Meningeal tumor: A rare extrahepatic association in patients with polycystic liver disease enrolled for liver transplantation

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Abstract. In the present study, we described a rare association of polycystic liver disease (PCLD) with intracranial meningiomas in patients included on a liver transplant list, focusing on the diagnosis, treatment and possible association with any genetic alterations. Two female patients, aged 39 and 49 years were included on a liver transplant list due to extensive PCLD, with symptoms related to an abdominal compartmental syndrome. Screening for extrahepatic manifestation revealed a right frontal meningioma in the first patient, and a parietal posterior calcified meningioma in the second patient, measuring 1 and 7x3x2 cm in diameter, respectively. Following tumor removal, the histological pattern was compatible with fibrous and transitional meningioma, respectively. Cytogenetic studies conducted following surgery did not reveal any changes in metaphase chromosomes. The postoperative follow-up for the two patients was uneventful, without complications, with the patients remaining on a liver transplant waiting list. We conclude that screening for extrahepatic manifestations of PCLD is mandatory, as certain lesions require treatment prior to liver transplantation. The lack of a genetic or familial association between these two cases show they are likely to have occurred by chance, rather than representing a previously unrecognized association between polycystic liver disease and cranial meningioma.

Introduction

Intracranial manifestations correlated with autosomal dominant polycystic kidney disease (ADPKD), including intraparenchymal hemorrhage and aneurysm formation, have been widely described (1), as has an increased incidence of intracranial arachnoid cysts (1,2). Hepatic cysts are relatively common in patients with ADPKD (3,4), increasing with advancing age, female gender, pregnancy and degree of renal lesions, which affect the course of polycystic liver disease (PCLD) (5). The majority of patients with multiple liver cysts are asymptomatic, recognized only after routine ultrasound investigation. However, the most common clinical patterns include abdominal pain, dyspnea and early satiety related to a compartmental syndrome. In the present study, we described a rare association of PCLD with intracranial meningiomas in patients included on a liver transplant waiting list, focusing on the diagnosis, possible association with any chromosomal alteration and mandatory treatment of those lesions prior to transplantation.

Case reports

Two female patients, 39 and 49 years of age, were referred for evaluation for extensive abdominal tumors, with symptoms related to a compartmental syndrome, which included dyspnea, abdominal pain and early satiety. The two patients provided informed consent, and the study was approved by the ethics committee of Sao Paulo State University.

Clinical investigation included an abdominal ultrasound and further computer tomography (CT), which revealed the presence of a right frontal meningioma in the first patient and a parietal posterior calcified meningioma in the second patient, measuring 1 and 7x3x2 cm in diameter, respectively. Following tumor removal, the histological pattern was compatible with fibrous and transitional meningioma, respectively. Cytogenetic studies conducted following surgery did not reveal any changes in metaphase chromosomes. The postoperative follow-up for the two patients was uneventful, without complications, with the patients remaining on a liver transplant waiting list. We conclude that screening for extrahepatic manifestations of PCLD is mandatory, as certain lesions require treatment prior to liver transplantation. The lack of a genetic or familial association between these two cases show they are likely to have occurred by chance, rather than representing a previously unrecognized association between polycystic liver disease and cranial meningioma.
and a parietal posterior calcified meningioma, plus the presence of osteoma and encephalic calcification, in the second patient (Fig. 3), each measuring 1 and 7x3x2 cm in diameter, respectively. The patients were submitted to a craniotomy for tumor removal, with histological patterns compatible with fibrous meningioma in the first patient, and transitional meningioma in the second patient, both with psammomatous bodies (Fig. 4). These histological features lead to a classification of Grade I according to World Health Organization (WHO) criteria. The postoperative course was uneventful, with the patients still awaiting a liver transplant.

Post-operative conventional cytogenetic studies. Cells were obtained from the two patients and cultivated for 24 or 48 h in MarrowMAX™ Bone Marrow Medium (Gibco; Invitrogen, Brazil) with 10% fetal calf serum without stimulation. The cells were then harvested using conventional techniques. The GTG banding analysis was performed according to Scheres (6). Metaphase chromosomes were analyzed using an Olympus BX61 microscope connected to BandView 4.5 software (Applied Spectral Imaging, Israel). Chromosomes were identified and classified according to the International System of Human Cytogenetic Nomenclature guidelines (7). The analysis of twenty metaphases for each patient did not reveal any cytogenetic changes.

Discussion

The symptoms of isolated PCLD are specifically correlated with the extension of liver involvement (8), with the possibility of life-threatening complications and a poor quality of life. No exact epidemiological data are currently available regarding the incidence of PCLD in any population. However,
PCLD, without ADPKD, is a rare condition with a prevalence of 0.05 or 0.13% in two autopsy series.

When associated with ADPKD, the prevalence reported was 16% in one study and 93% in another (9,10). In these cases, a relevant genetic defect was linked to the polycystic kidney disease 1 (PKD1) locus on chromosome 16 (the major locus responsible for the disease) (12) and PKD2 locus on chromosome 4. No evidence of further locus heterogeneity was described (11).

In a study conducted by Pirson et al (12) of a family with PCLD not associated with kidney cysts and transmitted through three generations, linkage to mutations of the genetic markers of PKD1 and PKD2 were excluded. One report concluded that isolated PCLD exists as a genetic disease, distinct from ADPKD1 and ADPKD2.

A third gene, protein kinase C substrate 80K-H (PRKCSH), accounts for a comparatively rare, isolated form of autosomal dominant PCLD, which displays no kidney involvement (4). Waanders et al (13) concluded that 16% of patients with PCLD were found to have either PRKCSH or SEC63 mutations.

In a study of 20 individuals with PCLD, Yang et al (14) reported that the PRKCSH gene was not a major genetic cause, and that there may be at least another locus responsible for the disease in Taiwanese patients. Through analysis of eight Finnish families with PCLD, Tahvanainen et al (15) concluded that, in most families, PCLD is linked to a locus on chromosome 19p13.2-13.1; however, the disease is genetically heterogeneous with at least one more locus, which remains to be found.

Associated morbidities were notably less frequent in patients with PCLD when comparing individuals with PCLD linked to ADPKD16, and included mitral valve prolapse, diverticuli, brain aneurisms and intracranial arachnoid cysts (17).

Intracranial lesions in association with polycystic diseases are typically incidental findings in routine investigations, while symptomatic lesions may include headaches, seizure or focal neurological deficits (18). However, the association of rare, developmental, solid tumors in meningeal membrane (meningiomas) with PCLD has yet to be reported.

The treatment of PCLD aims to symptomatically relieve symptoms related to cysts, and includes conservative approaches such as cyst decompression, liver resections or liver transplantation. The main reason for the consideration of liver transplantation in our patients was the large liver volumes, and included mitral valve prolapse, diverticuli, brain aneurisms and intracranial arachnoid cysts (17).

The histological characterization of fibrous and transitional meningiomas in the patients we studied lead to a classification of Grade I according to WHO criteria (19).

The postoperative follow-up for the two patients was uneventful, without complications, with the patients remaining on the liver transplant waiting list.

Bearing in mind that the polymorphism is a feature of extrahepatic lesions in PCLD, and is either associated, or not, to ADPKD, improved awareness is mandatory in order to determine the best approach for the treatment of these patients. The lack of a genetic or familial association between these two cases shows they are likely to have occurred by chance rather than represent a previously unrecognized association between polycystic liver disease and cranial meningioma.

The analysis of a large patient cohort may provide us with more detailed information and a better understanding of the genetic background of such occurrences.

At present, a more prudent course toward the identification of PCLD remains a combination of refinement of the genetic interval and continued gene identification based on the genomic sequence of the region, with emphasis placed on the understanding of liver cyst pathogenesis, which may lead to non-surgical therapy for patients affected with symptomatic liver disease (21).

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References