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Spontaneous Renal Hemorrhage in Hemodialysis Patients; a Case Series

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Abstract: Spontaneous renal hemorrhage (SRH) is characterized by the acute onset of non-traumatic subcapsular and/or perirenal hematoma formation. Idiopathic SRH is rare, as SRH is most commonly due renal neoplasms with renal angiomyolipoma (AML) followed by renal cell carcinoma (RCC). Idiopathic SRH is known as one of complication of hemodialysis (HD). It is often life-threatening due to hemorrhagic shock and requires prompt recognition and appropriate management. We herein report four cases of idiopathic SRH with HD. None of the patients had hematologic disease, congenital vascular anomalies or renal neoplasm, and none showed a bleeding tendency. Only one patient had taken anticoagulants. All of these patients were diagnosed with SRH by computed tomography (CT). Bleeding was stopped via transcatheter arterial embolization (TAE) with gelatin sponges in three and n-butyl-2-cyanoacrylate (NBCA) in one. No patients experienced rebleeding. Generally, the diagnosis of SRH is difficult due to its non-specific symptoms. Abdominal ultrasonography is not useful for identifying retroperitoneal hemorrhage. CT is useful for identifying not only perinephric hemorrhage with 100% sensitivity but also AML. Intravenously injected anticoagulants of HD seem to have a greater influence on the development of idiopathic SRH than oral anticoagulants. Indeed, HD with intravenous anticoagulants itself is a risk factor for idiopathic SRH. We can stop the bleeding of idiopathic SRH using gelatin sponges; TAE with gelatin sponges is therefore recommended to stop the bleeding of idiopathic SRH. This is because gelatin sponges can be used from the peripheral bleeding point to the main trunk of the renal artery. We do not recommend NBCA be used to stop bleeding of idiopathic SRH due to its technical difficulty and the ease with which NBCA can spread to other organs via the arteries.

Keywords: spontaneous retroperitoneal hemorrhage, renal bleeding, transarterial embolization (TAE), anticoagulant, Wunderlich Syndrome

INTRODUCTION

Spontaneous renal hemorrhage (SRH) was first described by Wunderlich as Wunderlich syndrome in 1856[1] and characterized by the acute onset of non-traumatic subcapsular and/or perirenal hematoma formation. SRH is a rare disease, with only 102 cases reported between 2000 and 2016 in a systematic review by Ahn [2]. SRH is often life-threatening due to hemorrhagic shock and requires prompt recognition and appropriate management [3]. It is most commonly due to renal neoplasms (56.9%), followed by renal angiomyolipoma (AML) renal cell carcinoma (RCC) and vascular disease (25.5%) [2]. Idiopathic SRH is known to occur with hemodialysis (HD) at a rate of 0.516 cases per 100 patients[4]. We herein report four cases of idiopathic SRH associated with HD.

CASE PRESENTATION

We treated four Japanese idiopathic SRH patients with HD in our intensive-care unit. On arrival, the patients showed normal vital signs. None of the patients had hematologic disease or congenital anomalies. SRH was diagnosed in these patients by computed tomography (CT). We investigated the patient's blood test results before and after bleeding and therapies. The patients' characteristics are listed in Table 1. They had all been on HD for a long time (average of 6.75 years; range 3-13) and received HD with unfractionated heparin. No patients showed a bleeding tendency, although one was taking anticoagulants (aspirin, clopidogrel and cilostazol). CT showed that all of the patients had renal subcapsular hematoma. None had AML, RCC or vessel malformations on CT or angiography. All of the bleeding points were located in the distal portion of the causative artery on angiography with extravasation. Bleeding was stopped via transcatheter arterial embolization (TAE) with gelatin sponges in three patients and n-butyl-2-cyanoacrylate (NBCA) in one. After TAE, we use nafamostat mesilate as an anticoagulant for HD.

Table-1: patient characteristics

patient	1	2	3	4
age	75	80	75	59
sex	female	male	male	female
etiology of ESRD	diabetes mellitus	chronic kidney disease	diabetes mellitus	diabetes mellitus
symptoms	abdominal pain	cannot move	shock	cannot move hypothermia
years on dialysis	3	4	13	7
anticoagulation	none	none	aspirin clopidogrel cilostazol	none
past history	reflux esophagitis hyper tension	hyper tension bladder cancer duodenum ulcer ileus	gastric cancer arteriosclerosis obliterans	Cerebellar hemorrhage hyper tension
Hb (before/after bleeding) <g/dL>	9.9/8.4	11/6.9	13.7/7.7	12.1/3.3
plt (before/after bleeding) <10^4μl>	14.7/10.2	11/12.9	8.1/6.9	14.4/6.7
PT-INR (before/after bleeding)	1/1	1.4/1.3	1.2/1.46	1.1/1.54
aPTT (before/after bleeding) <S>	28.2/29.3	46.4/47.3	28.8/43.3	36.3/47.0
fib (after bleeding) <mg/dl>	377	654	80	136
last HD day before bleeding	on the same day	2 days before	during HD	3 days before
the first HD day after bleeding	1 day after	1 day after	2 days after	1 day after
extravasation on CT	(no enhanced)	positive	positive	(no enhanced)
bleeding point	subcapsular	subcapsular	subcapsular	subcapsular in cyst
embolic materials	gelatin sponge	gelatin sponge	gelatin sponge	NBCA

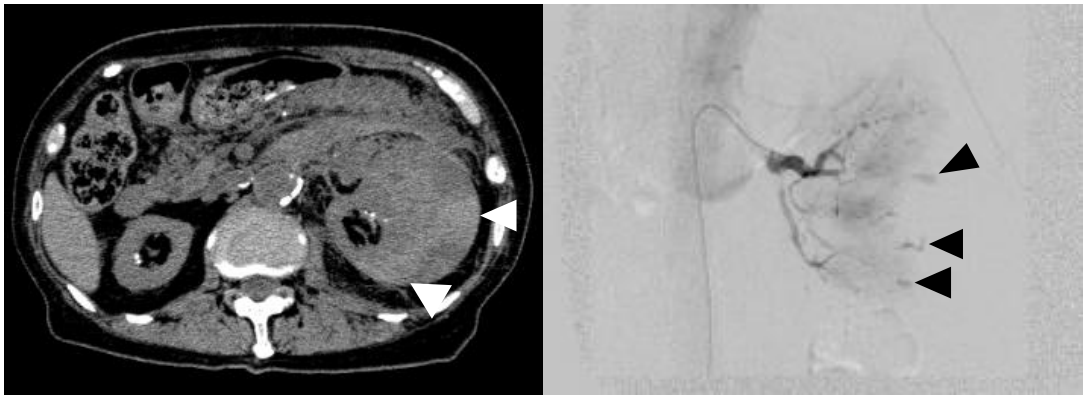

Fig-1: CT and angiography in case 1

Left (CT), a subcapsular hematoma (white arrowheads) in the left kidney is shown.
Right (angiography), Extravasations are found in the inferior area (black arrowheads).

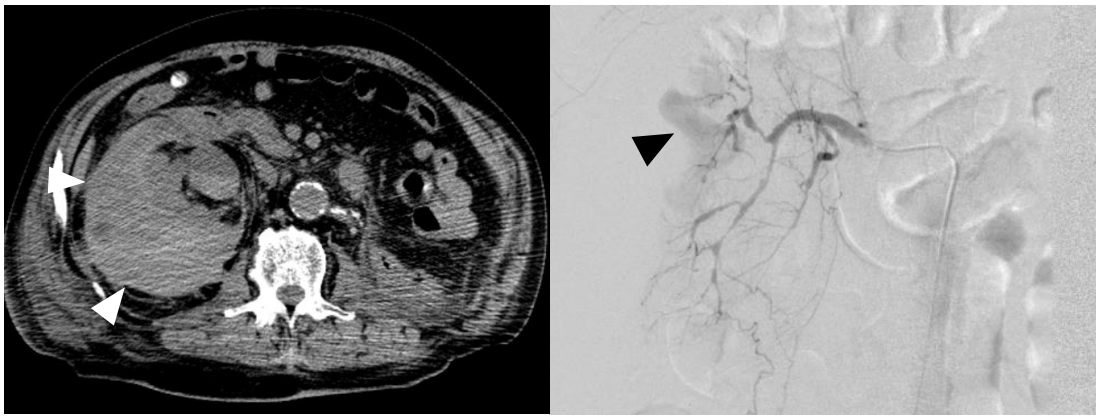

Fig-2: CT and angiography in case 2

Left (CT), a subcapsular hematoma (white arrowheads) in the right kidney is shown.
Right (angiography), Extravasations are found in the superior area (black arrowheads).

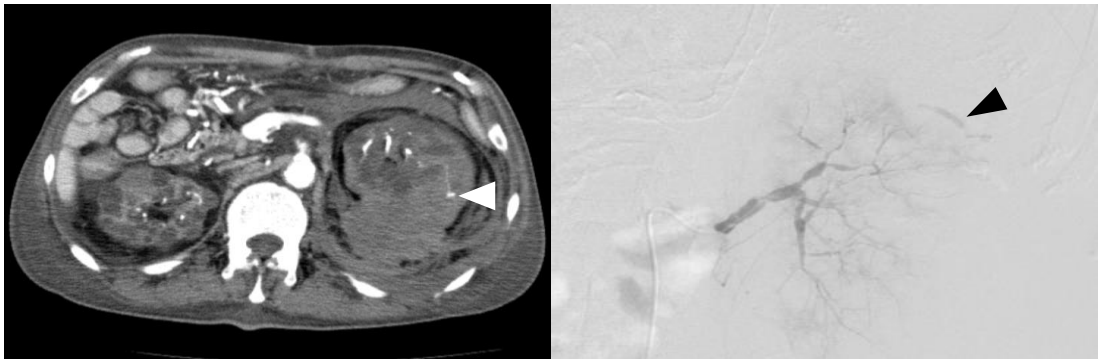

Fig-3: CT and angiography in case 3

Left (CT), A subcapsular hematoma (white arrowheads) in the left kidney are shown.
Right (angiography), Extravasations are found in the superior area (black arrowheads).

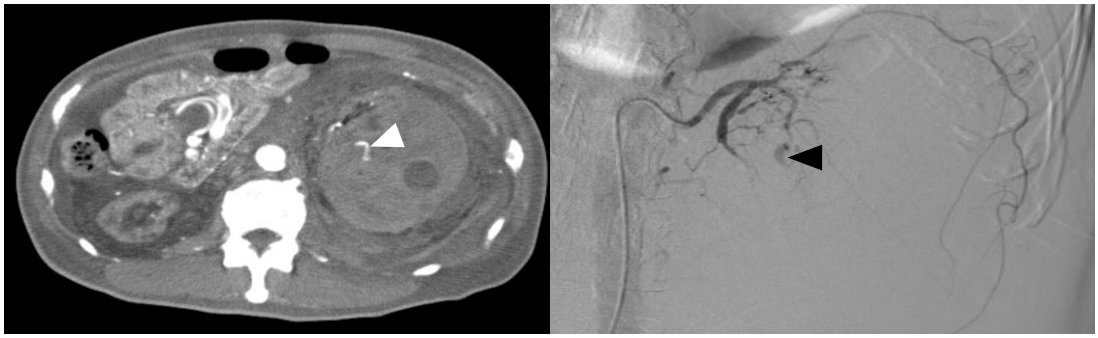

Fig-4: CT and angiography in case 4

Left (CT), a subcapsular/cystic hematoma (white arrowheads) in the left kidney are shown.
Right (angiography), Extravasations are found in the inferior area (black arrowheads).

DISCUSSION

Some SRH patients present with the triad of acute abdominal pain, a palpable flank mass and hypovolemia [5]. However, many show non-specific symptoms, such as nausea, vomiting, headache, a fever, weight loss, anemia and macroscopic hematuria [6]. SRH can therefore be difficult diagnose. Abdominal ultrasonography was reported not to be useful for identifying retroperitoneal hemorrhage, as patients often lack any retroperitoneal fluid [7]. CT was shown to be the most commonly used modality for the initial evaluation. CT identifies perinephric hemorrhage with 100% sensitivity [2], and its sensitivity for detecting renal masses or vascular abnormalities causing SRH can reach 100% [8]. For example, CT identifies AMLs as well-circumscribed renal masses with intratumoral fat (attenuation range −20 to −40 Hounsfield units) [9], and CT angiography can detect the source of hemorrhage, after which super-selective embolization can be performed to stop the bleeding [10].

In Japan, 25,391 patients have an HD vintage exceeding 20 years. Many cases of idiopathic SRH with HD exist, but there have only been a few case reports [11]. The four patients reported herein were all receiving HD, so we suspect that HD was a risk factor for their idiopathic SRH. The relative risk in HD patients compared to normal subjects is 10.7 times higher than that for cerebral hemorrhage in normal patients [12].

There are three suspected causes of idiopathic SRH due to HD. First, uremic patients have a bleeding tendency associated with platelet dysfunction, as the platelets of uremic patients have a reduced aggregating response to adenosine diphosphate, epinephrine and collagen [13-15]. Second, amyloid deposition was found in 90% of HD patients for 7 to 13 years in a prospective postmortem study [16]. Third, the anticoagulation used for HD may contribute to perinephric hemorrhage [17]. Anticoagulation via either oral or intravenous injections (both unfractioned and low-molecular-weight heparins) represents a major risk factor for SRH [18]. However, among our four patients, only one was taking any oral anticoagulants (three agents), and the others were taking none.

Some cases of bleeding during dialysis have been reported [4]. One case presented with SRH one month after starting HD with a history of five years on peritoneal dialysis (PD)[19]. The frequency of SRH reported to be higher with HD than with PD[4]. Heparinization during HD is said to cause SRH. HD patients may be particularly susceptible to idiopathic SRH due to intravenous anticoagulation injections. Recently, the mainstream treatment for SRH has shifted toward minimally invasive treatment. TAE was primarily chosen in 42.2% of cases, followed by conservative/medical management (29.4%) and surgery (27.5%)[2]. Conservative/medical management

included bed rest, blood transfusion and the discontinuation of anticoagulants with adequate monitoring of the blood pressure and hemoglobin (Hb) levels [17].

TAE is a minimally invasive way to stop bleeding and selectively embolize vessels using a micro-catheter and micro-guidewire [2]. At present various embolic materials, including gelatin sponges, coils and NBCA, are available, and the efficiency of TAE depends on the appropriate choice of such materials. These embolic materials can be either temporary or permanent; for example, gelatin sponges disappear within two weeks of placement. Only NBCA is useful for patients with coagulopathy, DIC and multiple injuries. Some physicians have reported limited success with gelatin sponges on SRH, describing complications of temporary embolization and late rebreeding [20].

However, the bleeding in our three patients treated with gelatin sponges stopped completely, and there were no rebleeding events. This is because gelatin sponges were used from the peripheral bleeding point to the main trunk of the renal artery.

After TAE using gelatin sponges, HD can be immediately restarted without rebleeding. We do not recommend NBCA be used to stop bleeding of idiopathic SRH due to its technical difficulty and the ease with which NBCA can spread to other organs via the arteries. We also recommend against using coils, as these cannot be delivered to the peripheral bleeding point through narrow arteries. In recent studies, surgery has been preferred for patients in shock as well as in AML patients with tuberous sclerosis [21].

Malek reported the existence of malignancy in 6 out 55 chronic HD patients with SRH[4]. It is difficult to detect malignancy in cases of SRH using CT. Careful scrutiny for solid masses using CT or magnetic resonance imaging is recommended to exclude RCC underlying SRH [22].

CONCLUSION

Idiopathic SRH is a known complication of HD. CT is useful for the diagnosis of SRH in HD patients. TAE with gelatin sponges from the peripheral artery to the main trunk of the renal artery is recommended to stop bleeding permanently.

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