Traditional & Kampo Medicine

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Japanese Traditional Medicine for the Treatment of Swelling Caused by *Gloydius blomhoffii* Snakebites

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In Japan, *Gloydius blomhoffii* (mamushi) is the most common venomous snake and accounts for the majority of snakebite consultations each year. Its venom is primarily hemotoxic and contains enzymes such as phospholipase A_2 and metalloproteinases, which induce significant subcutaneous hemorrhage and inflammatory swelling. Clinical severity is traditionally graded from I to V based on the proximal spread of swelling. Although the overall prognosis for *G. blomhoffii* envenomation is relatively favorable, with a low mortality rate of approximately 0.5%–0.8%, severe cases—particularly Grades IV and V—carry a high risk of systemic complications [1, 2]. Major complications include rhabdomyolysis, which may progress to acute kidney injury (AKI), disseminated intravascular coagulation (DIC), and multi-organ failure [3]. Prompt reduction of swelling is essential to prevent these sequelae and reduce the need for surgical interventions such as fasciotomy (Table 1).

We experienced five patients with *G. blomhoffii* envenomation (three Grade V and two Grade III) using a combination of Japanese traditional (Kampo) medicines: saireito (SRT) and eppikajutsuto (EPTJ). To evaluate the clinical course, we monitored serum creatine kinase (CK), creatinine (Cr), and platelet counts. Rhabdomyolysis was confirmed in three patients.

Patient 1 (28-year-old male, Grade V): Presented with swelling extending to the trunk. CK peaked at 18,893 U/L on hospital day 3, yet renal function remained stable (Cr 0.71 mg/dL).

Patient 2 (9-year-old male, Grade V): Swelling progressed from Grade IV to V. Peak CK reached 6025 U/L with no renal impairment (Cr 0.39 mg/dL).

Patient 5 (74-year-old female, Grade V): Exhibited severe rhabdomyolysis (peak CK 7175 U/L) but maintained normal creatinine levels (0.64 mg/dL).

Platelet counts remained stable in all cases, and no patient developed consumptive coagulopathy. Fluid management was strictly implemented to prevent AKI. Patients with rhabdomyolysis required higher volumes of intravenous fluids; for example, Patient 2 received 7500 mL of lactated Ringer's solution over 7 days.

SRT is composed of shosaikoto and goreisan, which are traditionally used to treat water retention, edema, and febrile illness. Goreisan and related formulas have demonstrated strong diuretic effects through aquaporin inhibition and subsequent reduction of tissue edema. SRT and comparable Kampo formulations also demonstrate antioxidant properties, which may contribute to the reduction of inflammatory swelling.

EPTJ, consisting of gypsum, ephedra, *Atractylodes lancea*, jujube, Glycyrrhiza roots, and ginger, is indicated for acute inflammatory conditions characterized by swelling, pain, and heat sensation. Ephedra and *Atractylodes* provide diuretic and analgesic effects, whereas gypsum exhibits anti-inflammatory activity. Glycyrrhiza suppresses prostaglandin production and enhances anti-inflammatory responses. Historically, EPTJ has been recommended for the treatment of snakebites in classical Kampo texts and is reported to have achieved favorable outcomes [4].

Conventional treatment typically includes antitoxin and cepharanthine. However, antitoxin administration carries a 2%–12%

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TABLE 1 | Kampo medicine treatment for *Gloydius blomhoffii* snakebites.

Case	Age/sex (years)	Bite site	Severity	CK (IU/L)			Creatinine (mg/dL)			Platelet count ($\times 10^3$/uL)		
				Pre	Peak	Post	Pre	Peak	Post	Pre	Peak	Post
1	28/M	Thumb	V	12,791	18,893	8403	0.78	0.71	0.66	231	190	222
2	9/M	Thumb	V	167	6025	1333	0.4	0.39	0.39	276	298	352
3	22/M	Index finger	III	171	171	152	0.85	0.85	0.84	263	263	240
4	74/M	Thumb	III	693	2065	1269	0.62	0.60	0.63	191	177	187
5	74/F	Little finger	V	5832	7175	2074	0.65	0.64	0.59	205	173	159

Case	Kampo medicines	Duration (Days)	Intravenous infusion (Type, dose, days)	Other specific treatments	Complications	Sequelae
1	SRT, EPTJ	6	Lactated Ringer's (7000 mL, 4 days) 10% glucose (3500 mL, 4 days)	None	Diplopia Rhabdomyolysis	None
2	SRT, EPTJ	39	Lactated Ringer's (7500 mL, 7 days)	None	Rhabdomyolysis	None
3	SRT, EPTJ	6	Lactated Ringer's (1500 mL, 2 days)	None	None	None
4	SRT, EPTJ	5	Lactated Ringer's (2500 mL, 4 days)	None	None	None
5	SRT, EPTJ	9	Lactated Ringer's (4000 mL, 6 days)	None	Rhabdomyolysis	None

Abbreviations: CK, creatine kinase; EPTJ, eppikajutsuto; F, female; M, male; SRT, sareito.

risk of allergic reactions, including serum sickness and anaphylaxis, and its impact on overall survival remains under discussion [5]. Corticosteroids are sometimes used to control inflammation but may cause rebound swelling during dose tapering.

From the perspective of traditional Japanese medicine, inflammatory swelling following envenomation is interpreted as "fluid retention". In our cases, alongside appropriate fluid therapy, the combined use of SRT and EPTJ, both of which possess diuretic properties, was associated with favorable control of severe swelling and rhabdomyolysis, without apparent adverse effects or sequelae. Although further studies are required to establish efficacy, traditional Japanese medicine may represent a safe and practical adjunctive option for managing severe snakebite-induced swelling.

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The authors have nothing to report.

Disclosure

SRT and EPTJ were administered as Tsumura Saireito Extract Granules and Tsumura Eppikajutsuto Granules (Tsumura & Co., Tokyo, Japan).

Consent

Informed consent was obtained from the patients and their family members.

Conflicts of Interest

Hajime Nakae received honoraria from Tsumura & Co. The other authors declare no conflicts of interest.

Data Availability Statement

Data supporting the findings of this study are available upon request from the corresponding authors. The data are not publicly available because of privacy and ethical restrictions.

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