

Ghosh-Laskar S, et al. Three-dimensional conformal radiotherapy (3D-CRT) versus intensity modulated radiation therapy (IMRT) in squamous cell carcinoma of the head and neck: a

randomized controlled trial. *Radiother Oncol* 2012;104:343-348.

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Drug-Induced Immune Hemolytic Anemia Caused by Postoperative Cefotetan Administration

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Dear Editor:

Drugs can induce almost any hematologic disorder that affects white blood cells, red blood cells (RBCs), platelets, and the coagulation system. Although the clinical manifestation of drug-induced immune hemolytic anemia (DIIHA) is usually mild, it may progress to acute severe hemolytic anemia (HA) and death. There is an increasing number of reports of second and third-generation cephalosporins causing clinical hemolysis¹. Cefotetan is a second-generation cephalosporin used frequently in postoperative condition. Here, we report a case of cefotetan-induced immune hemolytic anemia in a Korean (CIIHA).

A 68-year-old male with a small nasal nodule was diagnosed as basal cell carcinoma was referred to our hospital for further treatment. We removed the remaining lesion and the defect was repaired with a nasolabial flap (Fig. 1). Intravenous cefotetan 2 g daily was administered to the patient postoperatively for 7 days. Before discharge, the patient developed sudden mild fever (37.8°C) and fell down due to dizziness. Other symptoms including nausea, weakness, dark urine color, drowsiness, and pale appeared successively. During his hospitalization, there were no symptoms other than stomach discomfort. His he-

moglobin (Hb) and hematocrit were 3.5 g/dl and 12.8%, respectively. The total serum bilirubin was 6.86 mg/dl (Table 1). There was no evidence of internal bleeding upon physical examination. His reticulocyte and red cell production index were 2.93% (normal, 1% ~ 2%) and 0.916. We excluded chronic anemia, and acute gastrointestinal bleeding as a possible diagnosis. Therefore, we doubted a drug-induced condition. The patient was transferred to the Medical Intensive Care Unit. The patient's serum did not react with the antibody-detection RBCs. The

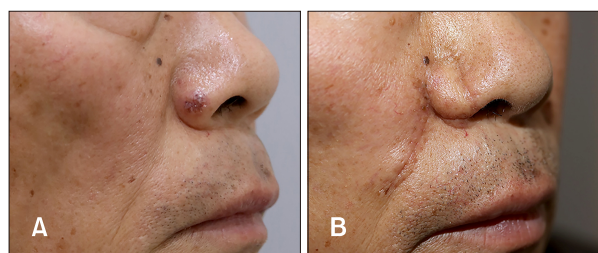


Fig. 1. A 1.0 cm×1.0 cm sized erythematous nodule with brown pigments on the nose (A) and at the 3 months follow-up (B). We received the patient's permission about publishing all photographic materials.

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Table 1. Characteristics of laboratory results and direct antiglobulin test of the patient

Hospital day	Hemo-globin (mg/dl)	WBC ($\times 10^9/L$)	MCV (fl)	Platelet ($\times 10^9/L$)	Total bilirubin (mg/dl)	AST (SGOT) (U/L)	ALT (SGPT) (U/L)	BUN (mg/dl)	Creatinine (mg/dl)	Iron ($\mu g/dl$)	Ferritin (ng/ml)	TIBC (U/L)	Haptoglobin	Creatinine (mg/dl)	LDH (U/L)	POLY	Anti-C3	
Pre-surgery	10.7	7.66	77.0	420	0.46	18	20	13.2	0.65	283	>16,500	295	<20	0.65	Not tested	Not tested	Not tested	
POD 8	3.9	22.98	80.5	262	6.86	247	22	88.6	1.6	283	>16,500	295	<20	1.6	3,505	+	+	
Post-intravenous systemic steroid																		
POD 9	6.7	19.31	86.9	215	1.94	134	36	106.2	0.87					0.87	1,207			
POD 13	7.9	16.02	92.5	196	0.55	32	30	34.5	0.68					0.68	1,147			
POD 15	9.4	10.21	92.4	147	0.46	18	27	18.8	0.65					0.65	1,003			

POD: postoperative day, WBC: white blood cell, MCV: mean corpuscular volume, AST: aspartate transaminase, SGOT: serum glutamic oxaloacetic transaminase, ALT: alanine aminotransferase, SGPT: serum glutamate-pyruvate transaminase, BUN: blood urea nitrogen, TIBC: total iron-binding capacity, LDH: lactate dehydrogenase, POLY: polyspecific anti-human globulin.

direct antiglobulin test was positive (polyspecific+ and anti-C3+) (Table 1). He was diagnosed with DIIHA due to cefotetan. His symptoms completely resolved after massive systemic steroid treatment and blood transfusion with 5 units of packed RBCs. The lactate dehydrogenase (LDH) level dropped from 3,005 to 1,003 U/L, and the Hb count was 9.6 g/dl at the time of discharge.

The induction of HA can be explained by four hypothetical mechanisms: 1) drug-induced production of antibodies leading to hemolysis. 2) The drug binds to the homologous site on the RBC membrane to form an antigen-neo complex. 3) The drug is absorbed into the cell membrane through direct covalent bonds. 4) The drug binds to the RBC membrane followed by the binding of proteins other than antibodies. In the case of cefotetan, hemolysis is most likely caused by 3) or 4).

Cefotetan accounts for 43% of all drugs which cause DIIHA over a 10 year period². The incidence of CIIHA was 1.4%³. The US FDA reported 18% fatalities and 8% renal failures³.

To our knowledge, this is the first reported case CIIHA in Korea. Prompt diagnosis, aggressive supportive measures, and appropriate treatments including systemic steroid treatment and blood transfusion are essential factors. Halting of the suspected drug is the first and most important step. The LDH level is a useful marker for the severity of hemolysis and for monitoring treatment responses⁴. Although DIIHA is rare, dermatologists should be aware of the causative drugs and clinical characteristics associated with severe HA.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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REFERENCES

- Chaudhry SB, Veve MP, Wagner JL. Cephalosporins: a focus on side chains and β -lactam cross-reactivity. *Pharmacy (Basel)* 2019;7:103.

2. Garratty G. Immune hemolytic anemia associated with drug therapy. *Blood Rev* 2010;24:143-150.
3. Martin ME, Laber DA. Cefotetan-induced hemolytic anemia after perioperative prophylaxis. *Am J Hematol* 2006;81:186-188.
4. Valent P, Lechner K. Diagnosis and treatment of autoimmune haemolytic anaemias in adults: a clinical review. *Wien Klin Wochenschr* 2008;120:136-151.

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Successful Removal of Angioleiomyoma with Ultrasonographic Evaluation

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Dear Editor:

Newer-generation ultrasonography devices are increasingly applied in the field of dermatology. Ultrasonography is less time-consuming and noninvasive. Portable ultrasonography devices enable point-of-care examination in the outpatient clinic. Minimal unwanted radiation exposure is an important reason ultrasonography is preferred.

Angioleiomyoma is a rare benign solitary tumor that originates from the vascular smooth muscle and can occur anywhere in the body, but more frequently in the lower extremities. It usually presents as a painful solitary slow-growing nodule¹.

A 33-year-old female presented with a purplish atrophic patch on her right lower leg (Fig. 1A). Three years before, she had presented to our clinic with a skin-colored firm nodule on her right lower leg, which is identical to the location of the present scar (Fig. 1B). We had performed a punch biopsy to diagnose the lesion. The histopathological

finding from the punch biopsy specimen was consistent with angioleiomyoma (Fig. 1C). As the patient did not have any discomfort after the biopsy and lesion became non-palpable, she refused further procedure. Two years later, she presented our clinic with intermittent pain on pressing the lesion. On physical examination, the patient felt mild tenderness, but no lesion was discernable under manual palpation. Further evaluation of the lesion was performed using ultrasonography (15 MHz, linear probe), which revealed a 5.7 mm × 4.7 mm sized, circumscribed homogenous hypoechoic mass in the deep subcutaneous tissue (Fig. 2A). We performed excisional biopsy of the solid mass under local anesthesia. The tumor removed appeared to be a grossly pearl-gray nodule (Fig. 2B). Its histopathological features were consistent with angioleiomyoma (Fig. 1D). We received the patient's consent form about publishing all photographic materials.

Angioleiomyoma is not commonly diagnosed preoperatively owing to its rarity and the lack of awareness among clinicians. However, high-resolution sonography has been increasingly used as the first-line modality to evaluate soft tissue tumors. Zhang et al.² investigated the clinical and sonographic features of subcutaneous angioleiomyoma. They demonstrated that the typical sonographic features of angioleiomyoma may include an oval shape, well-defined margins, a homogenous structure, and hypervascularity. By contrast, some studies reported that angioleiomyoma may show low or moderate vascular density^{3,4}.

Wortsman⁵ demonstrated sonographic features of dermatologic entities that are commonly examined with ultraso-

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