CASE REPORTS

Arteriovenous Fistulae Secondary to Renal Cell Carcinoma

Clinical and Cardiovascular Manifestations: Report of a Case

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SUMMARY
A 63-year-old woman presented with progressive congestive heart failure and unexplained cardiomegaly. Diagnostic workup revealed large arteriovenous fistulae in the lower pole of the left kidney. A total left nephrectomy was performed and microscopic exam revealed renal cell carcinoma. Following surgery, the congestive heart failure cleared and the patient has been asymptomatic for one year.

The pertinent findings of the 22 patients who have been reported previously in the literature with arteriovenous fistulae complicating renal cell carcinoma are reviewed. Thirty percent of the patients presented with cardiovascular complaints, and 60% had significant cardiovascular findings during the course of evaluation. An abdominal bruit was the most discriminating finding on physical exam, and it occurred in 72% of the reported cases. The diagnosis was unexpectedly established by surgery in 13%, and by angiography in 87% — usually in the course of a workup for hypertension, abdominal pain, hematuria, or during search for an occult malignancy. An extensive evaluation is required for early diagnosis of this correctible cause of hypertension and heart failure.

Arteriovenous Fistulae may occur from a variety of causes, and the cardiovascular effects of the altered circulatory state have been well described in the literature. Renal cell carcinoma with significant arteriovenous shunt formation is an uncommonly encountered entity, yet it is a reversible cause of hypertension and heart failure. We recently had the opportunity of seeing a patient with chronic, severe congestive heart failure secondary to arteriovenous fistulae complicating an unsuspected renal cell carcinoma. The case is being reported and the available English literature reviewed in order to summarize the clinical and cardiovascular manifestations of this disease entity.

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Case Report

M.L. (SMH #82-41-48) is a 63-year-old woman who was admitted to the Strong Memorial Hospital on October 7, 1972, with congestive heart failure and pulmonary edema. She had no history of hypertension, valvular heart disease or chest pain. Cardiovascular exam revealed a blood pressure of 175/80 mm Hg, pulse regular at 110 per minute, distended jugular veins, diffuse pulmonary rales, cardiomegaly without heart murmurs, and pitting pre-tibial edema. Routine laboratory studies were unremarkable including a urinalysis without gross or microscopic hematuria. She responded to digoxin, diuretics, oxygen, and low salt diet. During the course of this hospitalization a systolic bruit was heard over the left flank, but the patient refused an intravenous pyelogram for further evaluation. Twelve days after admission she was discharged in a markedly improved condition.

During the subsequent year, she developed progressive congestive heart failure despite an augmented cardiac regimen. She was readmitted on November 21, 1973, with congestive heart failure and a very rapid ventricular response to atrial fibrillation. Cardiac examination revealed a well-nourished woman with a blood pressure of 180/75 mm Hg, an irregular pulse at 130 per minute, a normal thyroid gland, elevated jugular venous pressure, and congestive rales. Cardiomegaly was present with enlargement of the heart to the anterior axillary line; the first heart sound was accentuated, a right ventricular heave was palpable, and a grade 2/6 ejection-type systolic murmur was heard.

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best along the left sternal border. A high pitched systolic bruit was heard in the left flank. Hepatomegaly was present without other palpable abdominal masses. There was pitting edema of the lower extremities. An electrocardiogram revealed atrial fibrillation with terminal S waves in the lateral precordial leads suggesting right ventricular hypertrophy (fig. 1). Chest X-rays revealed mild pulmonary congestion and generalized cardiomegaly with left atrial and right ventricular enlargement (fig. 2). Urinalysis was negative and red blood cells were absent from the sediment. Thyroid function tests were normal.

After appropriate stabilization, cardiac catheterization was performed for the evaluation of possible left atrial myxoma. Pressures in all chambers were normal, cardiac index was elevated at 4.45 L/min/m², and an oxygen step up was noted in the right atrium (table 1). A left ventricular angiogram revealed excellent contractility of the left ventricle and early recirculation of the contrast material into the right atrium. This latter finding together with the oxygen step up in the right atrium raised the question of a systemic left-to-right shunt. Aortic and renal arteriography revealed large arteriovenous fistulae in the lower pole of the left
Table 1

Hemodynamic Findings

| Parameter                                      | Value  |
|------------------------------------------------|--------|
| Arterial O₂ content, vol %                    | 16.60  |
| Pulmonary arterial O₂ content, vol %          | 13.92  |
| A-V O₂ difference, vol %                      | 2.68   |
| Superior vena cava O₂ sat, %                  | 50.0   |
| Right atrial O₂ sat., %                       | 67.5   |
| Inferior vena cava above renal vein O₂ sat., %| 87.0   |
| Inferior vena cava below renal vein O₂ sat., %| 62.0   |
| Cardiac index, L/min/M²                        | 4.45   |
| Heart rate, AP beats/min                      | 78     |
| Right atrial pressure, mm Hg                  | (3)    |
| Right ventricular pressure, mm Hg             | 31/4   |
| Pulmonary artery pressure, mm Hg              | 24/12 (17) |
| Left atrial pressure, mm Hg                   | (10)   |
| Left ventricular pressure, mm Hg              | 135/7  |
| Brachial artery pressure, mm Hg               | 135/60 |
| Pulmonary vascular resistance, dyne-sec/cm²   | 120    |
| Total systemic resistance, dyne-sec/cm²       | 1078   |

Figures in parentheses indicate mean values.

kidney (fig. 3). Inferior vena cava catheterization was then performed, and the venous blood above the renal veins had an oxygen saturation 25% higher than that below these vessels (table 1).

On December 10, 1973, a total left nephrectomy was performed. Cut section of the removed kidney revealed an irregular lobulated tumor in the lower pole with no identifiable capsule; microscopic exam of this area showed a renal cell carcinoma of the grade II-A clear-cell type. Both the renal vein and the surgical margin were free of tumor. Following operation, the patient’s cardiac state dramatically improved and the congestive heart failure cleared. During the subsequent one year follow-up, the patient has returned to normal activity and has been free of all congestive symptomology. There is no evidence of recurrent tumor.

Reported Cases

The present case is the twenty-third reported patient with arteriovenous fistulae complicating renal cell carcinoma (table 2). A few additional cases have been reported in the radiologic literature with emphasis on angiographic findings and these cases are not included in table 2. A summary of the frequency of clinical and cardiac findings in the 23 patients is presented in table 3. Cardiovascular complaints were the presenting problem in seven of the 23 patients (30%), with hypertension in five and congestive heart failure in two. However, a majority of the patients had significant cardiovascular findings during the course of evaluation with hypertension in 63%, a systolic cardiac murmur in 61%, and cardiomegaly by chest X-ray in 66%. The most discriminating finding on physical exam was an abdominal bruit which occurred in 72% of the reported patients. The abdominal bruit was described as continuous in some, systolic in

Figure 3

Selective left renal arteriogram showing multiple arteriovenous fistulae in the lower pole of the kidney. Left) arterial phase. Right) venous phase 2.5 sec later.

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Table 2

| Case number | Year | Source | Age | Sex | Presenting problem | BP mm Hg | Systolic cardiac murmur | X-ray cardiomegaly | Abdominal bruits | Palpable abdom. mass | Hematuria |
|-------------|------|--------|-----|-----|--------------------|----------|------------------------|-------------------|-----------------|-----------------|-----------|
| 1. Hamilton 3 | 1953 |        | 23  | M   | CHF                | 180/110  | +                      | +                 | +               | +               | -         |
| 2. Myhre    | 1959 |        | 60  | F   | Abd. pain          | 140/70   | +                      | -                 | -               | -               | +         |
| 3. Scheifley | 1961 |        | 33  | F   | HBP                | 205/110  | +                      | +                 | -               | -               | -         |
| 4. Abbott   | 1962 |        | 62  | F   | Abd. pain          | 206/110  | +                      | +                 | +               | +               | NR        |
| 5. Janet    | 1964 |        | 55  | F   | Abd. pain          | 130/80   | -                      | -                 | +               | -               | -         |
| 6. Nicoff   | 1964 |        | 74  | F   | Fatigue            | 210/108  | -                      | +                 | +               | +               | NR        |
| 7. Maldonado | 1965 |        | 67  | F   | Abd. pain          | 140/70   | +                      | +                 | +               | +               | NR        |
| 8. Love     | 1967 |        | 62  | M   | Hematuria          | 140/80   | +                      | -                 | NR              | NR              | +         |
| 9. Thomas   | 1967 |        | 60  | M   | Abd. pain          | 150/75   | +                      | +                 | +               | NR              | NR        |
| 10. Kelly   | 1967 |        | 58  | F   | Fatigue            | 150/80   | -                      | -                 | NR              | -               | -         |
| 11. Kelly   | 1967 |        | 51  | F   | Abd. mass          | 160/80   | -                      | -                 | +               | +               | -         |
| 12. Wise    | 1967 |        | 61  | F   | HBP                | 220/120  | +                      | +                 | +               | -               | -         |
| 13. Wise    | 1967 |        | 40  | F   | HBP                | 160/105  | +                      | +                 | +               | -               | +         |
| 14. Wise    | 1968 |        | 68  | F   | Abd. pain          | 112/60   | +                      | +                 | NR              | -               | +         |
| 15. MacLennan | 1969 |        | 54  | F   | HBP                | 185/110  | -                      | +                 | +               | -               | -         |
| 16. Lang    | 1970 |        | 46  | M   | Hematuria          | NR       | NR                     | NR                | NR              | NR              | +         |
| 17. Stahlsaker | 1973 |        | 48  | M   | HBP                | 160/110  | -                      | +                 | +               | +               | -         |
| 18. Sondag   | 1973 |        | 67  | F   | Weight loss        | 140/60   | +                      | +                 | -               | -               | -         |
| 19. Sondag   | 1973 |        | 45  | M   | Hematuria          | 210/140  | NR                     | NR                | -               | -               | -         |
| 20. Sondag   | 1973 |        | 76  | F   | Abd. pain          | 160/70   | NR                     | -                 | -               | -               | +         |
| 21. Sondag   | 1974 |        | 68  | M   | Hematuria          | 160/85   | NR                     | -                 | -               | +               | +         |
| 22. Curtiss  | 1974 |        | 38  | F   | Hematuria          | 160/80   | +                      | +                 | -               | -               | -         |
| 23. Rodgers  | 1974 |        | 63  | F   | CHF                | 180/75   | +                      | +                 | +               | -               | -         |

**Abbreviations:** CHF = congestive heart failure; HBP = high blood pressure; plus sign = present; minus sign = absent; NR = not reported.

Others, or as simply present in the remaining patients in which it was recorded. In contrast to what might be expected, a palpable abdominal mass or hematuria was reported in less than 50% of the patients. Patients with this condition were generally in the older age group (70% greater than 50 years of age), and the striking preponderance of women (70%) is unexplained. The diagnosis of renal cell carcinoma with arteriovenous fistulae was rarely made on initial clinical exam. The diagnosis was unsuspectingly established by surgery in 13% and by angiography in 87%, usually in the course of a workup for hypertension, abdominal pain, hematuria, or during search for an occult malignancy.

**Discussion**

Our patient presented with unexplained congestive heart failure, and clinically, an atypical atrial myxoma was suspected. High cardiac output and a left-to-right shunt were documented at cardiac catheterization, and renal arteriovenous fistulae were demonstrated angiographically. Etiologic considerations of the latter...
Table 3
Summary of Clinical Findings: 23 Patients with Renal Cell Carcinoma and Arteriovenous Fistulae

| Manifestation                  | Frequency |
|--------------------------------|-----------|
| Cardiac output                 | 25%       |
| Abdominal pain                 | 30%       |
| Hematuria                      | 30%       |
| Age > 50 years                 | 70%       |
| Female sex                     | 70%       |
| Hypertension > 100/100 mm Hg   | 65%       |
| Systolic cardiac murmur        | 61%       |
| X-ray cardiomegaly            | 66%       |
| Abdominal bruit                | 72%       |
| Pulpable abdominal mass        | 60%       |
| Hematuria                      | 47%       |

Finding include congenital angiomatosis with multiple arteriovenous connections, and acquired lesions due to trauma, renal biopsy, inflammation, arteriosclerosis, or renal cell carcinoma. Our patient is quite typical of the clinical picture which has evolved from a review of the literature. That is, the patient is a female in the older age group and presented with cardiovascular symptoms. Significant cardiovascular abnormalities were detected on exam including a systolic abdominal bruit, but the clinical diagnosis was not entertained by numerous physicians who examined the patient. There was no abdominal mass or hematuria, and the angiographic findings of renal cell carcinoma with arteriovenous fistulae were quite unexpected.

Certain angiographic criteria have been established to differentiate large arteriovenous fistulae from the small shunts which are commonly seen in most cases of renal cell carcinoma. Bosniak categorized renal arteriovenous fistulae as large when considerable opacification of the renal vein occurs within one second following opacification of the renal artery, or if renal vein and aorta opacify while there is still contrast medium within the aorta. The normal opacification of the inferior vena cava occurs approximately eight seconds after aortic injection, whereas it occurs in four-to-five seconds in patients with large arteriovenous fistulae.

Circulatory effects of renal arteriovenous fistulae are similar to fistulae between other vessels of similar size. The markedly reduced peripheral resistance is associated with a shortened circulation time, an augmented cardiac output, and an elevated systolic blood pressure. Secondary effects include an increase in the blood volume, venous pressure, heart rate, and progressive right and left sided cardiac enlargement from the systemic venous and arterial volume overload. Diastolic hypertension, which occurs in approximately one-half the reported cases, is thought to result from "renalvascular steal" with renal parenchymal ischemia on the side of the fistulae. The over-all cardiovascular manifestations of the arteriovenous fistulae are dependent on: 1) the magnitude of the shunt as determined by the size of the feeding artery and draining vein and by the level of systemic blood pressure; 2) the chronicity of the fistulae; and 3) the status of the cardiovascular system prior to the development of the fistulae. Thus, one could expect a spectrum of cardiovascular symptoms and signs in this condition as a result of variability in the severity of the aforementioned factors.

There is a paucity of reported data on quantification of the left-to-right shunt in arteriovenous fistulae complicating renal cell carcinoma. Curtis et al. reported one patient with a 1.23:1 shunt flow and minimal hemodynamic embarrassment. In our patient, sufficient data were not obtained to quantitate the shunt flow; however, it was estimated from the indicator dilution curves, the magnitude of the venous oxygen step up above the renal veins, and the angiographic findings that the shunt was greater than 2:1.

The formation of fistulae in renal cell carcinoma involves multiple connections between arteries and veins due to tumor invasion and the development of communicating vascular spaces within partially necrotic tumor. Although these arteriovenous fistulae are most marked in the primary carcinoma, similar fistulae have been reported in metastatic implants of renal cell carcinoma. The sparsity of arteriovenous fistulae in other types of malignancy suggests some unique characteristics in the local growth and invasive properties of renal cell carcinoma.

It is quite obvious that total nephrectomy of the involved kidney is the treatment of choice if local tumor extension does not preclude surgery. Even if metastatic lesions exist, and especially if they are solitary, nephrectomy may be indicated to eliminate the hemodynamic burden of the arteriovenous fistulae. The short-term follow-up results of surgical nephrectomy have been excellent from a cardiovascular standpoint with improvement in the congestive heart failure and reduction or normalization of the blood pressure. The long-term results are determined by the growth characteristics of the renal cell carcinoma.

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