Polycystic Kidney Disease as a New Risk Factor for Coronary Events

Rasmi Magadle MD, Paltiel Weiner MD, Marinella Rabner MD, Miri Mizrahi-Reuveni MD and Avi Davidovich MD

Department of Medicine A, Hillel Yaffe Medical Center, Hadera, Israel

Key words: polycystic kidney, coronary aneurysm, myocardial infarction

Abstract

Background: The association between coronary and/or other arterial aneurysms and polycystic kidney disease is well known. While myocardial infarction is a possible complication of atherosclerotic coronary aneurysms, it is reasonable to assume that CA in patients with PKD may make them prone for a similar complication.

Objective: To evaluate the possible occurrence of CA and MI in first-order relatives of a patient with PKD, CA and MI.

Patients: We studied 12 family members: 2 parents, 8 sisters and 2 brothers of a young woman who was incidentally diagnosed as having a MI, while her mother was known to have PKD. We used electrocardiogram, thallium-image test, and transthoracic echocardiography to determine MI, ultrasonography of the kidney to determine PKD, and coronary angiography and ventriculography to determine CA and MI, respectively.

Results: PKD was detected in seven family members, while CA and MI were found in five and three of them, respectively.

Conclusions: In a family with PKD we detected a high prevalence of CA, with MI as a complication of the latter.

IMAJ 2002;4:21–23

The pathognomonic hallmark of PKD is the presence of renal cysts. PKD accounts for approximately 5–6% of patients entering end-stage renal disease programs worldwide [1]. The well-recognized extrarenal associations of PKD with cardiac valve anomalies, gastrointestinal tract diverticula, hepatic cysts and hypertension suggest an underlying disorder in the connective tissue matrix formation [1,2]. Involvement of vascular walls may cause arterial aneurysms, including aorta, coronary arteries and, most frequently, intracranial berry aneurysms whose prevalence is 5–10% [3,4]. The incidence of CA in patients with PKD is still unknown. Most of the known information in the literature derives from small studies and individual case reports [2,4–6]. Swan et al. [4] found aneurysms in 5 of 32 angiograms (15%) performed in PKD patients with end-stage renal disease. Hadimeri and co-workers [2], in a recent controlled study, found that the prevalence of definite aneurysms was much lower (only 4 of 30 patients, 13%). However, this rate is significantly higher than the rate in the general population with suspected coronary atherosclerotic disease. The incidence of atherosclerotic coronary ectasia and/or aneurysms in patients undergoing coronary angiography and/or autopsy ranges from 0.2 to 4.9% [7]. The occurrence of an MI, as a complication of the latter, is about 4% [8].

However, the incidence of MI as a complication of CA in patients with PKD is unknown, and to the best of our knowledge was never investigated. The referral of a 23 year old female patient, the daughter of a woman with PKD, to our outpatient clinic because of incidental ECG signs suggesting old MI, led us to investigate the possible association between CA, PKD, and MI in all 12 members of her family.

Patients and Methods

Patients

We investigated 12 first-order relatives of a 23 year old apparently healthy female, who was initially referred to our center in June 1999 for evaluation for coronary artery disease because of incidental ECG changes suggesting old MI. The patient's mother was known to have PKD.

Laboratory studies and diagnostic criteria

ECG, transthoracic echocardiography and kidney ultrasonography were performed in all 13 subjects. Five of them, in whom ECG pattern suggested possible MI, had also undergone a ^{201}thalium-image test, coronary angiography and ventriculography. The institution's ethics committee approved the study and informed consent was obtained from all subjects.

PKD was diagnosed by an experienced radiologist according to the previously published criteria [1,2], and all ^{201}thalium-image tests were evaluated by an expert. MI was considered if a localized myocardial area with an irreversible defect in radiotracer uptake on both exercise and rest (delayed) images were identified [9]. An experienced cardiologist also evaluated the

CA = coronary aneurysms
PKD = polcystic kidney disease
MI = myocardial infarction

ECG = electrocardiogram

Table 1. Characteristics of the family members

No	Age (yr)	Gender	Smoking	Hyper-cholesterol	DM	Ht	MI	PKD	CA
1	67	M	+	–	+	–	+	–	–
2	62	F	–	–	–	–	–	+	–
3	42	M	+	+	–	+	–	–	+
4	40	F	+	–	–	–	–	–	–
5	39	F	–	–	–	–	–	+	+
6	35	F	+	–	–	–	+	+	–
7	33	M	–	–	–	–	+	+	+
8	32	F	–	–	–	–	–	–	–
9	27	F	–	–	–	–	–	–	–
10	25	F	–	–	–	–	+	+	+
11	23	F	–	–	–	–	+	+	+
12	22	F	–	–	–	–	–	–	–
13	19	F	–	–	–	–	–	+	–

DM = diabetes mellitus, Ht = arterial hypertension

angiograms and ventriculograms, diagnosing MI according to the international criteria [9].

Definitions

- *Polycystic kidney*: PKD was diagnosed if there was ultrasonographic evidence of grossly enlarged kidneys, with multiple spherical cysts that varied in size and studded the surface of the kidney, with or without straw-colored fluid [10].
- *Coronary aneurysm*: CA was defined as a segmental coronary dilation that exceeds the diameter of normal adjacent segments or the diameter of the patient's largest coronary vessel by 1.5 times [5].
- *Myocardial infarction*: MI was defined as a permanent Q-wave on ECG trace, and/or by permanent perfusion defect on a myocardial perfusion imaging test, and/or by identification of permanent akinetic segment of the myocardium on ventriculography [9] and/or by transthoracic echo [11].

Results

A total of 13 family members, 10 females and three males, mean age 35.9 ± 14.6 years (range 19–67), were enrolled in this study. Their clinical characteristics are summarized in Table 1. PKD was diagnosed in seven patients. Five subjects were diagnosed as having MI, four of them in association with PKD. CA was found in five subjects, four of whom had PKD. MI was found in three of the PKD and CA patients. The transesophageal echo was able to identify one of the CA, which confirmed the aneurysm (19 mm diameter) in the left main coronary artery with no thrombus or abnormal flow patterns. None of the patients with a combination of PKD, CA and MI (patients no. 7, 10, and 11) had any of the usual risk factors for coronary artery disease: namely arterial hypertension, smoking, diabetes mellitus, hypercholesterolemia, and family history. The subject who was diagnosed to have MI but without documented PKD and/or CA was a diabetic and heavy smoker (patient no. 1). There were no special coronary artery predilections for these CA. A distinctive huge aneurysm, in addition to angiography, was also identified by transesophageal echo in the left main coronary artery in one of these PKD patients (patient no. 5), but with no MI. His angiogram demonstrated a critical stenosis (about 95%) of the left descending coronary artery. Successful revascularization by angioplasty and stent implantation was performed. One year later, he was still asymptomatic and without complaints.

Discussion

Atherosclerosis is by far the most important cause of coronary artery disease, but a number of other non-atheromatous conditions may also play a role, such as arteritis, trauma, metabolic disease, coronary emboli, myocardial oxygen demand-supply disproportion, hematological *in situ* thrombosis, cocaine abuse, and myocardial contusion. Congenital coronary anomalies such as CA, anomalous origin of left coronary artery, and coronary arteriovenous and arteriocameral fistulas are also considered to be rare, non-atherogenic conditions that may lead to MI [9]. Generally, CA is of atherosclerotic origin, but congenital anomaly, coronary angioplasty, trauma, polyarteritis nodosa, scleroderma, syphilis, Ehlers-Danlos syndrome and Kawasaki's disease are also considered probable causes [12,13].

CA usually involves the major epicardial coronary artery and is present in 0.2–4.9% of patients with obstructive atherosclerotic coronary artery disease at autopsy or angiography [7]. Although it was previously suggested that CA does not appear to affect symptoms, survival, or the incidence of MI [14], few recent case studies report on the association between MI and CA. It was suggested that the association might be due to formation of thrombus within the aneurysm with or without embolization to distal vessels, resulting in MI [15,16].

The association of CA and PKD was recently reported in certain families [2,17,18]. The gene accounting for most cases of adult polycystic kidney disease has been mapped to a locus on human chromosome 16, but the biochemical defect is not yet characterized [19]. In the present study three young subjects (23, 25, and 33 years old) belonging to the same family were confirmed to have MI, PKD, and CA. No atherosclerosis or other non-atherosclerotic causes of MI and none of the internationally recognized risk factors of coronary artery disease were identified in these subjects. In addition, no non-atherogenic condition that may lead to the formation of CA was detected.

The association of PKD and CA in the same family members supports the hypothesis that local inflammation of the coronary vessels, creating the CA, is a part of the generalized defect of the extracellular collagen tissue in PKD patients. A similar disorder

in collagen metabolism has been noted for the Ehlers-Danlos (type I and III) and Marfan syndromes [20]. This inheritable abnormality of collagen metabolism may also explain the development of coronary artery aneurysms and ischemic heart disease in our study

Because of the rarity of information about patients with CA and PKD, the general therapeutic strategy for CA can be used. Systemic thrombolytic treatment can be helpful in the acute phase of myocardial infarction, while maintenance anticoagulant and/or anti-aggregant treatment needs more investigation. Because the coronary artery aneurysmatic spasm can also produce ischemia, nitroglycerine and calcium channel blockers may also be recommended as a first-line therapy. Surgical therapy or stent placement should be considered on the basis of symptoms, aneurysmal size, and underlying obstructive coronary disease [21]. To our knowledge, the family described here represents the first report of patients with PKD and CA further complicated by MI.

Conclusion

This paper describes several family members of an index patient with the association of PKD, CA and coronary disease. It is recommended that when a patient with PKD is found to have coronary disease, all the other family members, even if asymptomatic, should be investigated for PKD, CA and coronary disease.

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Correspondence: Dr. R. Magadle, Dept. of Medicine A, Hillel Yaffe Medical Center, Hadera 38100, Israel.
Phone: (972-4) 630-4526/1/0,
Fax: (972-4) 630-4522,
email: library@hillel-yaffe.health.gov.il