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# Loxoprofen-Induced Edema in an Elderly Male: A Case Report

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## Abstract

A 79-year-old male presented to the general medicine department with one-month history of pitting edema of the dorsum of the hands and lower legs. The patient had no recent history of such an episode. On arrival, his vital signs were as follows: Glasgow Coma Scale, E4V5M6; body temperature, 36.6˚C; blood pressure, 146/84 mmHg; heart rate, 87 beats/min; respiratory rate, 16 breaths/min; and oxygen saturation, 97% on room air. Laboratory investigations and imaging revealed no remarkable findings. After loxoprofen was prescribed by the orthopedic department for lower back pain, edema developed. Drug-induced edema due to loxoprofen was suspected and, approximately 1 month after discontinuing the drug, the edema fully disappeared. This report aims to raise awareness among physicians, who should consider the possibility of a drug causing symptoms such as edema.

## Keywords

Edema, Drug-Induced Edema, NSAIDs, Differential Diagnosis

## 1. Introduction

Edema is defined as the accumulation of fluid in the interstitial space that occurs when capillary filtration exceeds the limits of lymphatic drainage, producing noticeable clinical signs and symptoms [1], which are frequently encountered in primary care settings. A nationally representative longitudinal survey study from the United States reported that the weighted prevalence of edema among adults > 50 years of age was 19% - 20% [2]. Chronic edema persisting for 3 months affects at least 100,000 individuals in the United Kingdom alone [3]. According to a facility-based study from Japan, the prevalence of chronic edema was 5.0% in university hospitals, 7.7% in acute community hospitals, and 66.1% in long-term medical facilities [4]. However, the differential diagnosis is extensive, and identifying the

cause is often challenging. In fact, edema is a nonspecific symptom in many diseases, ranging from benign to life-threatening. Prompt and accurate diagnosis and treatment of patients with edema depends on a rational and systematic approach.

Drug-induced edema is a commonly underestimated—yet potentially debilitating—condition. Edema occurs in 2% - 5% of patients taking non-steroidal anti-inflammatory drugs (NSAIDs) and in 6% - 14% of patients taking calcium channel blockers [5] [6]; as such, this condition cannot be overlooked.

Herein, a case of loxoprofen-induced edema that was diagnosed through a careful diagnostic work-up is reported.

## 2. Case

A 79-year-old male presented to the general medicine department with a one-month history of pitting edema of the dorsum of the hands and lower legs. It was detected during the course of an examination at a clinic of a family orthopedic surgeon, who referred to the patient to the author's department. The patient's medical history included ossification of the posterior longitudinal ligament of the cervical spine, and hypertension. He reported no use of illicit drugs, tobacco, or alcohol, no known allergies, and no family history of hereditary diseases. His regular medications included 3 mecobalamin (1500 μg) tablets, magnesium oxide (750 mg) tablets, sarpogrelate hydrochloride (300 mg) 3 times per day with every meal, amlodipine besilate (5.0 mg), dutasteride (0.5 mg), vonoprazan fumarate (20 mg), furosemide (20 mg) once daily, silodosin (8 mg) twice daily after breakfast and dinner, Shakuyaku kanzo-to (5.0 g), a Japanese Kampo medicine, twice daily before breakfast and dinner, and eszopiclone (1 mg), once per day before bed. In addition to these medications, he was newly prescribed loxoprofen (180 mg) 3 times per day with every meal at a family orthopedic surgeon clinic for lumbar spondylosis one month previously and the patient had been taking loxoprofen until 9 days prior to arriving at the author's department.

On presentation, the patient's vital signs were as follows: Glasgow Coma Scale (GCS), E4V5M6; body temperature, 36.6˚C; blood pressure, 146/84 mmHg; heart rate, 87 beats/min; respiratory rate, 16 breaths/min; and oxygen saturation, 97% on room air. On physical examination, the patient's pupillary light reflex was prompt and his respiratory and cardiac sounds were normal. Pitting edema was observed on the dorsum of the hands and lower legs without erythema, heat, or pain. Laboratory investigations revealed an elevated brain natriuretic peptide (BNP) level (33.4 U/L [reference range < 18.4/pg/mL]), D-dimer of 6.5 μg/mL (reference range < 0.9 μg/mL), and a qualitative urine test was negative for protein (**Table 1**). Chest radiography revealed cardiomegaly (cardiothoracic ratio, 56.6%), but no evidence of pneumonia or pleural effusion. Electrocardiography revealed first-degree atrioventricular block. Suspecting a side effect of loxoprofen as the cause of the edema, the patient was instructed to discontinue taking loxoprofen, and a diagnostic work-up for edema of the dorsum of the hands and the lower legs was performed.

There was no evidence of renal dysfunction or proteinuria, thus ruling out nephrotic syndrome. Thyroid function tests revealed normal thyroid-stimulating hormone level of 1.20 μIU/mL (normal range, 0.35 - 4.94 μIU/mL) and free thyroxine (fT4) level of 1.09 ng/dL (normal range, 0.70 - 1.48 ng/dL), ruling out thyroid dysfunction. Although the BNP level was slightly elevated and cardiomegaly was observed on imaging, echocardiographic ultrasound examinations demonstrated a 73% left ventricular ejection fraction and no left ventricular wall motion abnormality or valvular heart disease, in other words, no structural or functional abnormalities in the heart could be observed, ruling out heart failure. D-dimer level was slightly elevated, whereas lower-limb venous ultrasonography revealed no evidence of venous thromboembolism in the lower limbs. One month after discontinuing loxoprofen administration, the patient was re-examined, and all edema had disappeared.

Overall, the clinical and laboratory findings were consistent with a diagnosis of loxoprofen-induced, bilateral, pitting peripheral edema. The patient had a Naranjo adverse drug reaction (ADR) probability score of 6 (**Table 2**); accordingly, his symptoms were classified as a probable ADR [7]. Due to these circumstances, a referral document outlining his therapy was sent to an orthopedic surgeon. The patient was not readmitted to the author's department.

**Table 1.** Laboratory investigation results on admission.

| **On admission** | |
|---|---|
| **Blood cell count** | |
| WBC (/μL) | 6400 |
| RBC (/μL) | $418 \times 10^4$ |
| Hb (g/dL) | 13.4 |
| Hct (%) | 41.4% |
| Plt (/μL) | 171000 |
| **Urine test** | |
| Cloudiness | - |
| pH | 7.5 |
| Nitrites | - |
| Protein | - |
| Glucose | - |
| Ketone body | - |
| WBC (/HPF) | 1 - 4 |
| RBC (/HPF) | 1< |
| **Biochemical test** | |
| TP (g/dL) | 7.1 |
| Alb (g/dL) | 4.2 |
| BUN (g/dL) | 17.0 |
| Cre (mg/dL) | 1.27 |

**Continued**

| | |
|---|---|
| eGFR (ml/min/1.73m$^2$) | 42.6 |
| AST (U/L) | 14 |
| ALT (U/L) | 11 |
| T-Bil (mg/dL) | 0.5 |
| Na (mEq/L) | 146 |
| K (mEq/L) | 4.1 |
| Cl (mEq/L) | 104 |
| Glucose (mg/dL) | 118 |
| CRP (mg/dL) | 0.22 |
| D-dimer (μg/mL) | 6.5 |
| BNP (pg/mL) | 33.4 |

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Hct: hematocrit, HPF: hi power field, TP: total protein, Alb: albumin, BUN: blood urea nitrogen, Cre: creatinine, eGFR: estimated glomerular filtration rate, AST: aspartate aminotransferase, ALT: alanine transferase, T-Bil: total bilirubin, Na; sodium, K: potassium, Cl: Chloride, HbA1c: Hemoglobin A 1c, CRP: C-reactive protein, BNP: brain natriuretic peptide.

**Table 2.** Naranjo adverse drug reaction probability scale calculated for the case reported.

| Question | Answer | Score |
|---|---|---|
| Are there previous conclusive reports on this reaction? | Yes | +1 |
| Did the adverse event appear after the suspected drug was given? | Yes | +2 |
| Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given? | Yes | +1 |
| Did the adverse reaction reappear when the drug was readministered? | Do not know | 0 |
| Are there alternative causes (other than the drug) that could have on their own caused the reaction? | No | +2 |
| Did the reaction reappear when a placebo was given? | Do not know | 0 |
| Was the drug detected in any body fluid in toxic concentrations? | Do not know | 0 |
| Was the reaction more severe when the dose was increased/increasing or less severe when the dose was decreased? | Do not know | 0 |
| Did the patient have a similar reaction to the same or similar drugs in any previous exposure? | No | 0 |
| Was the adverse event confirmed by any objective evidence? | No | 0 |

## 3. Discussion

Loxoprofen has long been used clinically as a standard nonsteroidal anti-inflammatory drug (NSAID), not only in Japan, but also worldwide. In 2007, a questionnaire survey of 1568 physicians in 6 East Asian countries reported that loxoprofen was the second most commonly used NSAID in China in 2007 [8]. Over-the-counter doses of NSAIDs are effective for short-term relief of minor aches and pain due to headache, backache, menstrual cramps, common cold, muscular aches,

and arthritis [9]. This drug is instantly metabolized through trans-alcohol formation, acts as a non-selective inhibitor of cyclooxygenase (COX) after oral administration, and reaches its maximum plasma concentration in <1 h [10]. It inhibits COX enzymes, thereby reducing the synthesis of prostaglandins, which mediate inflammation and pain [11]. It is well known that the major side effects of loxoprofen are gastric inflammation and renal dysfunction [12] [13]. However, physicians should be aware that the adverse effects of loxoprofen are multifactorial. Relatively rare cases of loxoprofen-induced interstitial pneumonia and colonic ulceration [14] [15].

NSAIDs may affect blood pressure and induce edema via the renin-angiotensin pathway, alter sodium and water retention in the kidneys, inhibit vasodilating prostaglandins and produce various vasoconstricting factors, including endothelin-1 and P450-mediated metabolites of arachidonic acid [16]. NSAIDs have the potential for sodium and water retention, increased systemic vascular resistance, and blunted responses to diuretics [17]. The net impact is increased blood volume and blood pressure, which may cause edema related to increased hydrostatic pressure [18]. Although the patient described in this case was prescribed furosemide (20 mg) once daily, the blunted response to diuretics with loxoprofen may have prevented the improvement of edema.

For edema, some diuretics can be administered to alleviate swelling; however, this often results in frequent urination, which can lead to dehydration and decreased renal function [2] [19]. The patient developed resistance to diuretics due to loxoprofen; thus, while increasing the diuretic dose may have improved his edema, it could have led to dehydration and renal impairment. Increasing the diuretic dosage indiscriminately without thoroughly identifying the cause of edema must be avoided because it can only harm the patient.

## 4. Conclusion

A case of loxoprofen-induced edema in an elderly male is reported. Despite the unknown incidence rate, the "take-home message" is that physicians should be aware of the potential development of edema after treatment with loxoprofen. The dilemma for physicians prescribing loxoprofen is to maintain its anti-inflammatory and analgesic benefits while reducing or preventing side effects, including edema.

## 5. Limitations

The case report has certain limitations:

1) No re-administration test of loxoprofen have been conducted in this case.

2) As this report discussed only one illustrative case, the findings may not be generalizable.

3) This patient had been taking a lot of medications in addition to loxoprofen; therefore, the possibility of multifactorial edema could not be completely ruled out.

## Informed Consent

Informed consent was obtained from the patient by the corresponding author. Details of the patient have been anonymized as much as possible.

## Author Contributions

TT contributed substantially to the conception and design of this study. The author agreed to be responsible for all aspects of the work, ensuring that any questions related to the accuracy or completeness of any part of the work were properly investigated and resolved. The author approved the submitted version.

## Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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## References

[1] Trayes, K.P., Studdiford, J.S., Pickle, S. and Tully, A.S. (2013) Edema: Diagnosis and Management. *American Family Physician*, **88**, 102-110.

[2] Besharat, S., Grol-Prokopczyk, H., Gao, S., Feng, C., Akwaa, F. and Gewandter, J.S. (2021) Peripheral Edema: A Common and Persistent Health Problem for Older Americans. *PLOS ONE*, **16**, e0260742. https://doi.org/10.1371/journal.pone.0260742

[3] Moffatt, C.J., Franks, P.J., Doherty, D.C., Williams, A.F., Badger, C., Jeffs, E., *et al.* (2003) Lymphoedema: An Underestimated Health Problem. *QJM*, **96**, 731-738. https://doi.org/10.1093/qjmed/hcg126

[4] Dai, M., Nakagami, G., Sugama, J., Kobayashi, N., Kimura, E., Arai, Y., *et al.* (2019) The Prevalence and Functional Impact of Chronic Edema and Lymphedema in Japan: LIMPRINT Study. *Lymphatic Research and Biology*, **17**, 195-201. https://doi.org/10.1089/lrb.2018.0080

[5] Walker, C. and Biasucci, L.M. (2017) Cardiovascular Safety of Non-Steroidal Anti-Inflammatory Drugs Revisited. *Postgraduate Medicine*, **130**, 55-71. https://doi.org/10.1080/00325481.2018.1412799

[6] Makani, H., Bangalore, S., Romero, J., Htyte, N., Berrios, R.S., Makwana, H., *et al.* (2011) Peripheral Edema Associated with Calcium Channel Blockers: Incidence and Withdrawal Rate—A Meta-Analysis of Randomized Trials. *Journal of Hypertension*, **29**, 1270-1280. https://doi.org/10.1097/hjh.0b013e3283472643

[7] Naranjo, C.A., Busto, U., Sellers, E.M., Sandor, P., Ruiz, I., Roberts, E.A., *et al.* (1981) A Method for Estimating the Probability of Adverse Drug Reactions. *Clinical Pharmacology and Therapeutics*, **30**, 239-245. https://doi.org/10.1038/clpt.1981.154

[8] Arakawa, T., Fujiwara, Y., Sollano, J.D., Zhu, Q., Kachintorn, U., Rani, A.A., *et al.* (2009) A Questionnaire-Based Survey on the Prescription of Non-Steroidal Anti-Inflammatory Drugs by Physicians in East Asian Countries in 2007. *Digestion*, **79**, 177-185. https://doi.org/10.1159/000211713

[9] Hersh, E.V., Moore, P.A. and Ross, G.L. (2000) Over-the-counter Analgesics and Antipyretics: A Critical Assessment. *Clinical Therapeutics*, **22**, 500-548. https://doi.org/10.1016/s0149-2918(00)80043-0

[10] Riendeau, D., Salem, M., Styhler, A., Ouellet, M., Mancini, J.A. and Li, C.S. (2004) Evaluation of Loxoprofen and Its Alcohol Metabolites for Potency and Selectivity of Inhibition of Cyclooxygenase-2. *Bioorganic & Medicinal Chemistry Letters*, **14**, 1201-1203. https://doi.org/10.1016/j.bmcl.2003.12.047

[11] Voilley, N. (2004) Acid-Sensing Ion Channels (ASICs): New Targets for the Analgesic Effects of Non-Steroid Anti-Inflammatory Drugs (NSAIDs). *Current Drug Target - Inflammation & Allergy*, **3**, 71-79. https://doi.org/10.2174/1568010043483980

[12] Scheiman, J.M. (2016) NSAID-Induced Gastrointestinal Injury: A Focused Update for Clinicians. *Journal of Clinical Gastroenterology*, **50**, 5-10. https://doi.org/10.1097/mcg.0000000000000432

[13] Scarpignato, C., Lanas, A., Blandizzi, C., Lems, W.F., Hermann, M. and Hunt, R.H. (2015) Safe Prescribing of Non-Steroidal Anti-Inflammatory Drugs in Patients with Osteoarthritis—An Expert Consensus Addressing Benefits as Well as Gastrointestinal and Cardiovascular Risks. *BMC Medicine*, **13**, Article No. 55. https://doi.org/10.1186/s12916-015-0285-8

[14] Kato, M., Sasaki, S., Sekimoto, Y., Arano, N., Jo, H., Suina, K., *et al.* (2016) Loxoprofen-induced Interstitial Pneumonia: A Case Report. *Journal of Medical Case Reports*, **10**, Article No. 128. https://doi.org/10.1186/s13256-016-0919-2

[15] Nakase, H., Itani, T., Mimura, J., Kawasaki, T., Komori, H., Hashimoto, K., *et al.* (1999) Colonic Ulceration Caused by Administration of Loxoprofen Sodium. *Internal Medicine*, **38**, 249-251. https://doi.org/10.2169/internalmedicine.38.249

[16] Frishman, W.H. (2002) Effects of Nonsteroidal Anti-Inflammatory Drug Therapy on Blood Pressure and Peripheral Edema. *The American Journal of Cardiology*, **89**, 18-25. https://doi.org/10.1016/s0002-9149(02)02233-6

[17] Robert, L., O'Bryant, C.L., Cheng, D., *et al.* (2016) Drugs That May Cause or Exacerbate Heart Failure: A Scientific Statement from the American Heart Association. C*irculation*, **134**, e32-e69.

[18] Sinnathamby, E.S., Urban, B.T., Clark, R.A., Roberts, L.T., De Witt, A.J., Wenger, D.M., *et al.* (2024) Etiology of Drug-Induced Edema: A Review of Dihydropyridine, Thiazolidinedione, and Other Medications Causing Edema. *Cureus*, **16**, e53400. https://doi.org/10.7759/cureus.53400

[19] Keast, D.H., Despatis, M., Allen, J.O. and Brassard, A. (2014) Chronic Oedema/Lymphoedema: Under-Recognised and Under-Treated. *International Wound Journal*, **12**, 328-333. https://doi.org/10.1111/iwj.12224