Stroke in adult polycystic kidney disease

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Summary: In order to assess the incidence of acute cerebrovascular events, 142 patients with adult polycystic kidney disease were retrospectively reviewed. Fourteen patients (9.8%) had 19 cerebral attacks. Six patients (4.2%) had intracranial haemorrhage attacks (three ruptured intracranial aneurysms and three cerebral haemorrhages). Ischaemic events occurred in nine patients (five cerebral infarctions and four transient ischaemic attacks). Patients with ischaemic attacks had a better outcome than patients with haemorrhagic events even when transient ischaemic attacks were excluded. Patients with ruptured intracranial aneurysms were younger. Cerebral complications are an important cause of morbidity and mortality in patients with adult polycystic kidney disease. They can prove disabling prior to or after dialysis and transplantation.

Introduction

Adult polycystic kidney disease (APKD) is a genetic disorder transmitted as an autosomal dominant trait. In Spain the disease accounts for 10.4% of the new adult patients who started renal replacement therapy during both 1986 and 1987. In the dialysis era, the survival of APKD patients is mainly dependent on non-renal complications. So, cardiac events due to mitral valve prolapse, abdominal aneurysms and cerebral complications are important causes of morbidity and mortality in APKD.

There are many reports regarding the coexistence of APKD and berry aneurysms. In addition, it is generally accepted that cerebral haemorrhage and rupture of intracranial aneurysms (ICA) are leading causes of death in patients with APKD.

A total of 142 APKD patients were retrospectively reviewed in order to assess the incidence and outcome of acute cerebrovascular events.

Patients and methods

A total of 142 patients with APKD seen over the period June 1977 to October 1990 were retrospectively reviewed. Many of these patients were included in a previous study. The mean follow-up of the patients was 6 years (range 2–10 years). The diagnosis of APKD was confirmed by unequivocal excretory urography or sonography and a family history of the disease compatible with an autosomal dominant inheritance. In the asymptomatic patients who were at risk, having one affected first degree relative, the diagnosis of APKD was made if at least three cysts were detected in each kidney.

Definitions: Chronic renal failure—serum creatinine higher than 115 μmol/l. End-stage renal disease—serum creatinine higher than 885 μmol/l and/or creatinine clearance lower than 15 ml/min/l. 73 m². Hypertension—systolic or diastolic blood pressure higher than 140 and 90 mmHg, respectively, or a known history of hypertension on therapy. Transient ischaemic attacks (TIA)—transient neurological deficits with total recovery in minutes or hours.

Head computerized tomography (CT) was performed on all patients having cerebral symptoms. When findings on CT were suggestive of ICA, that is, subarachnoid haemorrhage, intraparenchymal haemorrhage in an atypical site for hypertensive haemorrhage, or an ICA directly viewed on contrast CT, four vessel angiography was performed.

Results

Fourteen out of 142 patients (9.8%) with APKD had 19 episodes of acute cerebrovascular disturbance (10 male and four female). The mean age at the time was 55 years (range 17–70 years) and there was no significant difference between males and females (55 and 58 years, respectively). The age,
sex, renal function, type and anatomical location of the cerebrovascular event and outcome are summarized in Table I.

Cerebral haemorrhage occurred in three patients at a mean age of 65 years (range 64–66 years) and three patients were found to have a ruptured ICA at a mean age of 41 years (range 17–58 years).

Three patients had seven episodes of TIA at a mean age of 62 years (range 40–70 years). Cerebral infarction occurred in five patients at a mean age of 54 years (range 38–66 years). All patients with ischaemic attacks had severe generalized arteriosclerosis. Five out of eight patients with an ischaemic attack undertook treatment with aspirin (three aspirin alone and two with dipyridamole). Three patients did not receive antiaggregants.

ICA was located in the anterior communicating artery in two patients and in the carotid siphon in one. Subarachnoid haemorrhage was found on CT in all of them. Cerebral haemorrhage was located in the temporal lobe, basal ganglia and thalamus, typical sites for hypertensive haemorrhage. Therefore, findings on CT can help to differentiate ICH from ruptured ICA.

Eight patients were hypertensive. Hypertension was of mild to moderate severity in all of them and none of these patients had accelerated hypertension with grade 3 or 4 retinopathy. Blood pressure was normal in five patients. Hypertension was adequately controlled in six patients (two with ischaemic attacks, two with intracranial haemorrhage) and uncontrolled in two (two with ischaemic attacks).

Two patients with cerebral infarction recovered fully, two had hemiparesis and one had dementia. With respect to cerebral haemorrhage, one patient had hemiparesis and two had dementia. All patients with ruptured ICA had hemiparesis. Patients with TIA recovered completely.

It is worth stressing that in seven patients the first clinical symptom of APKD was a cerebral complication. None of these patients suffered from embolic cardiopathy.

**Discussion**

In our series, cerebral haemorrhage occurred in three patients (2.1%). That incidence is lower than the 8% reported by Shan-Jin in living patients and 13.9% reported by Zeier in an autopsy series.

The association of APKD and ICA was first

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<th>Table I Clinical data from 14 patients with APKD at the time of the acute cerebrovascular event</th>
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*Data from the last attack.
noted by Dunger in 1904 and it has been repeatedly reported since then.\textsuperscript{1,3-5,9-12} Wakabashi \textit{et al.}\textsuperscript{12} observed saccular aneurysms in 40% of asymptomatic carriers by angiography. However, Torres \textit{et al.}\textsuperscript{13} did not find any case of ICA in 40 APKD patients prospectively studied with nuclear magnetic resonance angiography which combines sensitivity and specificity in the diagnosis of ICA. In autopsy series, from 2.3%\textsuperscript{2} to 19.7%\textsuperscript{10} of patients have been found to have one or more aneurysms. However, the diagnosis of ICA in living symptomatic patients has been reported less frequently. Three of our patients (2.1%) had a confirmed ruptured ICA. That incidence agrees with 3% reported by Gabow \textit{et al.}\textsuperscript{3} and 2% by Shan-Jin\textsuperscript{4} in APKD patients. A familial aggregation of ICA in patients with APKD has been described. The reported prevalence of family history of ICA varies from 76% according to Kaehny \textit{et al.}\textsuperscript{14} to 22% observed by Schievink.\textsuperscript{15} In our series, a history of stroke in our patients’ first degree relatives was not obtained. Taking into account all published series, we can suggest that the incidence of ICA in APKD is lower than previously thought.

Hypertension is a well-known risk factor for stroke, but the risk varies for each type of stroke. So, hypertension is a risk factor for cerebral haemorrhage, since it conditions the formation of Charcot-Bouchard aneurysms. However, the link between hypertension and ICA is not completely determined.\textsuperscript{16,17} In the review of Shan-Jin\textsuperscript{4} eight out of 98 patients had cerebral haemorrhage. Like our patients the haemorrhage was located in the thalamus and putamen, the usual sites for hypertensive haemorrhage. It is important to note that the patients studied by Shan-Jin had inadequate blood pressure control or undetected hypertension. Therefore, we think that since an early and high incidence of hypertension has been described in APKD, effective blood pressure control is essential.

The degree of disability after stroke depends on the severity of the vascular neuroanatomical lesion.\textsuperscript{18} In our series, patients having ischaemic attacks had a better outcome than the patients with haemorrhagic events, none of whom totally recovered. Furthermore, two patients with cerebral haemorrhage had terminal renal failure and had to be excluded from dialysis because of severe mental and motor deficits. Haemorrhagic attacks are an important cause of morbidity and mortality in patients with APKD prior to or after dialysis and transplantation.\textsuperscript{11,19}

Routine conventional angiography has been considered impractical.\textsuperscript{13} However, in view of the poor course of ruptured ICA, it is believed that in patients who are likely to have an ICA (family clustering or symptoms thought to be due to an unruptured ICA as migraine headache or acute cerebrovascular events) should be promptly examined if an ICA is to be discovered in time to permit adequate treatment. Arterial digital angiography or nuclear cerebrovascular events\textsuperscript{20} are warranted in these patients.

References


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