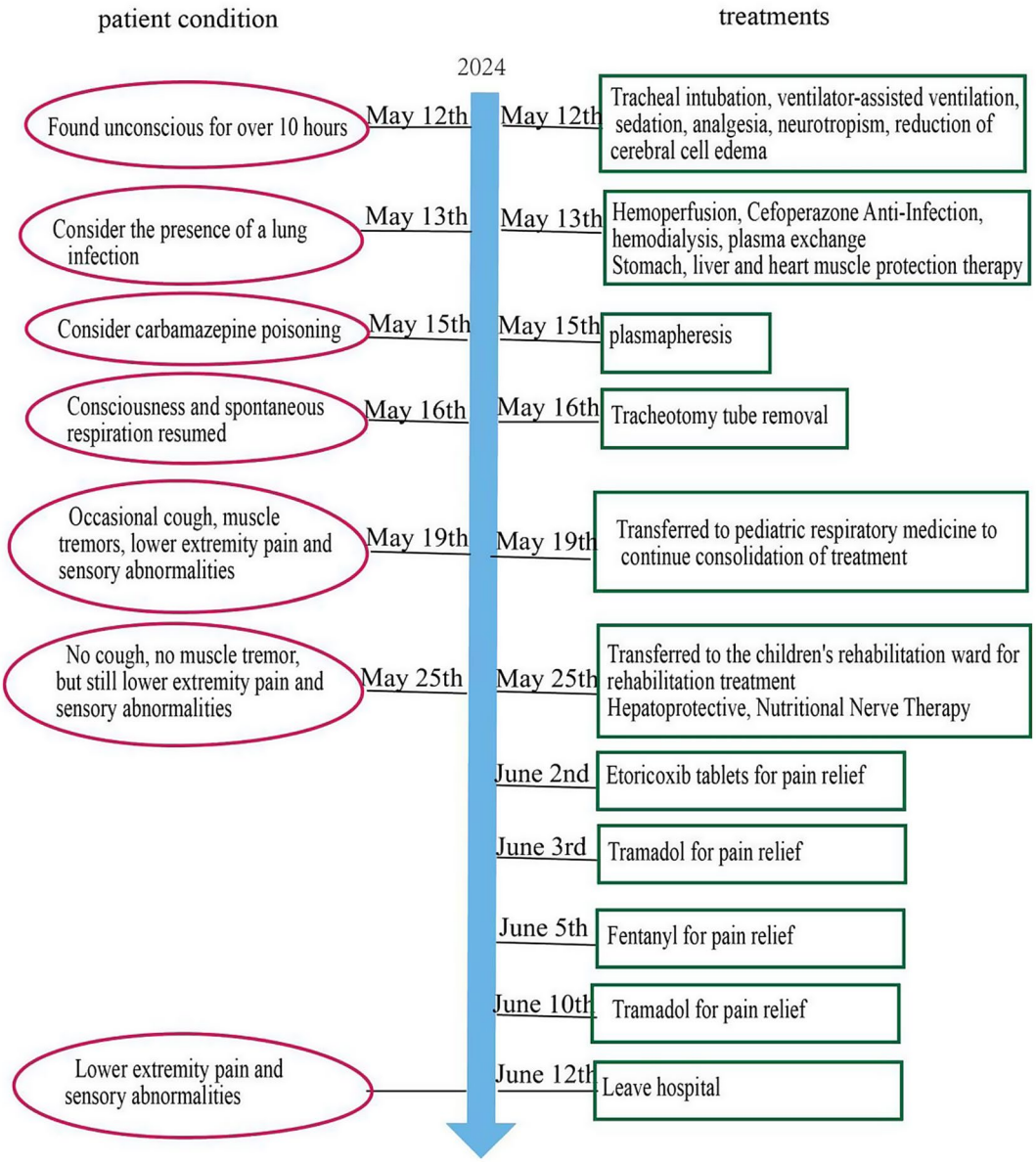

Fig. 1 Timeline of treatment for the patient

resuscitation. Endotracheal intubation was administered to assist respiration. Subsequently, he was treated successively with hemoperfusion, plasma exchange, hemodialysis, and antiinfective therapy. After regaining consciousness, the child experienced abnormal sensations and intolerable pain in his left lower limb; therefore, he was transferred to the pediatric neurological rehabilitation ward for treatment. After transfer, acetylglutamide, vitamin B6, and vitamin B1 were continuously administered for nerve nourishment. Dexamethasone sodium phosphate was used for anti-inflammatory and immunosuppressive purposes. Murine nerve growth factor was administered for nerve nourishment. Diclofenac suppositories, ibuprofen, and etoricoxib tablets were administered for pain relief. Nevertheless, the child did not experience pain relief and was unable to sleep quietly at night. Tramadol administration significantly relieved pain, and the patient could sleep at night. However, approximately 24 h after intramuscular injection, pain returned to its previous state. Fentanyl was subsequently administered as an external patch and significantly relieved pain. However, after approximately 72 h, the child experienced the same level of pain as before. The fentanyl external patch was replaced after approximately 20 h; afterward, the pain was the same as before, and the effective duration of pain relief with the drug was significantly shorter. After treatment, the child's condition stabilized, and the pain was slightly alleviated. The patient

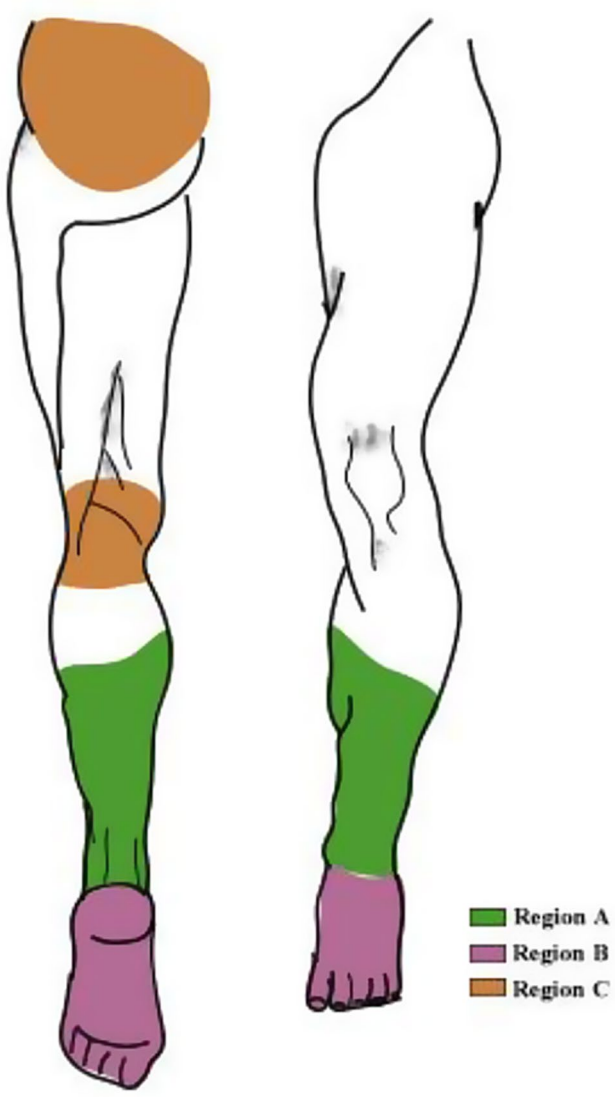

Fig. 2 The patient experienced decreased tactile sensation, prickling sensation, loss of proprioception, spontaneous burning sensation, tingling, and pin-and-needle-like pain in Region **A** The warm nociceptive sensation remained. The patient experienced persistent burning pain, electric shock-like pain, numbness, tingling, pin-and-needle-like pain, decreased tactile sensation, increased pain due to friction in the area of pain, complete loss of heat and cold sensations and paresthesia in Region **B** The patient experienced significant pain sensation in Region C

was discharged for further treatment at an outside hospital. During a one-month follow-up after discharge, the child made several visits to other hospitals. However, he did not experience pain relief.

Discussion

ANFH leads to trabecular fractures, necrotic collapse of bone tissue, and hip dysfunction [21]. There are many microvessels in the femoral head, which has an important influence on the mechanism underlying ANFH development [22]. When coagulation dysfunction, vascular endothelial cell damage, and vascular inflammation occur, thrombi are easily formed, leading to ischemic necrosis of the femoral head [21, 23]. This patient was admitted to the hospital with abnormal coagulation factor levels, which may have contributed to femoral head necrosis. Abnormalities in coagulation increase the risk of thrombus formation, which impedes blood flow, exacerbates tissue ischemia and delays tissue repair [24]. The delicate balance between vasoconstriction and vasodilatation is disrupted by various factors (e.g., coagulation abnormalities) that impair the normal function of vascular endothelial cells [25]. This dysfunctional state affects the regulation of blood flow and the release of vasoactive molecules, which results in the failure to address the urgency of the blood supply to the femoral head, leading to ischemia and subsequent bone tissue damage and worsening the condition by initiating a proinflammatory state [23]. Several inflammatory cytokines and adhesion molecules contribute to immune cell aggregation, which causes further damage to bone tissue [1]. As a result, when microvascular hypercoagulability and coagulation in the femoral head are impaired, this affects blood flow to the femoral head and leads to its necrosis [21]. However, more research is needed to confirm this conclusion. In addition, many diseases and medications may cause necrosis of the femoral head [26]. However, there are no reports to date that CBZ causes femoral head necrosis.

The long-term use of CBZ frequently leads to abnormal bone metabolism, hypocalcemia, and disturbances in vitamin D metabolism [9, 12, 14]. These factors may be the primary causes of femoral head necrosis. This patient was found to have a low level of 25-hydroxyvitamin D (25(OH)D), which was undoubtedly due to prolonged oral CBZ use. Previous studies have demonstrated that long-term treatment with CBZ has a negative effect on bone mineral density (BMD). An increased risk of fracture and accelerated age-related osteoporosis have been observed [11]. Studies have shown that these effects may be due to the induction of cytochrome P450 enzymes by CBZ, which can lead to metabolic alterations resulting in vitamin D deficiency and decreased calcitonin levels. This can further lead to secondary hypoparathyroidism, which can increase bone turnover and lead to decreased bone density [27]. Moreover, childhood and adolescence are critical periods for bone mineralization. The peak BMD, which is achieved at the end of adolescence, determines the risk of pathological fractures and osteoporosis later in life [28]. Thus, patients receiving long-term CBZ therapy require regular bone assessment, bone health monitoring and measurement of serum 25(OH)D levels prior to therapy initiation [9, 11]. Vitamin D supplementation therapy should be provided if necessary.

The main manifestations in our patient throughout the course of disease were intolerable unilateral lower

Table 1 Selected test results

Metabolic Panel										
Marker	Value								Reference Range	unit of measure
	May 12th	May 13th	May 14th	May 15th	May 16th	May 17th	May 18th	May 23rd		
N-terminal pro-B-type natriureticpeptide	973.00	/	/	/	/	/	/	/	<125	pg/mL
C-reactive protein	14.29	156.92	/	/	62.91	/	14.22	3.64	0-5	mg/mL
procalcitonin	0.46	2.95	/	/	1.59	/	0.40	/	<0.046	ng/mL
calcium	2.01	1.91	1.96	/	/	/	2.02	2.43	2.1-2.8	mmol/L
creatinine	181.00	176.00	208.00	166.00	155.00	93.00	67.00	64.00	37-93	umol/L
alanine amiotransferase	71.00	106.00	98.00	120.00	56.00	74.00	73.00	50.00	7-43	U/L
aspartate aminotransferase	264.00	/	483.00	475.00	190.00	207.00	132.00	36.00	12-37	U/L
creatine kinase	43953.00	/	34225.00	27507.00	9385.00	9584.00	4221.00	588.00	50-310	U/L
creatine kinase-MB	396.74	/	326.94	255.87	102.86	106.55	77.96	25.80	0-25	U/L
troponin T	23.90	17.50	13.60	14.50	10.90	37.80	17.00	31.00	0-14	pg/mL
myoglobin	>3000.0	>3000.0	12960.00	4298.00	1071.00	383.00	112.00	/	<72	ug/L

blood routine examination									
Marker	Value							Reference Range	unit of measure
	May 12th	May 14th	May 15th	May 16th	May 17th	May 18th	May 23rd		
white blood cell	7.77	5.76	4.53	5.03	6.96	7.28	10.81	4.1-11	$\times 10^9$/L
red blood cell	5.60	3.96	3.88	3.56	3.55	3.60	4.00	4.5-5.9	$\times 10^{12}$/L
hemoglobin	159.00	113.00	110.00	99.00	99.00	102.00	112.00	129-172	g/L
platelet	285.00	128.00	114.00	110.00	134.00	157.00	386.00	150-407	$\times 10^9$/L
percentage of neutrophils	78.00	84.00	76.70	68.40	52.20	41.80	66.40	37-77	%
percentage of lymphocytes	10.70	11.70	14.70	20.30	34.50	42.90	22.60	17-54	%

coagulation function							
Marker	Value					Reference Range	unit of measure
	May 12th	May 13th	May 14th	May 15th	May 18th		
prothrombin time	12.20	16.30	14.00	12.60	14.70	9.4-12.5	sec
activated partial thromboplastin time	30.50	122.50	33.20	34.80	32.20	25.1-36.5	sec
thrombin time	15.00	>180	16.70	13.20	16.50	10.3-16.6	sec
fibrinogen	3.07	3.33	3.55	4.80	2.27	2.38-4.9	g/L
D-dimer	1.66	1.40	2.08	1.71	2.78	0-0.5	ug/mL
Fibrin degradation product	3.90	3.60	6.20	6.70	7.90	0-2.01	ug/mL

Urinalysis				
Marker	Value		Reference Range	unit of measure
	May 13th	May 19th		
specific gravity	1.011	1.011	1.003-1.03	
blood	weak positive	negative	negative	
white blood cell	0.8	0.8	0-13	
red blood cell	168.7	7.5	0-18	pcs/ul
epithelial cell	11.8	0.5	0-8	pcs/ul

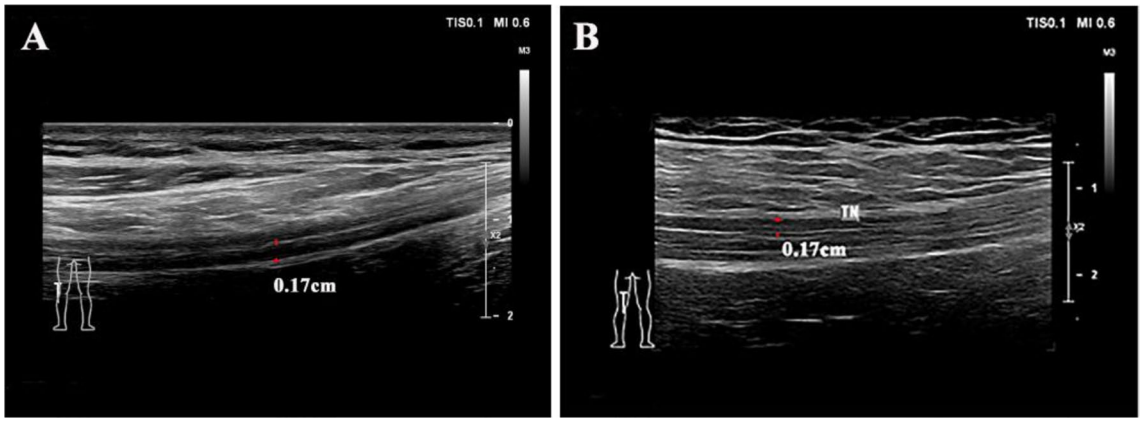

Fig. 3 (**A**) Ultrasound of the left common peroneal nerve showing a thickened segment of the nerve bundle, measuring approximately 0.17 cm in thickness and located in the popliteal fossa. (**B**) Ultrasound of the left tibial nerve also revealed a thickened segment of the nerve bundle, which was approximately 0.17 cm thick, in the popliteal fossa

extremity pain, abnormal sensation (DN4 score of 8), decreased muscle strength, and limited movement. Neurosonography revealed that the common peroneal nerve and tibial nerve (popliteal segment) were injured and that damage to the peripheral nerve had occurred. These findings are consistent with previous findings indicating that CBZ can cause peripheral nerve damage [14, 25]. In peripheral nerves, temperature sensitivity is transmitted

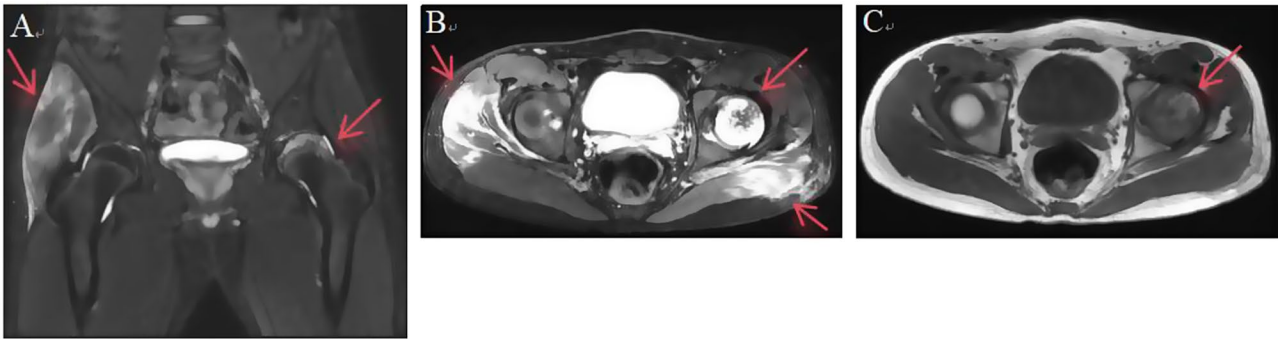

Fig. 4 (**A**) On the magnetic resonance imaging (MRI) coronal T2-weighted (T2WI) compression fat image of the hip, patchy high signals of the left femoral head epiphysis and the right gluteus maximus and minimus muscles are observed. (**B**) On the axial T2WI compression fat image of the hip, patchy high signals of the left femoral epiphysis, the right gluteus medius, the left gluteus maximus, and the adjacent subcutaneous soft tissues are noted. (**C**) On the axial T1WI image of the hip, a low signal from the left femoral head epiphysis was detected

only by very small myelinated A fibers and unmyelinated C fibers. Nerve fiber damage leads to increased sensory thresholds. This child presented with distal sensory deficits in the left lower extremity. CBZ-caused peripheral nerve damage may be closely related to its antidiuretic effect. Relevant experimental animal studies have shown that CBZ causes peripheral nerve damage, mainly in the form of demyelination [29]. Our findings may validate the findings of this animal study, but more clinical studies or monitoring of children on CBZ are needed to confirm these results. The effects observed may be closely related to the disruption of the superoxide–antioxidant balance in vivo, especially in neural tissues [30–32].

The lower limb pain was obvious in our patient, and MRI revealed muscle/soft tissue edema. The blood CBZ concentration was significantly elevated. There were abnormalities in myoglobin and creatine phosphokinase levels, which were accompanied by abnormal levels of liver and kidney function parameters. Thus, rhabdomyolysis was considered. It has been previously reported that decreased drug excretion may lead to increased serum concentrations of CBZ and cause toxicity, resulting in hepatic injury, neurotoxicity, and acute kidney injury, along with the development of rhabdomyolysis [17]. The child's liver and kidney function parameter levels were suggestive of injury; simultaneously, the urine was positive for occult blood and protein.

There are many causes of ANFH, such as Legg–Calve–Perthes disease and slipped capital femoral epiphysis. Legg–Calve–Perthes disease (LCPD) is an idiopathic form of osteonecrosis or idiopathic avascular necrosis of the femoral epiphysis. The highest prevalence of LCPD is observed between 5 and 7 years of age, and it is most common in males. HIV infection, thrombophilia, deficient fibrinolysis, secondhand smoke exposure, the birth weight less than 2.5 kg for boys, and a short stature are risk factors for LCPD [33]. LCPD is often acute or insidious claudication and is usually painless (for 1 to 3 months) [34]. If pain is present, it may be confined to the hip or may move to the knee, thigh or abdomen, and as the disease progresses, the pain usually worsens with activity, but there should be no systemic symptoms [33]. Slipped capital femoral epiphysis (SCFE) is a common hip lesion in prepubertal children and adolescents [35]. Typically, young adult patients complain of traumatic pain in the hip, thigh or knee, which may be accompanied by a limp or an inability to bear weight [36]. Obesity is the most important risk factor for SCFE [37]. Our patient denied chronic secondhand smoke exposure, was free of AIDS, and did not have a short stature or obesity. The movement limitations included significant pain, notably in the distal muscles; weakness of the dorsiflexion and plantar flexion of the left toe; and hyperreflexia of the Achilles tendon and knee tendons. The blood CBZ concentration was 32.60 μg/mL. There were significant abnormalities in laboratory test results, such as aspartate aminotransferase (26471.00 U/L), creatine kinase isoenzyme (396.74 U/L), myoglobin (> 3000.00 μg/mL), and creatine kinase (43953.00 U/L) levels. Urinalysis revealed positive results for occult blood (++++), and therefore, the influence of the drug is a preferential diagnosis. However, as the child did not have regular health checkups, ANFH caused by these two factors could not be completely excluded.

The distinguishing features of this case were unilateral femoral head necrosis with peripheral nerve injury, a history of long-term CBZ drug use, and a significantly elevated blood CBZ concentration. The child's condition was considered to be due to long-term CBZ administration. Notably, however, ischemic necrosis of the femoral head is usually a chronic change, and a combination of factors other than the long-term effects of carbamazepine may be involved.

Conclusion

For patients receiving long-term CBZ treatment, careful monitoring for osteoarthritis, bone pain, and decreased sensation and range of motion of the extremities, as well as detailed medical history-taking and complete imaging, EMG, and neurosonography of the hip joint, are needed.

Acknowledgements
The authors thank the patient for providing consent to publish his clinical information.

Author contributions
All the authors have contributed to this manuscript in terms of planning, conception and design and writing and editing the final manuscript.

Funding
None.

Data availability
The data that support the conclusions of this article are included within the article.

Declarations

Ethical approval
The content of the article has been agreed upon by the patient and his family members. Moreover, the article does not contain any information that can clearly identify the patient. All procedures were conducted according to the principles of the Declaration of Helsinki.

Consent for publication
Written informed consent was obtained from family members for the personal or clinical details, along with any identifying images, to be published in this study.

Competing interests
The authors declare no competing interests.

Received: 7 February 2025 / Accepted: 18 April 2025
Published online: 16 May 2025

References

1. Singh M, Singh B, Sharma K, Kumar N, Mastana S, Singh P. A Molecular Troika of Angiogenesis, Coagulopathy and endothelial dysfunction in the pathology of avascular necrosis of femoral head: a comprehensive review. Cells 2023;12(18).
2. Ha AS, Chang EY, Bartolotta RJ, Bucknor MD, Chen KC, Ellis HB Jr., Flug J, Leschied JR, Ross AB, Sharma A, et al. ACR appropriateness Criteria® osteonecrosis: 2022 update. J Am Coll Radiol. 2022;19(11s):S409–16.
3. Kim KJ, Lee J, Wang W, Lee Y, Oh E, Park KH, Park C, Woo GE, Son YJ, Kang H. Austalide K from the fungus penicillium rudallense prevents LPS-induced bone loss in mice by inhibiting osteoclast differentiation and promoting osteoblast differentiation. Int J Mol Sci 2021;22(11).
4. Pack AM, Morrell MJ. Epilepsy and bone health in adults. Epilepsy Behav. 2004;5(Suppl 2):S24–29.
5. Rahimdel A, Dehghan A, Moghadam MA, Ardekani AM. Relationship between bone density and biochemical markers of bone among two groups taking carbamazepine and sodium valproate for epilepsy in comparison with healthy individuals in Yazd. Electron Physician. 2016;8(11):3257–65.
6. Fricke-Galindo I, Jung-Cook ALL, López-López H. Carbamazepine adverse drug reactions. Expert Rev Clin Pharmacol. 2018;11(7):705–18.
7. Sukkarieh HH, Khokhar AA, Bustami RT, Karbani GA, Alturki FA, Alvi SN. A highlight on carbamazepine-induced adverse drug reactions in Saudi Arabia: a retrospective medical records-based study. Naunyn Schmiedebergs Arch Pharmacol. 2023;396(11):3177–82.
8. Vieta E, Cruz N, García-Campayo J, de Arce R, Manuel Crespo J, Vallès V, Pérez-Blanco J, Roca E, Manuel Olivares J, Moríñigo A, et al. A double-blind, randomized, placebo-controlled prophylaxis trial of oxcarbazepine as adjunctive treatment to lithium in the long-term treatment of bipolar I and II disorder. Int J Neuropsychopharmacol. 2008;11(4):445–52.
9. Zhang X, Zhong R, Chen Q, Li M, Lin W, Cui L. Effect of carbamazepine on the bone health of people with epilepsy: a systematic review and meta-analysis. J Int Med Res. 2020;48(3):300060520902608.
10. Fernández-López L, Mancini R, Rotolo MC, Navarro-Zaragoza J, Hernández D, Rincón JP, Falcón M. Carbamazepine overdose after psychiatric conditions: a case study for postmortem analysis in human bone. Toxics 2022;10(6).
11. Verrotti A, Coppola G, Parisi P, Mohn A, Chiarelli F. Bone and calcium metabolism and antiepileptic drugs. Clin Neurol Neurosurg. 2010;112(1):1–10.
12. Arora E, Singh H, Gupta YK. Impact of antiepileptic drugs on bone health: need for monitoring, treatment, and prevention strategies. J Family Med Prim Care. 2016;5(2):248–53.
13. Nicholas JM, Ridsdale L, Richardson MP, Grieve AP, Gulliford MC. Fracture risk with use of liver enzyme inducing antiepileptic drugs in people with active epilepsy: cohort study using the general practice research database. Seizure. 2013;22(1):37–42.
14. Pack AM, Gidal B, Vazquez B. Bone disease associated with antiepileptic drugs. Cleve Clin J Med. 2004;71(Suppl 2):S42–48.
15. Shiek Ahmad B, Hill KD, O'Brien TJ, Gorelik A, Habib N, Wark JD. Falls and fractures in patients chronically treated with antiepileptic drugs. Neurology. 2012;79(2):145–51.
16. Jetté N, Lix LM, Metge CJ, Prior HJ, McChesney J, Leslie WD. Association of antiepileptic drugs with nontraumatic fractures: a population-based analysis. Arch Neurol. 2011;68(1):107–12.
17. Soliman N, Alsultan M, Alhusseini A, Alsamarrai O, Basha K. Status epilepticus resulted in rhabdomyolysis-induced AKI associated with hepatotoxicity induced by synergistic carbamazepine and Diazepam: A case report. Med (Baltim). 2024;103(8):e36834.
18. Ben Aziz M, Cascella M. Neurolytic procedures. *StatPearls*. Treasure Island (FL): StatPearls publishing 2025. StatPearls Publishing LLC.; 2025.
19. Radó P. Water intoxication during carbamazepine treatment. Br Med J. 1973;3(5878):479.
20. Kato DB. Dilutional hyponatremia and water intoxication during carbamazepine therapy. A case report and review of the literature. Drug Intell Clin Pharm. 1978;12(7):392–6.
21. Ma T, Wang Y, Ma J, Cui H, Feng X, Ma X. Research progress in the pathogenesis of hormone-induced femoral head necrosis based on microvessels: a systematic review. J Orthop Surg Res. 2024;19(1):265.
22. Zheng ZW, Chen YH, Wu DY, Wang JB, Lv MM, Wang XS, Sun J, Zhang ZY. Development of an accurate and proactive Immunomodulatory strategy to improve bone substitute Material-Mediated osteogenesis and angiogenesis. Theranostics. 2018;8(19):5482–500.
23. Poredos P, Poredos AV, Gregoric I. Endothelial dysfunction and its clinical implications. Angiology. 2021;72(7):604–15.
24. Glueck CJ, Freiberg RA, Wang P. Heritable thrombophilia-hypofibrinolysis and osteonecrosis of the femoral head. Clin Orthop Relat Res. 2008;466(5):1034–40.
25. Sandoo A, van Zanten JJ, Metsios GS, Carroll D, Kitas GD. The endothelium and its role in regulating vascular tone. Open Cardiovasc Med J. 2010;4:302–12.
26. Guerado E, Caso E. The physiopathology of avascular necrosis of the femoral head: an update. Injury. 2016;47(Suppl 6):S16–26.
27. Sheth RD. Bone health in epilepsy. Epilepsia. 2002;43(12):1453–4.
28. Sheth RD. Bone health in pediatric epilepsy. Epilepsy Behav. 2004;5(Suppl 2):S30–35.
29. Zhong M, Cai FC, Zhang XP, Song Y. [Peripheral nerve damage and its pathogenesis induced by antiepileptic drugs in rats]. Zhonghua Er Ke Za Zhi. 2008;46(8):574–8.
30. Vincent AM, Russell JW, Low P, Feldman EL. Oxidative stress in the pathogenesis of diabetic neuropathy. Endocr Rev. 2004;25(4):612–28.
31. Aycicek A, Iscan A. The effects of carbamazepine, valproic acid and phenobarbital on the oxidative and antioxidative balance in epileptic children. Eur Neurol. 2007;57(2):65–9.
32. Sobaniec W, Solowiej E, Kulak W, Bockowski L, Smigielska-Kuzia J, Artemowicz B. Evaluation of the influence of antiepileptic therapy on antioxidant enzyme activity and lipid peroxidation in erythrocytes of children with epilepsy. J Child Neurol. 2006;21(7):558–62.
33. Mills S, Burroughs KE. Legg-Calve-Perthes disease. *StatPearls*. Treasure Island (FL): StatPearls publishing 2025. StatPearls Publishing LLC.; 2025.

34. Beni R, Hussain SA, Monsell F, Gelfer Y. Management of Legg-Calve-Perthes disease: a scoping review with advice on initial management. Arch Dis Child 2024.
35. Mathew SE, Larson AN. Natural History of Slipped Capital Femoral Epiphysis. *J Pediatr Orthop* 2019, 39(Issue 6, Supplement 1 Suppl 1):S23-s27.
36. Johns K, Mabrouk A, Tavarez MM. Slipped capital femoral epiphysis. *StatPearls*. Treasure Island (FL): StatPearls publishing 2025. StatPearls Publishing LLC.; 2025.
37. Perry DC, Metcalfe D, Lane S, Turner S. Childhood obesity and slipped capital femoral epiphysis. Pediatrics 2018;142(5).

Publisher's note