Case Series

Clinical Characteristics of Renal Infarction in an Asian Population

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Abstract

Introduction: Renal infarction is a rare and easily missed disease. There is even less meaningful information on renal infarction in the Asian population. Thus, the aim of this study was to clarify the clinical characteristics of the disease in Asian patients. Clinical Picture: Over a period of 10 years, 38 Chinese patients with renal infarction diagnosed by contract-enhanced CT or angiography were enrolled in this study. Their demographic data, clinical characteristics, laboratory and image results, risk factors or suspected causes, treatment and final outcomes were retrospectively reviewed. The results were also compared with the analogous Western data. The mean age of the sample population was 60.8 ± 17.6 years, with patients aged over 50 years and males predominating. The most common symptoms/signs were abdominal (57.9%) and flank pain/tenderness (50%). Only 23.7% of patients had suffered previous thromboembolic events such as coronary or peripheral artery diseases, or cerebral infarction. Cardiogenic factors, such as atrial fibrillation, intra-cardiac thrombus, infective endocarditis and valvular heart disease, were the main causes of renal infarction (57.9%). The most common laboratory abnormalities were elevated serum LDH (92.1%) and proteinuria (76.3%). Only half of the cases involved haematuria at initial presentation. Treatment and Outcome: One-third of the sample suffered renal impairment after the renal infarction. Overall mortality rate during admission was 13.2% (n = 5). The cause of death was usually not the renal infarction itself but rather the underlying disease and its complications. There was no difference in outcome for anticoagulation treatment with or without thrombolytics. Compared to their Western counterparts, the proportion of males (71.1% versus 48.3%) and bilateral renal infarctions (31.6% versus 12.4%) were significantly higher, and the percentage of leukocytosis (50% versus 85%) significantly lower in our Asian patients. Conclusion: Clinical presentation of renal infarction is usually non-specific and differs for Asian and Western populations. In our Asian patients, the most common clinical characteristics were abdominal pain/tenderness, flank pain/tenderness, elevated serum LDH and proteinuria. Early diagnosis and treatment are imperative because of the high rate of renal impairment and associated mortality. If this disease is suspected, contrast-enhanced CT is suggested to exclude or confirm renal infarction and anticoagulation alone is currently the favored treatment.

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Introduction

Renal infarction is a rare disease. Domanovits et al[1] reported an incidence rate of 0.007% (17/248,842) during a study period of 45 months. As the presentations are usually non-specific, diagnosis is difficult and the disease is frequently mistaken as other common entities such as urolithiasis, abdominal disease, lumbago or even myocardial infarction.[1-7] If the diagnosis proves incorrect and treatment is delayed or absent, there is a high risk of renal failure and other complications such as embolic events to other organs may occur.[1,3] Information with respect to renal infarction is limited, however, with almost all of the published research having been carried out on Western populations. As Asian investigation and comparative study with other races are still lacking, the objective of this investigation was to provide some insights into these important issues.

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Case Series

This setting for this investigation was a 2900-bed tertiary medical centre in Taiwan. Permission from the institute's ethics review committee was not needed for this retrospective analysis. The hospital computer database was searched for medical records with the International Classification of Diseases code 593.81 (vascular disorders of kidney). The records of 45 patients hospitalised between 1 January 1996 and 31 December 2005 were found. The definition of duration before diagnosis was the time after hospital visit or appearance of symptoms/signs during admission. Diagnosis of renal infarction was based on the findings of contrast-enhanced computed tomography (CT) and angiography. CT diagnosis of renal infarction was determined by the presence of a wedge-shaped parenchymal perfusion defect, with or without a cortical rim sign and without mass effect or major perirenal stranding.[1,3,7] Angiography diagnosis relied on demonstration of occlusion or filling defect in the renal artery.[3] By the definition of renal infarction above and after excluding cases involving traumatic causes, patients aged less than 14 years, and incomplete records, a total of 38 Taiwanese patients with renal infarction were enrolled. Two experienced physicians participated independently in the reviewing process. Demographic data, clinical characteristics, laboratory and image results, risk factors or suspected causes, treatments and final outcomes were retrospectively collected and analysed from the relevant medical records. Conclusion was only made after discussion by these 2 physicians if any question arose during the data collection and analysis. Our findings were also compared with those of previous Western research to determine whether there were any ethnic differences.

SPSS 13.0 software (SPSS, Chicago, IL) was used for the statistical analysis. Results were presented as number (%) or mean ± SD. Categorical variables between groups were compared using the χ^2 test or Fisher's exact test. $P < 0.05$ was considered statistically significant for all tests.

A total of 38 patients were enrolled in the study. Diagnosis was based on contrast-enhanced CT in 37 cases, with angiography used for the remaining individual. As shown in Table 1, the mean patient age was 60.8 ± 17.6 years (range, 21 to 91), with most aged over 50 years (n = 27; 71.1%). Although both patients who needed haemodialysis and the 5 who died during admission were over 50 years of age, no significant differences were demonstrated for any of the study parameters comparing individuals above or below this threshold. The majority of the patients were male (n = 29; 76.3%). The mean duration before diagnosis was 4.1 ± 6.5 days. Only 15 patients (39.5%) were diagnosed within 1 day of hospital visit or appearance of symptoms/signs during admission. If renal impairment and normal function were categorised according to new-onset creatinine ≥1.5 or <1.5 mg/dL, respectively, the diagnostic interval was longer for the former subgroup (7.6 ± 12.5 versus 3.0 ± 3.2 days), but the result was not statistically significant. Pain or tenderness was the initial symptom/sign in the majority of the patients (n = 32; 84.2%), including 22 abdominal pain/tenderness (57.9%) and 19 flank pain/tenderness (50.0%). Other symptoms/signs were nausea/vomiting, fever/chills and constipation. Only 9 of the subjects had suffered previous thromboembolic events such as coronary artery disease, cerebral infarction, and peripheral artery disease. Common risk factors or suspected causes of renal infarction were: hypertension (n = 18; 47.4%); atrial fibrillation or intra-cardiac thrombus (n = 17; 44.7%); and, infective endocarditis or valvular heart disease (n = 8; 21.1%). Other less common risk factors included diabetic mellitus, malignancy, coagulation or

Table 1. Summary of Demographic Data, Symptoms/Signs, Risk Factors or Suspected Causes, and Affected Sites

Age (y)	60.8 ± 17.6
Male	29 (76.3)
Duration before diagnosis (day)	4.1 ± 6.5
Pain/tenderness	32 (84.2)
Abdominal	22 (57.9)
Flank	19 (50.0)
Back	5 (13.2)
Nausea/vomiting	5 (13.2)
Fever/chills	2 (0.05)
Previous thromboembolic events*	9 (23.7)
Risk factor or suspected cause+	
Cardiogenic	22 (57.9)
Atrial fibrillation or intra-cardiac thrombus	17 (44.7)
Infective endocarditis or valvular heart disease	8 (21.1)
Hypertension	18 (47.4)
Diabetes mellitus	7 (18.0)
Malignancy	4 (10.5)
Coagulation or haematological disease	2 (0.05)
Renal artery dissection	2 (0.05)
Involved kidney	
Right	13 (34.2)
Left	13 (34.2)
Bilateral	12 (31.6)
Concomitant splenic infarction	7 (18.4)

Note: all the data were presented as mean ± SD or number (%)

* Including coronary artery disease, cerebral infarction, and peripheral artery disease

\+ Some patients may have multiple risk factors or causes

haematological disease, renal artery dissection, vasculitis, sepsis and antiphospholipid antibody syndrome. Twelve patients (31.6%) had suffered bilateral renal infarction. Involvement was unilateral in two-thirds of the sample (n = 26; 68.4%), but there was no significant difference between sides. Seven patients (18.4%) suffered concomitant splenic infarction.

The initial laboratory data for all patients are shown in Table 2. Common laboratory abnormalities, in descending order of prevalence, were: elevated serum lactate dehydrogenase (LDH) (n = 35; 92.1%); proteinuria (n = 29; 76.3%); haematuria (n = 20; 52.6%); and leukocytosis (n = 19; 50.0%). Only 31.6% and 42.1% of the sample had elevated AST and ALT, respectively.

Twenty-six individuals received anticoagulation therapy alone (Table 3), and 8 underwent combined treatment with anticoagulants and thrombolytics. There was no significant difference in follow-up outcomes between the 2 treatment groups. Only 2 patients needed haemodialysis during the treatment period. Neither of them received anticoagulation or thrombolytics due to underlying coagulopathy and both died during admission. In total, 5 patients (13.2%) died and the effects were: sepsis (n = 3); end-stage malignancy (n = 1); and aortic dissection (n = 1). Of these, 3 did not receive anticoagulation, 1 received anticoagulation alone, and the remaining individual received combined anticoagulation and thrombolytic therapy. None of the survivors experienced recurrence during the follow-up period (32 to 330 days).

Asian and Western populations were compared to determine whether there were any ethnic differences (Table 4). The comparison showed that 3 of the study parameters were significantly different, with greater male predominance, higher rate of bilateral renal infarction and lower rate of leukocytosis demonstrated for the Asian sample.

Table 2. Summary of the Initial Laboratory Data

Blood test (reference range)	**Mean ± SD**
WBC (4500-10500/cumm)	12067.6 ± 5095.1
LDH (95-215 U/L)	707.5 ± 555.2
BUN (0-20 mg/dL)	28.7 ± 22.5
Creatinine (0-1.5 mg/dL)	1.8 ± 1.6
AST (5-45 U/L)	42.6 ± 28.0
ALT (0-40 U/L)	38 ± 25.4
Urine test	**No. (%)**
Proteinuria	29 (76.3)
Haematuria (dipstick)	20 (52.6)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; LDH: lactate dehydrogenase; SD: standard deviation; WBC: white blood cell count

Discussion

As in Western populations, older patients predominated in this study. By contrast, the proportion of males was significant higher in our sample (71.1% versus 48.3%; Tables 1 and 4). The initial symptoms/signs, such as abdominal, flank or back pain, nausea/vomiting and fever, were typically non-specific in both populations. The mean time to diagnosis was about 4 days, with only 15 of our cases (39.5%) correctly diagnosed as renal infarction within 1 day of admission or symptom/sign presentation. Hazanov et al[3] found that only 40% of patients were correctly diagnosed at admission, with most of the determinations made within the first 3 days. Further, all 11 cases of the sample of Korzets et al[2] were initially misdiagnosed. It is

Table 3. Summary of Treatment and Outcome

Treatment	**No. (%)**
Anticoagulation alone*	26 (68.4)
Anticoagulation + thrombolytics†	8 (21.1)
Need haemodialysis	2 (5.3)
Mortality during admission	5 (13.2)

* Oral wafarin or/with IV or SC heparin
† IV or intra-renal artery urokinase injection

Table 4. Comparison between Asian (current) and Western (previous) Data

	Asian Data (N = 38)	**Western Data* (N = 89)**	***P* value**
Mean age (y)	60.8	65.7	NA†
Gender (male/female)	29/9	43/46	0.04
Previous thromboembolic events‡	9 (23.7)	20 (22.5)	NS
Unilateral/bilateral	26/12	78/11	0.02
Splenic involvement‡	7 (18.4)	4 (9.1)§	NS
Pain/tenderness‡	32 (84)	81 (91)	NS
Elevated lactate dehydrogenase‡	35 (92)	78 (91)	NS
Leukocytosis‡	19 (50)	76 (85)	0.000
Protenuria‡	29 (76)	12 (71)¦¦	NS
Haematuria (dipstick)‡	20 (53)	59 (72)	NS
Mortality‡	5 (13.2)	9 (10.1)	NS
Follow-up creatinine ≥1.5 mg/dL‡	13 (34)	30 (41)	NS

* Including reports by Hazanov et al (2004),[3] Korezets et al (2002),[2] Domanovits et al (1999),[1] and Lessman et al (1978),[4] a total of 89 patients were reported.
† NA: not available
‡ The data are presented as number (%)
§ Only data reported by Hazanov et al, 44 patients reported in total.
¦¦ Only data reported by Domanovits et al, 17 patients reported in total.

remarkable that renal infarction is so often overlooked by clinicians despite the great advances in medicine and technology. Given this advancement, therefore, it appears reasonable to speculate that the main problem is a lack of specific knowledge and a relative deficit in vigilance for this serious disease. More education and effective diagnostic strategies are required for this uncommon disease with non-specific manifestation.

Previous studies have demonstrated that, as in the cerebral/myocardial variants, the cause of renal infarction is thromboembolism. Thus, previous history of this condition should increase suspicion of renal infarction.[1-5,7] Only 9 of our sample (23.7%) had suffered thromboembolic events, however, and the low positive rate suggests that history is not especially useful in the diagnosis of renal infarction. The most common causes or risk factors for this event are cardiogenic thromboembolism, including atrial fibrillation, intracardiac thrombus, infective endocarditis, and valvular heart disease (n = 22; 57.9%), in line with the results of Western studies (40% to 60%).[2,7] Further, sickle cell disease, thrombophilia, autoimmune disease, cocaine use, trauma and medical intervention may reportedly contribute to renal infarction.[1]

Twelve of our Asian subjects (31.6%) suffered bilateral renal infarction, a significantly higher proportion compared to the Western samples (31.6% versus 14.1%; $P = 0.02$; Tables 1 and 4). This predominance gives us a reference for studying renal infarction, but the definitive factor for the difference cannot be identified and quantified based on the available data.

The most common abnormality in our laboratory analysis was the serum LDH (92.1%), which was 3 times higher than the normal upper limit (Tables 2 and 4). Serum LDH, which is a characteristic marker for cell necrosis and known to be elevated in patients with acute renal infarction,[1-5,7] was also shown to have the highest sensitivity in our patients. However, little is known with respect to the interval from pain onset to occurrence of LDH elevation. In 1 of the subjects of Domanovits et al,[1] elevated LDH was not detected at admission, but detected after 12 hours, which suggests that follow-up LDH is necessary because if may not be elevated on initial examination. Because LDH is highly sensitive but not specific for acute renal infarction, other causes of LDH elevation, such as mesenteric ischaemia and haemolysis, intra-abdominal infection, and acute myocardial infarction, and tumour must, therefore, be excluded as soon as possible.[1]

Proteinuria is the second most common laboratory abnormality, and about three-quarters of our patients had this at presentation. However, the presence of proteinuria is mentioned only by Domanovits et al[1] whose results are similar to our own (Tables 2 and 4). Western studies also reported a high frequency of haematuria (72%) in renal infarction. In the present study, however, the frequency of hematuria was significantly lower at only 53%. Theoretically, proteinuria and hematuria are caused by glomerular damage.[8] Renal infarction leads to tissue necrosis, which may involve the glomeruli and produce proteinuria and haematuria. However, both of these dysregulations may be considerably delayed because the associated structural damage takes several hours to develop. Thus, an initial lack of proteinuria and haematuria does not rule out renal infarction. If renal infarction is still suspected, follow-up urinalysis should be considered. In our opinion, these 2 markers may be used as indicators for renal infarction, but the relationship with other clinical characteristics should be established because they are also non-specific.

Up to 85% of the Western samples had leukocytosis. By contrast, the proportion of our Asian patients with this presentation was significant lower (50%; Table 4). Leukocytosis is usually a reaction to disease. It can only assist in resolution of the differential diagnosis; it is not suitable as an indicator of renal infarction, especially in Asian populations.

The current golden standard is still angiography, but contrast-enhanced CT has gradually replaced it in mainstream image study due to its convenience, noninvasive character and high accuracy.[1-5,7] Furthermore, CT may detect extrarenal causes of abdominal or flank pain including appendicitis, diverticulitis, biliary tract disease, leaking aortic aneurysm, and gynaecological disease.[3] For the above reasons, we suggest that contrast-enhanced CT should be the first choice in suspected renal infarction or where there is uncertainty with respect to abdominal or flank pain.

Ultrasound is relatively inexpensive and widely available, and it has even been tested for diagnosis of renal infarction.[3] It is not suggested for diagnosis now, however, due to its low sensitivity and because any abnormal findings require confirmation through additional investigation.[3] Despite its many limitations, ultrasound can still play a role in excluding urolithiasis and obstructive uropathy.[1] By contrast, renal scintigraphy is noninvasive, simple, and safe for detection and diagnosis of renal infarction. In addition, the renal function can be evaluated at presentation for subsequent comparison on follow-up. However, it is not available in the emergency setting and can only demonstrate the presence of an area of decreased perfusion and not the aetiology of the infarction.[3]

Although the treatment of choice for renal infarction remains unclear, early anticoagulation with heparin and/or warfarin is the most favoured method.[1-3] Better outcome has not been demonstrated for anticoagulation with thrombolytic therapy, and it is seldom used in current

practice due to the associated risks of haemorrhage.[3] In addition, these patients with renal infarction are also at high risk for repeated thromboembolism in other organs (intestine or cerebrum) with possibly fatal outcome, which may be prevented by long-term anticoagulation.[1] Most of our patients were treated with anticoagulation alone, however, outcome did not differ from the 8 receiving additional thrombolytics. Based on this evidence, therefore, it appears reasonable to suggest anticoagulation alone for renal infarction in the absence of evidence favouring alternative treatment.

Our results were similar to the Western findings, with 30% to 40% of our patients suffering renal impairment after renal infarction. Although the subsequent renal impairment does not usually result in uraemia necessitating haemodialysis, the associated mortality is not low (Table 4). Further, the fact that the cause of death is not always the renal infarction itself but the underlying disease and complications of the infarction highlights the necessity of early diagnosis and prompt treatment.[1-3]

This investigation did have some limitations. Firstly, it was a retrospective study and some clinical manifestations or records may not have been completely documented. However, it seems unpractical to perform a prospective study because renal infarction happens rarely in clinical practice. Secondly, we did not use golden standard of angiography as the diagnostic tool in all the patients. With the improvement in CT technology (especially spiral CT) in recent years, the accuracy of diagnosing renal infarction using contrast-enhanced CT has been accepted and applied in recent studies.[1-3] Thirdly, this study was conducted in a single tertiary medical centre, which may not be representative of the population. Further research involving more patients would be useful in this regard.

Conclusion

Renal infarction is a rare and easily missed disease. In this study of an Asian sample population, the associated symptoms/signs, such as abdominal pain, flank pain, nausea and fever, were non-specific. Cardiogenic thromboembolism was the main cause of the disease. Other causes and risk factors were hypertension, diabetes mellitus and malignancy. Elevated serum LDH and proteinuria were the most common laboratory abnormalities; however, both are non-specific. Only half of our patients had leukocytosis or haematuria. Compared to the Western populations, our Asian sample had a higher proportion of males and bilateral renal infarctions, and a lower rate of leukocytosis. Early diagnosis and treatment are imperative as 34% of our patients suffered renal impairment after their renal infarction, with 13.2% expiring due to the effects of the associated diseases. We suggest that contrast-enhanced CT should be performed as soon as possible to exclude or confirm renal infarction where it is suspected. We recommend treatment with anticoagulants alone, as there is no definitive evidence to support superior outcome when anticoagulation is used in combination with thrombolysis.

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