Intracranial Hemorrhage in Patients With Polycystic Kidney Disease

Shan-Jin Ryu, MD

To emphasize the important association of polycystic kidney disease and hypertensive cerebral hemorrhage, a registry of 900 consecutive cases of hemorrhagic stroke was reviewed. Eleven patients (1.2%) had intracranial hemorrhage (eight had hypertensive cerebral hemorrhage and the other three had aneurysmal subarachnoid hemorrhage) found to be associated with polycystic kidney disease. These 11 patients also accounted for 11% of the 98 cases of polycystic kidney disease during the 28-month study period. As verified by computed tomography, parenchymal hemorrhage occurred mainly in the putamen and the thalamus, the usual sites for hypertensive cerebral hemorrhage. One patient with cerebral hemorrhage was autopsied and one was studied angiographically, but in neither patient was an intracranial aneurysm identified. In the patients with polycystic kidney disease and intracranial hemorrhage, hypertension had been inadequately treated or even undetected; therefore, I emphasize early detection and more effective control of hypertension in patients with polycystic kidney disease for prophylaxis against hemorrhagic cerebrovascular events. (Stroke 1990;21:291-294)

The association of polycystic kidney disease (PKD) with intracranial hemorrhage—aneurysmal subarachnoid hemorrhage (SAH) or cerebral hemorrhage without saccular aneurysms—was reported early in the beginning of this century.1,2 In most subsequent reports,3-9 attention was drawn to the association of PKD with intracranial aneurysm. Cerebral hemorrhage complicating PKD, though not rare, has been underestimated.3-9 Cerebral hemorrhage and aneurysmal SAH are among the leading causes of death in patients with PKD. Detection and surgical treatment of unruptured cerebral aneurysms for prophylaxis against future occurrence of SAH in such patients remain controversial.7,8,10 Cerebral hemorrhage, on the other hand, is often related to hypertension, a common complication of PKD and a treatable risk factor for stroke. I report 11 cases of PKD associated with intracranial hemorrhage (hypertensive cerebral hemorrhage in eight and aneurysmal SAH in the other three). Clinical profiles and computed tomograms (CT scans) in these 11 cases are further described; the important association of PKD with hypertensive cerebral hemorrhage is reappraised.

Subjects and Methods

From August 1984 to January 1987, 900 consecutive cases of hemorrhagic cerebrovascular disease (763 cases of cerebral hemorrhage and 137 cases of SAH) were registered from Chang Gung Memorial Hospital Lin-Kou Medical Center. During the same period in the same hospital, 98 patients were diagnosed as having PKD. The medical records of the cases of hemorrhagic stroke or PKD were retrospectively reviewed; among those, PKD was found to be associated with intracranial hemorrhage in 11. Only one patient with PKD had an ischemic stroke, and one had a brain tumor; I excluded both from the present series.

Cranial CT was performed ≤72 hours after the onset of hemorrhagic stroke in all 11 cases. PKD was diagnosed before the onset of intracranial hemorrhage in six cases and after onset in the remaining five. Imaging procedures employed in the diagnosis of PKD were renal ultrasonography in nine cases, intravenous pyelography in eight, isotope liver scanning in three, abdominal CT in two, and renal angiography in one. For further study of the intracranial hemorrhage, cerebrospinal fluid was examined in three cases and cerebral angiography was performed in three. Pathologic study included autopsy in one case, liver biopsy via laparotomy in one, and examination of the nephrectomized kidney in two.

From the Department of Neurology, Chang Gung Medical College and Chang Gung Memorial Hospital, Tao-Yuan, Taiwan (Republic of China).

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Address for correspondence: Shan-Jin Ryu, MD, Department of Neurology, Chang Gung Memorial Hospital, Tao-Yuan 33333, Taiwan (Republic of China).

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Table 1. Summary of 11 Cases of Polycystic Kidney Disease Associated With Intracranial Hemorrhage

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age at PKD diagnosis (yr)</th>
<th>Duration of hypertension (yrs)</th>
<th>Symptoms and signs of ICH</th>
<th>Type and location of ICH</th>
<th>Uremia</th>
<th>Other cystic organs</th>
<th>Outcome of ICH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>30</td>
<td>4</td>
<td>Hemiplegia, vomiting, unconsciousness</td>
<td>CH, putamen</td>
<td>-</td>
<td>Liver</td>
<td>Dead</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>55</td>
<td>10</td>
<td>Hemiplegia, dysarthria</td>
<td>CH, thalamus</td>
<td>+</td>
<td>Lung</td>
<td>Alive</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>34</td>
<td>3</td>
<td>Motor aphasia, hemiplegia</td>
<td>CH, putamen</td>
<td>-</td>
<td>Liver</td>
<td>Dead</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>44</td>
<td>6</td>
<td>Headache, hemiplegia</td>
<td>CH, putamen</td>
<td>+</td>
<td>Liver</td>
<td>Dead</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>73</td>
<td>20</td>
<td>Headache, vomiting, unconsciousness</td>
<td>CH, thalamus</td>
<td>-</td>
<td>Liver</td>
<td>Alive</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>46</td>
<td>?</td>
<td>Headache, hemiplegia</td>
<td>CH, thalamus</td>
<td>-</td>
<td>Liver</td>
<td>Alive</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>53</td>
<td>5</td>
<td>Dizziness, vomiting, hemiplegia</td>
<td>CH, thalamus</td>
<td>+</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>24</td>
<td>10</td>
<td>Headache, hemiplegia</td>
<td>CH, putamen</td>
<td>-</td>
<td>Liver</td>
<td>Alive</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>32</td>
<td>2</td>
<td>Headache, vomiting, incontinence</td>
<td>SAH, ACoA aneurysm</td>
<td>-</td>
<td>Liver</td>
<td>Alive</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>45</td>
<td>10</td>
<td>Dizziness, vomiting, headache</td>
<td>SAH, basilar tip aneurysm</td>
<td>-</td>
<td>Liver</td>
<td>Alive</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>44</td>
<td>10</td>
<td>Unconsciousness, seizure, stiff neck</td>
<td>SAH</td>
<td>+</td>
<td>Liver</td>
<td>Dead</td>
</tr>
</tbody>
</table>

PKD, polycystic kidney disease; ICH, intracranial hemorrhage; M, male; F, female; CH, cerebral hemorrhage; SAH, subarachnoid hemorrhage; -, absence; +, presence; ACoA, anterior communicating artery.

Results

Eight patients with cerebral hemorrhage and three with SAH were found to have PKD; these 11 patients accounted for 1.2% of the 900 cases of hemorrhagic stroke and 11.2% of the 98 cases of PKD.

The clinical profiles of these 11 patients are summarized in Table 1. Case 1 has been reported in Chinese. Cerebral hemorrhage occurred in six men and two women; SAH occurred in one man and two women. Their ages at the onset of intracranial hemorrhage ranged from 28 to 73 (mean 46.4) years.

Hypertension had been present for 2–20 (mean 8) years in 10 patients; none had adequate antihypertensive treatment. A history of hypertension was not obtained in case 6; however, preexisting hypertension was suspected due to retinal changes seen by funduscopy and left ventricular hypertrophy shown on chest roentgenogram and electrocardiograms. Case 6 also sustained hypertension during and after her cerebral hemorrhage.

Five patients were unaware of the existence of PKD until the ictus of intracranial hemorrhage; the clinical manifestations of PKD (besides hypertension) in these five patients included a palpable renal mass in four cases, hepatomegaly in three, hematuria in three, uremia in two, and urinary tract infection in one. None of the 11 patients had a definite family history suggestive of PKD.

Neurologic symptoms and signs were characteristic of a hemorrhagic stroke in all 11 patients, that is, a sudden onset of headache in six, dizziness in two, vomiting in five, unconsciousness in four, hemiplegia in seven, incontinence in one, and seizure in one.

Cranial CT showed parenchymal hemorrhage in cases 1–8; the hemorrhage occurred in the putamen in four patients and in the thalamus in the other four. Cases 1, 4, 5, 6, and 7 were complicated with intraventricular hemorrhage, and cases 4 and 5 were complicated with obstructive hydrocephalus. No CT evidence of parenchymal hemorrhage, but signs of SAH, was noted in cases 9, 10, and 11. Cerebral angiography was carried out in cases 6, 9, and 10; berry aneurysms were verified in case 9 (in the anterior communicating artery) and in case 10 (at the tip of the basilar artery).

Four cases of PKD and intracranial hemorrhage were associated with chronic renal insufficiency. Cystic lesions involving the liver, proved by abdominal CT, ultrasonography, isotope scanning, or laparotomy, were found in seven patients (63.6%). Case 3 was found to have lung cysts.

The intracranial hemorrhage was treated surgically in four patients. In case 3, evacuation of the putaminal hematoma was performed, and case 5 received a ventriculoperitoneal shunt for complicated obstructive hydrocephalus. Saccular aneurysms were clipped in cases 9 and 10.

Cases 1, 4, and 11 died ≤1 week after the onset of intracranial hemorrhage, giving a mortality rate of 27.3%. Case 1 was autopsied; massive putaminal hemorrhage with transtentorial herniation and polycystic lesions involving the kidneys and the liver were pathologically verified (Figures 1 and 2); however, no intracranial aneurysm was discovered.

Discussion

Adult-type PKD (Potter type 3) is pathologically characterized by replacement of normal renal tissue...
by numerous cysts, which results in massive enlargement and functional failure of the kidneys.\textsuperscript{12} The cystic lesions are present at birth but usually become clinically apparent after age 30. Cysts may also occur in the liver (33\%), pancreas (9\%), spleen, and lung. PKD is considered a hereditary malformation with autosomal dominant transmission; in many cases, however, family history suggestive of this disease cannot be obtained.\textsuperscript{8,12}

There is a significant association between PKD and congenital berry aneurysms; in autopsy series from 7.3\%\textsuperscript{5} to 16.6\%\textsuperscript{6} of patients with PKD were found to have one or more aneurysms, and aneurysmal SAH accounted for the cause of death in nearly 10\% of the PKD patients. Intracerebral hemorrhage without associated aneurysms also occurred in 4.7–11.9\% of autopsied PKD patients\textsuperscript{1-2}; nevertheless, antemortem diagnosis of cerebral hemorrhage in patients with PKD has been described only rarely.

In this series, 8\% of 98 patients with PKD sustained cerebral hemorrhage occurring mainly in the putamen and thalamus, the usual sites for hypertensive cerebral hemorrhage. Intracranial berry aneurysms were not found in the autopsied case nor in the angiographed case. Almost all patients in this study had long-standing hypertension with no adequate treatment. Hypertension is a common presentation of PKD; up to 75\% of patients develop such a complication during their clinical course.\textsuperscript{9}

Hypertension may play an important role in the pathogenesis of cerebral hemorrhage and SAH in patients with PKD. Long-standing uncontrolled hypertension is suspected to cause intracerebral microaneurysms (so-called Charcot-Bouchard aneurysms\textsuperscript{13}) or lipohyalinosis\textsuperscript{14} of the perforating arteries, which results in rupture of the aneurysm or artery and parenchymal hemorrhage. Such arterial or
arteriolar changes are not demonstrable by cerebral angiography. Furthermore, hypertension may also be a predisposing factor for aneurysmal SAH; a congenital defect of the cerebral arteries in patients with PKD complicated by hypertension may increase the risk of SAH.

Intracranial hemorrhage, either cerebral hemorrhage or aneurysmal SAH, can cause high mortality and morbidity in PKD patients. Angiographic detection and surgical treatment of unruptured berry aneurysms to prevent SAH in such patients has been reported. In view of cost-effectiveness, however, routine cerebral angiography and prophylactic surgery for asymptomatic aneurysms remain impractical. Hypertension, a common complication of PKD, is a powerful risk factor for cerebral hemorrhage and may also predispose to rupture of cerebral aneurysms. More effective control of hypertension may decrease the occurrence of cerebral hemorrhage and SAH. In developing countries such as Taiwan, unfortunately, almost one fourth of patients with hypertensive cerebral hemorrhage were unaware of their hypertension, and only few persons with hypertension have proper control of their blood pressure. Early detection and adequate treatment of hypertension in patients with PKD, therefore, can be a beneficial and inexpensive medical approach for prophylaxis against catastrophic cerebrovascular events.

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S J Ryu

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