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Original Research

A preliminary study on classification and therapeutic strategies for spontaneous perirenal hemorrhage

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ABSTRACT

Background: The aim of our study was to report our experience in the classification and therapeutic management strategies for spontaneous perirenal hemorrhage (SPH).

Methods: From September 2005 to April 2015, 20 patients with SPH were newly diagnosed in our hospital. Their clinical features, image findings, identification of underlying causes, and therapeutic management were retrospectively analyzed, and relevant literature was reviewed. In this study, patients were classified according to the degree of severity of the disease or emergency imaging diagnosis of underlying causes. On the basis of the former, patients were classified as critical and noncritical, and on the basis of the latter, patients were classified as renal cell carcinoma (RCC), undefined solid neoplasm, angioleiomyolipoma (AML), and unknown cause.

Results: In the acute stage, contrast-enhanced computed tomography (CT) was superior to ultrasonography for both diagnostic accuracy of SPH ($p = 0.02$) and etiology discovery power ($p = 0.004$). The results of contrast-enhanced magnetic resonance imaging (MRI) were identical to those of contrast-enhanced CT. We summarized a flowchart in the whole classification and therapeutic strategies of SPH. According to the imaging diagnosis of underlying causes, all the patients with undefined solid neoplasm or RCC underwent emergency operation. Patients with AML or unknown cause underwent selective arterial embolization (SAE) or conservative management according to the critical degree. Acute hemorrhage was controlled in 19 cases, of which 14 were cured by the operation and only one critical patient with severe shock died shortly despite rescue efforts.

Conclusions: Contrast-enhanced CT or MRI is the first choice of imaging examination, which could not only accurately diagnose SPH but also detect the underlying causes. Choice of therapeutic strategies for SPH should vary according to the identification of critical patients and imaging diagnosis of underlying cause.

1. Background

Spontaneous perirenal hemorrhage (SPH) is a relatively uncommon but often diagnostically challenging condition. Carl Wunderlich is credited with the first clinical description of Wunderlich syndrome (WS) in 1856, as SPH was confined to the subscapular and perinephric space in patients with no history of trauma. The incidence of this disease is low, and most of the literature are case reports [1,2]. Usually, patients with SPH have potential pathological changes of the kidney. Renal neoplasms are the most common causes of SPH, which account for 60%–65% of all cases. Renal angioleiomyolipoma (AML) is the most common benign neoplasm responsible for SPH (accounting for 30%–40%), whereas renal cell carcinoma (RCC) is the most common malignant neoplasm (accounting for 25%–35%). SPH caused by other neoplasms such as nephroblastoma, nephrosarcoma, urothelial carcinoma, and renal oncocytoma is rare [1–3]. Vascular diseases are the second common cause of SPH, which account for 20%–30% of SPH cases, in which polyarteritis nodosa accounts for half of the vascular pathology. Other vascular etiologies include renal aneurysm, arteriovenous malformations (AVMs), arteriovenous fistulas (AVFs), and so on [4,5]. Furthermore, other underlying causes of SPH such as hereditary and acquired renal cystic diseases as well as infectious disease (suppurative renal disease and pyelonephritis) were also reported [2,3].

SPH is typically characterized by acute flank pain, hypovolemic shock, hematuria, and flank mass. The onset of this disease is abrupt, and it causes excessive bleeding, thereby leading to a quick hypovolemic shock. Owing to massive retroperitoneal bleeding in patients, the underlying causes of SPH could not be revealed in around 20% of the cases by emergency imaging findings, and this makes it difficult to choose an optimal management. As the majority of the underlying

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etiologies causing SPH are benign diseases such as AML, vascular diseases, and renal cyst, it is therefore important to avoid unnecessary nephrectomy, and standard procedures might contribute to diagnosis and management of SPH.

In this study, we retrospectively analyzed and evaluated the outcomes of various diagnostic imaging modalities and different management approaches in 20 patients with SPH treated in our hospital, and relevant literature was reviewed. We proposed a simple and effective flowchart for SPH therapeutic management, and this might facilitate physicians to select an optimal management and ensure maximum benefit for patients.

2. Patients and methods

2.1. Patient information

We retrospectively collected information of 20 patients who were confirmed as having SPH between 2008 and 2015 at a hospital. The Clinical Research Ethics Committee at our institute had approved the study and granted permissions to access the patient records. This work has been reported in line with the STROCSS criteria [4]. Patients' demographics are described in Table 1. The median age of the patients was 53 years (range, 14–83 years). Among the 20 patients, 11 cases were initially confirmed in our hospital and nine cases were transferred from other hospital. None of these patients had a history of trauma or previously any anticoagulant therapy.

All patients presented with acute flank or abdominal pain. Six cases displayed hypovolemic shock. Among them, five cases had moderate shock (systolic blood pressure ≤ 90 mmHg) and one patient had severe shock (systolic blood pressure ≤ 60 mmHg). All the patients had percussion pain in the renal region and only one patient had ecchymosis on the flank and back. There were no signs of peritoneal irritation such as obvious tenderness, rebound tenderness, and muscle rigidity in all cases.

2.2. Laboratory examination

Blood routine tests, urine routine tests, liver function, renal function, and coagulation function were performed in all cases. Ten patients presented with anemia, including six cases with severe anemia (Hb < 60 g/L) and four cases with mild-to-moderate anemia. Five cases had coagulation abnormalities and two cases had microscopic hematuria.

2.3. Imaging examination

Color Doppler ultrasound and contrast-enhanced computed tomography (CT) were performed in all patients. Contrast-enhanced magnetic resonance imaging (MRI) was performed in five patients. On color Doppler ultrasound, SPH with acute hematoma appeared as an isoechoic or hyperechoic subcapsular or perinephric collection, thus causing compression and displacement of renal parenchyma. Blood-rich mixed masses with hyperechoic fat component ingredient indicated an AML. On contrast-enhanced CT, SPH with acute hematoma was categorized as those occurring in renal subcapsular space, perirenal space, and pararenal space according to the scope of hematoma; its CT values varied from 60 to 80 HU (Hounsfield units). As hemorrhagic lesions contain mixture of density masses with fat density (CT value ≤ −20 HU), imaging diagnosis indicated rupture of AML (Fig. 1 A, B). During the corticomedullary phase of contrast-enhanced CT, heterogeneous enhancing hypervascular soft tissue mass within the hematoma indicates rupture of RCC (Fig. 1 C, D). On contrast-enhanced MRI, relative to the muscle, acute hematoma (< 7 days) showed equal or slightly low signal intensity on I, which stands for “image,” and low signal intensity on II, which stands for “image. If the predominant component of hematoma was fat, it could present with a high signal on I, which stands for “image,” and slightly high on II, which stands for “image,” and displayed a low signal on the fat-suppressed sequence of I, which stands for “image” and II, which stands for “image.” This evidence indicated the rupture of AML.

2.4. Treatment and follow-up

In our study, considering the severity of hemorrhagic shock caused by SPH, the critical degree of a patient was judged on the basis of blood pressure and shock index, which indicates moderate shock. Meanwhile, kidneys, located in the retroperitoneum, cause a relatively lower spped of blood loss than abdominal organs; therefore, the hemoglobin level can be a reliable indicator of the severity of blood loss. Critical patients with SPH are defined as patients with systolic blood pressure ≤90 mmHg, shock index ≥1.5, and Hb level < 60 g/L. Six critical cases were then diagnosed. The shock index was separately 2.2, 1.7, 1.6, 1.6, 1.8, and 1.5. The hemoglobin level was separately 29 g/L, 46 g/L, 51 g/L, 52 g/L, 42 g/L, and 58 g/L. Management of patients with hemorrhagic shock was by deep venous catheterization, monitoring of vital signs, shock index and urine volume, fluid resuscitation,

Table 1
Characteristics of patients with WS.

No.	Gender	Age	Critical patient	Imaging diagnosis of underlying cause	Management	Confirmed etiology
1	F	43	YES	AML	Transferred from other hospital, emergency RN	AML
2	M	64	YES	AML	Transferred from other hospital, died after transient rescue efforts	AML
3	F	60	NO	AML	Conservative management, selective PN	AML
4	F	43	NO	AML	Conservative management, selective RAPN	AML
5	F	53	NO	AML	Conservative management, selective RAPN	AML
6	M	35	NO	AML	Conservative management	AML
7	M	73	NO	AML	Conservative management	AML
8	F	66	YES	RCC	Emergency RN	RCC
9	M	14	NO	RCC	Emergency RN	RCC
10	F	52	YES	Renal metastasis from lung cancer	Emergency SAE	Renal metastasis from lung cancer
11	F	63	NO	Undefined solid neoplasm	Emergency RN	RCC
12	F	40	NO	Undefined solid neoplasm	Emergency PN	Complex renal cyst
13	M	54	YES	Unknown cause	Emergency SAE	Renal cyst
14	M	23	NO	Unknown cause	Conservative management, selective PN	AML
15	M	83	NO	Unknown cause	Conservative management	Renal cyst
16	F	38	YES	AML	SAE invalid, emergency RN	AML
17	F	53	NO	AML	Conservative management, selective PN	AML
18	F	28	NO	AML	Conservative management, selective PN	AML
19	F	59	NO	AML	Conservative management, selective RAPN	AML
20	F	60	NO	AML	Conservative management, selective RAPN	AML

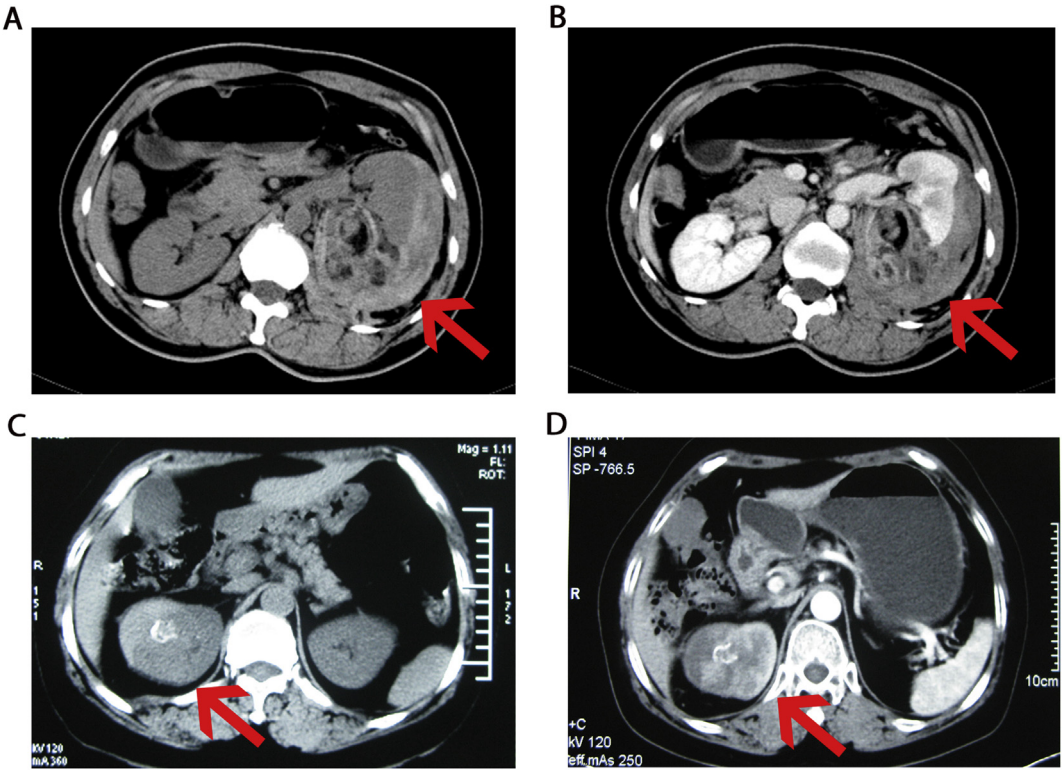

Fig. 1. CT image of a solid neoplasm. A. plain CT image of angioleiomyolipoma (AML), B. enhanced CT image of AML, C. plain CT image of renal cell carcinoma (RCC), and D. enhanced CT image of RCC.

and hemostatic and vasoactive agents. All patients meeting the above critical degree definition had a quick progress in shock, and conservative management was effective in none of them. According to imaging diagnosis for underlying causes, critical patients underwent emergency operation or transcatheter renal artery angiography plus selective arterial embolization (SAE). Emergency operations include radical nephrectomy (RN) and partial nephrectomy (PN). Noncritical patients underwent conservative management, or emergency operation or renal arteriography plus SAE. Further treatment options were offered to patients following conservative management according to the imaging follow-up. All patients underwent blood routine, urine routine, renal function, color Doppler ultrasound, and contrast-enhanced CT every three months after the treatment. No patient failed the follow-up during the study.

2.5. Statistical analyses

All statistical analyses were processed using statistical software SPSS ver. 17.0 (SPSS, Inc., Chicago, IL). Categorical variables were assessed by the chi-square test. *P* values were estimated, and $p < 0.05$ was considered as statistically significant.

3. Results

3.1. Imaging diagnosis

All patients initially underwent contrast-enhanced CT and ultrasonography. CT was superior to ultrasonography for both the diagnostic accuracy of SPH ($p = 0.02$) and the underlying cause discovery power ($p = 0.004$) (Tables 2 and 3). Contrast-enhanced MRI was performed in five cases, and the results were identical to those of CT.

Table 2
Diagnostic accuracy of WS in the acute bleeding stage.

	CT	US	P
Yes	20	14	0.02
No	0	6	

Table 3
Diagnostic accuracy of underlying cause in the acute bleeding stage of WS.

	CT	US	P
Yes	15	5	0.004
No	5	15	

3.2. Treatment

Clinical characteristics of all patients are summarized in Table 1.

The clinical condition of six critical patients deteriorated shortly despite undergoing active supporting therapy. Their blood pressure and hemoglobin levels declined, and blood coagulation function deteriorated progressively. Two of them were transferred from other hospital to our hospital owing to failure of conservative management; one patient with severe hypovolemic shock rapidly declined and died soon despite emergency rescue efforts. The remaining five patients underwent SAE or/and emergency operation, and their diseases were alleviated or cured.

In 14 noncritical cases, two undefined solid neoplasms and one RCC were identified by imaging examinations. All these three cases underwent emergency operation; the postoperative pathology confirmed RCC diagnosis in two cases and a complex renal cyst in the third case. Two patients had unknown causes; the remaining nine cases with AML initially received conservative management. For the former two people, the imaging follow-up confirmed that one case was AML and the other one was a renal cyst.

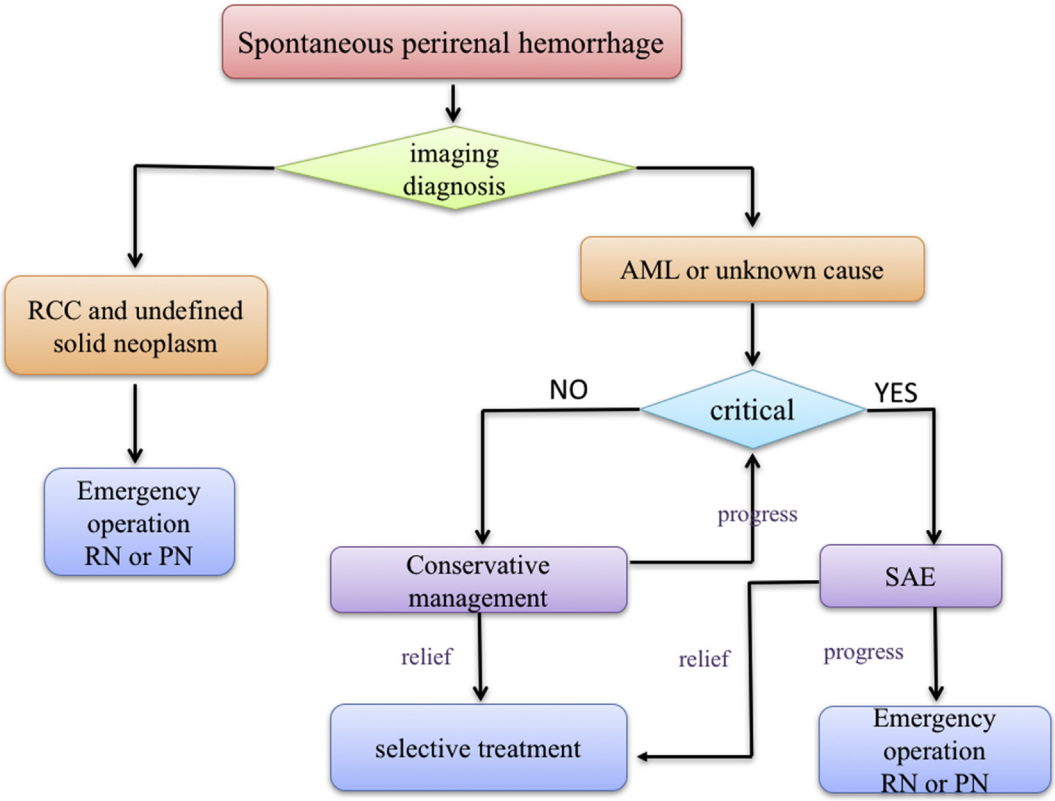

Fig. 2. Classification and therapeutic management strategies for spontaneous perirenal hemorrhage.

3.3. Follow-up

The mean follow-up time in our study was 34 months (range: 13–79 months). Emergency operations were performed in six cases and SAE was performed in two cases. Among 11 cases undergoing successive conservative management, hematomas were absorbed completely in 3–6 months. Eight of them then underwent PN, and no recurrence of neoplasm or SPH was detected afterwards. Further treatment was rejected in the remaining three cases, of which one patient presented tumor progression and SPH recurrence during the follow-up and was again relieved after conservative management. A patient with renal metastasis from lung cancer died of tumor progression after 11 months but with no recurrence of SPH.

4. Discussion

It is very difficult to diagnose SPH because of the absence of specific clinical manifestation and a wide variety of causes. Patients usually present with acute flank or abdominal pain, a palpable flank mass, hematuria, and hypovolemia. In this study, the main clinical manifestation included acute flank or abdominal pain, percussion pain in the renal region, hypovolemia, and hematuria. No one presented with signs of peritoneal irritation. Thus, when emergency patients presented with acute flank or abdominal pain, especially persistent pain with hypovolemia and hematuria, urologists should consider not only acute renal colic but also SPH.

Color Doppler ultrasound is the most commonly used imaging examination in emergency. In our study, the diagnostic power of SPH and its disease causes were much higher for contrast-enhanced CT than that for color Doppler ultrasound. Thus, contrast-enhanced CT is the first choice of imaging examination for emergency patients with suspected SPH. Continuous thin-layer spiral CT scanning and 3D image reconstruction could show the extent of hematoma and detect the underlying causes of SPH more accurately [5–8]. For patients allergic to CT contrast agents, MRI is preferred [3].

Currently, there are no systematic analysis and summary for the therapeutic management of SPH. Moreover, many controversies exist in this area. The main management options for SPH treatment include conservative management, SAE, and emergency operation. The advantage of conservative management is that there is a chance to choose optimal management when the hematoma subsides, and the general condition of the patient and local tissue response of the kidney ameliorate. This could enhance the success rate of subsequent nephron-sparing surgery. Particularly, when the cause of SPH is not identified or uncertain in the acute bleeding phase, follow-up CT scans could detect the underlying cause and help the doctor select the optimal treatment. However, once an emergency operation is inevitable because of failure of conservative management and occurrence of hemorrhagic shock, vital sign instability of the patient and enlarged hematoma might lead to not only the failure of nephron-sparing surgery but also life-threatening risk. For emergency surgical exploration, the advantages to patients are the quick control of bleeding and the direct management of lesions. But in this situation, RN is usually mandatory and applying nephron-sparing surgery is very difficult for the following reasons: First, during fast bleeding, especially when the cause of SPH is unknown, it is difficult to find the lesion and identify its properties. Second, bleeding and inflammation might lead to severe abdominal adhesion and unclear boundaries between the lesion and surrounding normal anatomical structures. In addition, the renal tissue had edema and brittle texture [9]. Hence, it becomes difficult to remove the lesion and suture the renal tissue. As for the advantage of SAE, renal arteriography could localize bleeding lesions and SAE could control hemorrhage quickly to avoid unnecessary nephrectomy. However, it also has some disadvantages. First, incomplete embolization or recurrent bleeding may occur because of complicated tumor blood supply [10]. Second, patients with malignant tumor undergoing SAE instead of emergency radical surgery might increase the risk of tumor progression or metastasis [11,12]. For the above reasons, based on our clinical study and the

latest relevant literature on SPH, we think that the choice of therapeutic strategy for SPH is more reasonable according to identification of critical patients and imaging diagnosis of the underlying cause, and hence, we developed a simple and effective flowchart of SPH therapeutic strategies (Fig. 2); the details are explained in the next few paragraphs. This flowchart is not a formal guideline but own working tool that can offer a reference to facilitate physicians to choose an optimal management. More cases are expected to be recruited to verify its feasibility in the future. SPH caused by metastatic renal tumor is rare but easy to diagnose; hence, it is not summarized in the flowchart. In our study, a patient with SPH together with renal metastasis from lung cancer was successfully managed with SAE. SAE is a safe and effective option for metastatic renal tumor–related SPH [13].

AML is the most common benign neoplasm that could cause SPH. The blood vessels within AMLs are abnormal, with no internal elastic lamina. The smooth muscle is replaced by fibrous tissue, which might lead to aneurysm formation and rupture [2,10,14]. Approximately 20–30% of patients with AML have tuberous sclerosis (TSC) [2,10,14,15]. Larger tumor size (> 4 cm) and diameter of the intralesional aneurysms (> 5 mm) directly correlate with tumor-related hemorrhage in AMLs [2,10,15,16]. Patients with AML accompanied with symptoms (such as back pain, hematuria, and so on), pregnancy, and TSC also increase the risk of SPH [14,15,17,18]. Fortunately, CT and MRI are highly accurate in detecting typical AML [1,2,19].

Recently, some literature showed that emergency SAE could be used to treat acute bleeding and at the same time protect the renal function [20]. Most AMLs lead to tumor shrinkage after SAE. However, 30%–40% of patients with AML undergoing SAE need re-embolization or surgical intervention because of re-canalization of the treated abnormal vessels or creation of new pathological vessels [10,14,15]. In our study, imaging findings of 12 cases showed that AML was the underlying cause of SPH. In three critical patients, one case failed to SAE and underwent emergency surgical exploration; finally, he had to be performed nephrectomy because of failure of nephron-sparing surgery. The remaining two critical patients, who failed to conservative management in other hospital, were transferred to our hospital, one with severe hypovolemic shock who died soon after transient rescue efforts and the other one underwent emergency surgical exploration and nephrectomy because of failure of nephron-sparing surgery. All noncritical patients achieved remission after conservative management. Most of them underwent selective PN after hematomas were absorbed, and the success rate of nephron-sparing surgery was 100%. Generally, if conservation management for patients with SPH was successful, the hematomas could be completely absorbed within 3–6 months. Selective operation at that time might increase success rate of PN. In summary, in the acute bleeding phase, if imaging findings indicate that the cause of SPH is typical AML, then selective operation following conservation management is the optimal choice for noncritical patients. However, in addition to critical patients, if noncritical patients fail to respond to conservative management, then renal arteriography + SAE is the first-line treatment and emergency surgical exploration should not be performed until hemostasis of SAE is invalid so as to avoid the risk of nephrectomy for benign lesions.

RCC is the most common malignant neoplasm leading to SPH, and clear cell RCC, which possess a rich network of blood vessels and rapid growth characteristics, is the most common histological type. Large size, intratumoral necrosis and hemorrhage, and extension into the renal vessels are risk factors for rupture of the RCC. Increase in the intratumoral pressure related to edema resulting from vascular invasion of the tumor, acute increase in the renal vein pressure, and rapid tumor growth with associated hemorrhage and necrosis are proposed mechanisms for spontaneous rupture of the RCCs [1,3]. During the acute hemorrhage phase of SPH, contrast-enhanced CT is the first diagnostic approach to detect underlying RCC. Furthermore, after excluding typical AML by CT scans, the majority of the solid renal neoplasms leading to SPH are malignancy, including RCCs or other neoplasms with malignant potential (such as epithelioid angiomyolipoma) [1–3,19]. Delay in surgical removal after rupture of the RCC increases the risk of tumor progression and metastasis, and surgical resection as early as possible could improve the prognosis of patients [11,12].

In this study, the CT scan finding of four cases showed solid renal neoplasms without imaging characteristics of typical AML, and emergency surgical exploration were performed in all of them. Finally, RN was performed in three patients with pathologically proven RCCs. PN was performed in one case and pathologically confirmed complex renal cyst. Thus, in the acute phase of SPH, if imaging findings of the underlying cause indicate solid renal neoplasm without imaging characteristics of typical AML, then we suggest that emergency surgical exploration is the first treatment so as to excise the renal malignancies as early as possible.

The major underlying causes of SPH are benign renal diseases such as AML, vascular diseases, renal cyst, and so on. In this study, in the acute phase of SPH, the underlying causes could not be detected by imaging examination in three cases. One critical patient underwent SAE, and the remaining two noncritical cases underwent conservative management. Benign renal diseases were identified in all three cases; one case was AML and the remaining two cases were renal cyst. Renal arteriography along with SAE is the optimal diagnostic and therapeutic approach to renal vascular diseases, which is the most common cause of SPH except renal neoplasms [1–3]. Therefore, as the underlying causes of SPH cannot be detected by imaging examination, we recommend that renal arteriography and SAE should be considered as the first therapy for critical patients, which can not only control hemorrhage quickly and effectively but also timely diagnose and treat renal vascular diseases. On the other hand, we recommend conservative management should be the first option for noncritical patients, so that physicians can take appropriate treatment after identifying the underlying cause by sequential follow-up imaging.

5. Conclusion

SPH is a rare, acute-onset, and potentially life-threatening condition with myriad causes. Contrast-enhanced CT or MRI is the first choice of imaging examination, which could not only accurately diagnose perirenal hemorrhage and show the extent of hematoma but also detect the underlying causes. Choice of therapeutic strategies for SPH should vary according to the identification of critical patients and imaging diagnosis of the underlying cause.

Ethical approval

Zhongshan Hospital Fudan University (Shanghai, China). Clinical Research Ethics Committee of Zhongshan Hospital, Fudan University had approved the study and granted permissions to access the patient records.

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Author contribution

LL performed statistical analysis and drafted the manuscript. RW took charge of the study design and revising manuscript critically for important intellectual content. YX, JW, YX, YQ, QL, LS and JG participated in the collection of patient materials and correction of words in the manuscript. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Research registration number

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Guarantor

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