

Imaging of Caroli's disease : a case report with review of literative.

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The diagnosis of Caroli's disease of an eight-month female infant was established by computer tomogram, ultrasound and hepatobiliary scintigraphy. The imaging clues were specifically demonstrated. CT, with strong contrast enhancement, showed the central dot sign within the saccular dilated intrahepatic bile ducts or multiple cyst-like structures. US showed multiple cysts with central tubular and dot echoes representing protrusion and bridge formation in the dilated intrahepatic bile ducts. The Tc-99m-¹²³I-IDA hepatobiliary scan confirmed through excretion of the radiotracer into the cystic structures that the multiple cysts in the liver were non-obstructive cystic dilatation of the bile ducts.

Key words: Caroli's disease, Imaging of caroli's disease, CT and ultrasoud of caroli's disease.

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Caroli's disease เป็นโรคของท่อน้ำดีโป่งพองที่เป็นมาแต่กำเนิด อาจร่วมกับความผิดปกติแต่กำเนิดของระบบไต อาการที่พบบ่อยส่วนใหญ่ได้แก่ ตับ ม้ามโต ดีซ่าน การติดเชื้อหรืออาการทางไตล้มเหลว รายงานผู้ป่วยเด็กหญิง อายุ 8 เดือน 1 ราย ที่สามารถให้การวินิจฉัยโรคโดยการตรวจด้านการเห็นภาพ ได้แก่ ซีทีสแกน อัลตราซาวด์ และนิวเคลียร์ซินติกราฟฟี ซึ่งจะให้ลักษณะภาพที่เฉพาะของโรคนี้

Congenital saccular dilatation of intrahepatic bile ducts is a rare congenital anomaly and is invariably associated with renal tubular ectasia or other forms of cystic disease of the kidney.⁽¹⁻⁴⁾ The first reported case with calculi within intrahepatic ducts and cavities without jaundice was described by Vschal & Stevens⁽⁵⁾ in 1906, but it was first prescribed as Caroli's disease in 1958 by Caroli et al.⁽¹⁾ It was characterized by : (1) congenital saccular dilatation of intrahepatic bile ducts; (2) a high incidence of stone formation and cholangitis; (3) the absence of hepatic cirrhosis and portal hypertension; (4) and an association with renal tubular ectasia or other forms of cystic disease of the kidney.⁽¹⁾ And in 1968, Caroli classified it into 2 types⁽⁶⁾: (1) the pure or simple form which was not associated with hepatic fibrosis; and (2) the periportal fibrotic form that was associated with hepatic fibrosis.

The disease is famial and is probably inherited by autosomal recessive trait.^(3,7,8) The simple form of disease is less common and is usually found in young adults with recurrent cholangitis and intrahepatic duct stone formation. The second periportal fibrotic type is usually found with upper gastrointestinal tract bleeding cawed by ruptured esophageal varices due to portal hypertension. This type is more often found in infants or children and there is a more serious prognosis.⁽⁷⁾

In the past, preoperative radiologic dianosis of Caroli's disease was difficult. Operative cholangiogram was the best procedure to observe the characteristic segmental saccular dilatation of the intrahepatic ducts.⁽³⁾ Nowadays, ultrasonograms (US) and computer tomograms (CT) play a major role in the diagnostic investigation, as does hepatobiliary scan. ERCP, intravenous cholangiogram (IVC), percutaneous transhepatic cholangiogram (PTC), also take part in

diagnosis. The advantages and disadvantages of these investigations will be discussed later.

In 1982, Nakamura et al⁽⁹⁾, described intraluminal bulbar protrusions of the ductal wall and bridge formation across dilated lumina as additional typical findings of Caroli's disease. In 1986, Marchal et al⁽¹⁰⁾ described an additional macroscopic feature; portal radicles partially or completely surrounded by dilated bile ducts which was possibly significant in the pathogenesis of Caroli's disease and which was detected by high frequency ultrasound. The central dot sign in CT was described by Byung Ihn Choi in 1990.⁽¹¹⁾ This central dot represented portal radicles in the dilated duct. We have reported a case of Caroli's disease which had all of these characteristic signs.

A case report

An eight-month female infant was referred to the Pediatric Department of Chulalongkorn hospital in September, 1990 with problems of anemia, hepatosplenomegaly and ascities. At brith, she had been well except for slight abdominal distension. Her first admission was for one month due to increased abdominal distension and she was discharged with no definite diagnosis. Three monthes later she had fever off and on, without jaundice, but looked pale. Few weeks later she had mucous bloody diarrhea, dyspnea, pedal edema and marked abdominal distension. She was admitted and siven antibiotics and a blood tranfusion. Diuretic and digoxin were given but her condition did not improve.

Physical examination revealed a malnourished body looking distressed, and with marked abdominal distension. She was pale without jaundice. Her vital signs were RR = 46/min, HR = 130/min, BP = 100/60 mmHg, and BT = 38.2° C. The lungs were clear. No heart murmur was detected. Marked hepatospleno-

megaly was detected with questionable ascites. Superficial vein dilatation was noted along the anterior abdominal wall. Palmar Erythema was observed with pitting edema of both legs. The laboratory values are provided in table 1. A computed blood count revealed anemia (Hb 7.9 g/dl) and leukocytosis (Wbc 38,700 cells/cu.mm), PMN 60 % and adequate platelets. Urine analysis was normal, as was a renal functional test. A liver function test showed a reverse albumin/globulin ratio with total bilirubin 0.64 % direct bilirubin 0 mg %, total protein 6.6 g/dl, albumin 2.8 g/dl, globulin 3.8 g/dl, SGOT 30 U/L, SGPT 12 U/L, and alkaline phosphatase 385 U/L. A prolonged prothrombin time of 20 seconds (control 12 seconds) was also noted.

Imaging studies:

Intravenous pyelography (Fig.1) showed normal excretory urography but marked hepatomegaly. A large well-defined rounded radiolucent area in the liver was observed. An ultrasonogram (Fig.2) revealed a huge hepatomegaly with diffuse cystic dilatation of the intrahepatic bile ducts throughout both lobes of the liver. Evidence of central tubular and dot echoes representing bullar protrusion and bridging formation of the ductal walls was observed in the dilated ducts. No evidence of intrahepatic duct stones or gall stones was noted. The gall bladder was normal. The spleen was enlarged. CT (Fig.3) revealed marked hepatomegaly with multiple large well-defined tubular or cystic structures of variable size from 1 cm. up to 10 cm, representing saccular and cystic dilatation of intrahepatic bile ducts. Evidence of linear shadows and tiny dots in all of the dilated ducts were noted with strong contrast enhancement, and this was

suggestive of a vascular nature. Prominent portal and splenic veins were noted with splenomegaly. The diagnosis of Caroli's disease was suggested.



Figure 1. Intravenous pyelography showed a well-defined rounded radiolucent area in liver (arrow-heads).

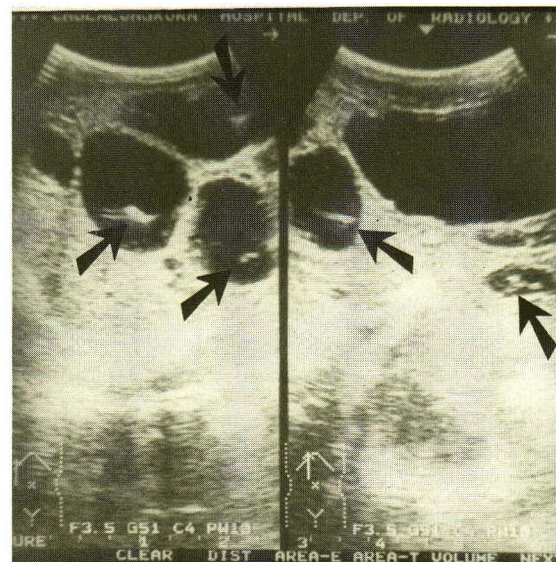


Figure 2. Ultrasonogram of liver showed diffusely dilated intrahepatic bile ducts with central tubular and dot echoes representing bullar protrusion and bridging formation of ductal wall. (arrows).

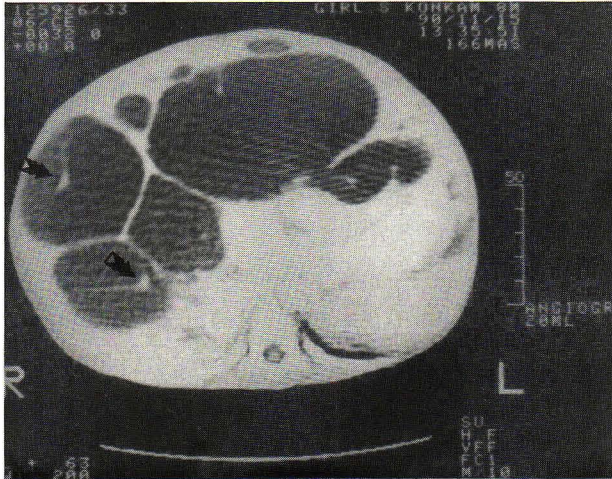


Figure 3. Enhanced CT scan showee strong enhancement of the linear and dot shadows locating in these cystic structures or dilated bile ducts (arrows).

However, since large oval cysts were seen in both the US and CT, an alternate diagnosis of polycystic liver was raised. A hepatobiliary scan was performed to confirm the diagnosis. Use of Tc-99m-sulfur colloid (Fig.4a,b) revealed hepatomegaly with variable size of multiple areas of photon deficiency throughout both lobes. The largest one was in left lobe. A Tc-99m-IODIDA scan demonstrated excretion of radiotracer into the cold areas mentioned above. Activity in the bowel was also noted at the delayed 3-hour-image. Almost no radioactiv-



Figure 4A. Tc-99-m. Sulfur collorid liver scan showed hepatomegaly with variable sizes of multiple photon deficiency areas.

ity in the liver was observed in the delayed 24-hour image. The diagnosis of Caroli's disease was undoubted.

This patient had clinical signs of portal hypertension (splenomegaly, dilated superficial veins on the anterior abdominal wall), suggestive of periportal fibrosis. Her signs of chronic liver disease (palmar erythema, pedal edema) and findings of reverse albumin/globulin ratio, prolonged prothrombin time were all indicative of a decompensated liver. She had gram negative septicemia (*Klebsiella* spp) obtained form hemoculture. Antibiotics, blood and fresh frozen plasma transfusions were given. She was discharged after a one-month admission and was clinically improved.

Discussion:

Cystic disease of the liver are simply classified into two groups (Table 1).⁽¹²⁾ Caroli's disease is congenital cysts of the biliary tract in origin, and is thus differentiated from the other group.

Polycystic liver disease and simple cysts differ from Caroli's disease in that these cysts contain a clear serous fluid and no communication with the biliary tree or each other. Complications are usually due to the associated polycystic kidney disease rather

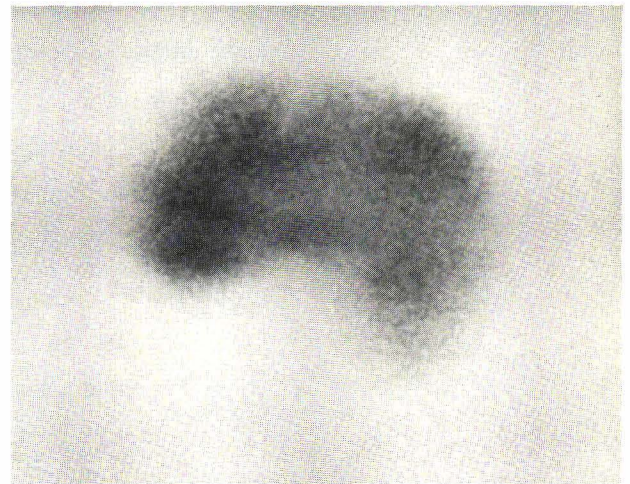


Figure 4B. Tc-99-m. 10DIDA liver scan showed excretion of radiotracer into those cold areas noted in Fig. 4A.

than liver dysfunction.⁽⁷⁾ Cysts in Caroli's disease and congenital hepatic fibrosis (CHF) both communicate to the biliary tract and contain bile.⁽⁷⁾ CHF is characterized histologically by diffuse portal and perilobular fibrosis and excessive proliferation of the small intrahepatic bile ducts forming cyst-like structures, usually microscopic, but occasionally they dilate and reach 2-3 cm. in diameter.^(7,12)

As previously mentioned, Caroli's disease is classified into two types, simple and periportal fibrotic type. These entities belong to the family of fibropoly cystic diseases of the hepatobiliary system and

kidneys. This spectrum of biliary dysplasias includes biliary microhamatomas, congenital hepatic fibrosis, adult polycystic disease and choledochal cysts. The more common periportal fibrotic type indicates that the saccular dilatation of the intrahepatic bile ducts is not usually an isolated entity but represents a part of the spectrum of developmental abnormality involving the biliary system.⁽¹³⁾ Renal tubular ectasia is the most common association between CHF and also Caroli's disease.^(4,13-15) True differentiation between these two types of disease can only be made with histopathologic specimens.⁽¹³⁾

Table 1. Classification of cystic diseases of the liver

I. Congenital intrahepatic cysts
parenchymal in origin
solitary
polycystic disease
childhood
adult
biliary tract in origin
cystic dilatation of intrahepatic bile ducts (Caroli's disease)
congenital hepatic fibrosis
II. Acquired intrahepatic cysts
inflammatory
pyogenic
amoebic
echinococcal
neoplastic
benign
malignant
traumatic

Embryology and pathogenesis:

The liver primordium or hepatic diverticulum appears in the middle of the third week of gestation. This soon splits into two components (1) the pars cystica which will form the gall bladder and cystic duct (2) and the pars hepatica which will become the liver and intrahepatic bile ducts. The topographic development of the intrahepatic biliary tract follows the branching of the portal veins. The formation of the biliary ducts begins at eight weeks, first as a single cell layer (Fig.5a) and later as a double layer (Fig.5b) surrounding the portal vein. Normally, the largest part of the primitive duct is reabsorbed and remodelled, leaving a small bile duct that parallel to the portal vein (Fig.5c).⁽⁶⁾

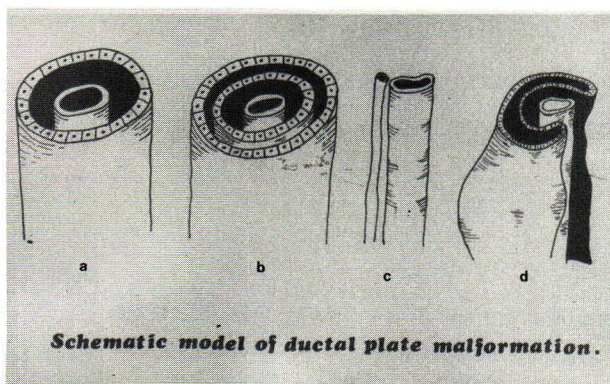


Figure 5. Formation of the biliary ducts.

- a. a single layer surrounding the portal vein
- b. a double layer surrounding the portal vein
- c. Resorbed and remodelled primitive duct in normal formation
- d. Dilated bile ducts in Caroli's disease

There are two hypothesis for Caroli's disease. First, in 1974 Jorgensen⁽¹⁶⁾ suggested that it was a disturbance of the reabsorption phase, resulting in the persistence of a dilated primitive bile duct surrounding the portal vein (Fig.5d) which may be located either in the center or peripheral part of

the duct. The second hypothesis was that the malformation may be caused by a disproportion in the speed of growth between the connective tissue and the biliary epithelium, resulting in elongation and irregular dilatation of the bile ducts.⁽⁹⁾

Clinical course of the disease:

The clinical manifestation of Caroli's disease is usually recognized initially in childhood or as a young adult.^(7,13) The nature depends on whether hepatic fibrosis or biliary ductal ectasia is prominent lesion.⁽¹³⁾ If hepatic fibrosis is predominant, the presence of portal hypertension, usually hematemesis due to ruptured esophageal varices, is common. In the simple type, recurrent cholangitis and intrahepatic duct stone formation are the most frequent manifestations.^(1,7,13,14) Hepatic decompensation is rare.⁽¹³⁾ Other complications are liver abscess,⁽¹³⁾ subphrenic abscesses⁽¹⁷⁾ gram negative septicemia which is the most common cause of death, biliary fistula, amyloidosis,⁽⁷⁾ and cholangiocarcinoma which occurs in 7 % of cases.⁽¹⁸⁾

Our patient had gram negative septicemia, diagnostic of portal hypertension and liver decompensation in the final stage of the disease. No evidence of associated kidney abnormality was detected.

Diagnostic work up:

Liver function tests yield non-specific results for this disease. Most of these cases are normal.^(7,21) Increased serum bilirubin and alkaline phosphatase may occur, associated with intrahepatic duct stone formation which is common in the simple type. Synthetic function may not change until late stages of the disease.

Imaging study: (table 2)

In the past, diagnostic procedures included intraoperative cholangiography, T-tube cholangiography, percutaneous transhepatic cholangiography (PTC), and less invasive endoscopic retrograde cholangiopancreatography (ERCP). All of these produced the image of characteristic cystic or saccular dilatation of the intrahepatic bile ducts. ^(4,5,19,21) Operative cholangiogram and T-tube cholangiography were invasive and only used in the cases where

surgery was indicated, or in the time prior to other preoperative diagnostic procedures. PTC, ERCP were preoperative studies and less invasive but still had morbidity. ERCP sometimes failed to demonstrate intrahepatic bile ducts. Some authors believed that ERCP would be important in preoperative evaluation of the biliary tract and also to provide a safe means of following the progression of the disease.⁽²⁰⁾ Esophageal varices was simultaneously evaluated with ERCP.⁽²⁰⁾

Table 2. Imaging of Caroli's disease.

Invasive studies:-

- Operative cholangiogram
- T-tube cholangiogram
- Percutaneous transhepatic cholangiogram (PTC)
- Endoscopic retrograde cholangiopancreatography (ERCP)

Non-invasive studies:-

- Ultrasonogram
 - CT cholangiography
 - Conventional CT with IV contrast enhancement
 - Hepatobiliary scan
 - MRI
 - Oral cholecystogram
 - IV cholangiogram
-

Intravenous cholangiography (IVC) also detected cystic dilatation of intrahepatic bile ducts⁽²²⁾ but due to high morbidity of the contrast material, the study was rarely done. Preoperative non-invasive imaging studies were developed in the last ten years. Ultrasonograms, computer tomography and hepatobiliary scintigraphy with newer cholescintigraphic agents are the main types.

US findings of Caroli's disease are tubular or cystic sonolucent structures in the liver converging toward the porta hepatis.⁽³⁾ In the case of large cystic dilatation of ducts as in our case, connection between these cysts or to the hepatic duct was hardly demonstrated. Depending on the pathogenesis, we could demonstrate echoic bridge formation across the dilated lumina and bulbar protrusion into the duct.^(8,10)

CT scan of our patient demonstrated branching areas of water-attenuation throughout the liver, representing dilated ducts.⁽¹¹⁾ In 1979 and 1982⁽²³⁻²⁵⁾ there were reports of CT cholangiogram (CT scan performed after intravenous cholangiography) in Caroli's disease to prove the biliary or non-biliary nature of the hepatic cysts. It was not necessary in our case since the pathogenesis of the disease helped us to understand the characteristic finding, the central dot sign, in Caroli's disease. Findings on the image were multiple central tiny dots or strings in the dilated bile ducts with strong contrast enhancement, representing the portal radicles in the biliary trees.

Radioisotope imaging performed with Tc-99m-labelled cholescintigraphic agents was a noninvasive study that proved the biliary nature of the disease.^(13,26) The study revealed nonhomogeneous hepatic uptake initially, followed by progressive and persistent accumulation of the radiotracer within those cold areas during the next hour, suggesting bile duct dilatation and stasis. Excretion of radiotracer into the bowel and complete clearance of radio activity in the liver in the delayed 24-hour image in our case suggested a non-obstructive disease. This study also provided functional information about the liver which could not be obtained by US or CT.

US and CT were more useful in the diagnosis of complications such as liver abscess, subphrenic abscess, intrahepatic duct stones and they also provided indirect signs of portal hypertension eg. varices, splenomegaly, dilated portal vein. Kidney diseases could also be studied.

The new modalities that we prefer to mention are doppler US and MRI. Doppler US may be used to evaluate flow in the portal radicles in dilated bile ducts and to also provide an evaluation of portal hypertension. MRI may demonstrate flow void phenomenon of the portal radicles.

Conclusion

We have reported a case of Caroli's disease, periportal fibrotic form, that had all of the characteristic and pathognomonic signs of the disease on US (bulbar protrusion and bridge formation in the dilated bile ducts) and CT (central dot signs). The non-obstructive biliary nature of the disease was also proven by Tc-99m-IODIDA hepatobiliary scintigraphy. An extensive review of literature was performed. The pathogenesis of the disease was mentioned and was according to all findings in our patient. We suggest that US and CT are the perfect diagnostic tools for accuracy of diagnosis and the detection of complications.

References

1. Caroli's J, Soupault R, Kossakowski J, Plocker L, Paradowska M. Lo dilatation polykystique congenitale des voies biliares intrahepatiques : essai de classification. *Semin Hop Paris* 1958; 34: 128-35
2. Bass EM, Funston MR, Shaff MI. Caroli's disease : an ultrasonic diagnosis. *Br J Radiol* 1977; 50(593): 366-9
3. Mittelstaedt CA, Volberg FM, Fischer GJ, McCartney WH. Caroli's disease : sonographic findings. *AJR* 1980 Mar; 134(3): 585-7
4. Mall JC, Ghahremani GG, Boyer GL. Caroli's disease associated with congenital hepatic fibrosis and renal tubular ectasis. *Gastroenterology* 1974 May; 66(5): 589-92
5. Barros JL, Polo JR, Sanabia J, Garcia-Sabrido JL, Gomez-Lorenzo FJ. Congenital cystic dilatation of the intrahepatic bile ducts (Caroli's disease) : report of a case and review of the literature. *Surgery* 1979 May; 85 (5): 589-92

6. Caroli J. Disease of intrahepatic bile ducts. *Israel J Med Sci* 1968 Jan; 4 (1): 21-35
7. Mujahed Z, Glenn F, Evans JA. Communicating cavernous ectasis of the intrahepatic ducts (Caroli's disease). *AJR* 1971 Sep; 113(1) : 21-6
8. Høglund M, Muren C, Schmidt D. Caroli's disease in two sisters. Diagnosis by ultrasonography and computed tomography. *Acta Radiol* 1989 Sep-Oct; 30(5): 459-62
9. Nakamura Y, Terada T, Ohta G, Kuracki M, Matsubara E. Caroli's disease in congenital hepatic fibrosis and infantile polycystic disease. *Liver* 1982; 2 : 346-54
10. Marchal GJ, Desmet VJ, Proesmans WC, Moerman PI, Van Roost WW, Van Holsbeeck MT, Baert AL. Caroli disease : high-frequency us and pathologic findings. *Radiology* 1986 Feb; 158(2): 507-11
11. Choi BI, Yeon KM, Kim SH, Han MC. Caroli disease : central dot sign in CT. *Radiology* 1990 Jan; 174 (1) : 161-3
12. Doty JE, Tompkins RK. Management of cystic disease of the liver. *Surg Clin N Am* 1989 Apr; 69(2): 285-95
13. Sty JR, Hubbard AM, Starshak RJ. Radionuclide hepatobiliary imaging in congenital biliary tract ectasis (Caroli disease). *Pediatric Radiol* 1982; 12(3): 111-4
14. Davies CH, Stringer DA, Whyte H, Daneman A, Mancor K. Congenital hepatic fibrosis with saccular dilatation of intrahepatic bile ducts and infantile polycystic kidneys. *Pediatric Radiol* 1986; 16(4) : 302-5
15. Six R, Oliphant M, Grossman H. A Spectrum of renal tubular ectasis and hepatic fibrosis. *Radiology* 1975 Oct; 117(1): 117-22
16. Jorgensen M. A serological study of intrahepatic bile ducts. 4. Congenital hepatic fibrosis. *Acta Pathol Microbiol Scand (A)* 1974 Jan; A 82: 21-9
17. Rogstad K, Freeman J, Moorghen M, Record CO. Difficulty in diagnosis complications of Caroli's disease. *J Clin Gastroenterol* 1986 Oct; 8(5) : 582-5
18. Dayton MT, Longmire WP. Jr., Tompkins RK. Caroli's disease : a premalignant condition? *Am J Surg* 1983 Jan; 145(1): 41-8
19. Hermansen MC, Starshak RJ, Werlin SL. Caroli disease : the diagnostic approach. *J Pediatrics* 1979 Jun; 94(6): 879-82
20. Missavage AE, Supawa C. Caroli's disease : role of endoscopic retrograde cholangiopancreatography. *Am J Gastroenterology* 1983 Dec; 78(12): 815-7
21. Foulk WT. Congenital malformations of the intrahepatic biliary tree in the adult. *Gastroenterology* 1970 Feb; 58(2) : 253-6
22. Lucaya J, Gomez JL, Molino C, Atienza JG. Congenital dilatation of the intrahepatic bile ducts (Caroli's disease). *Radiology* 1978 Jun; 127(3): 746
23. Kaiser JA, Mall JC, Salmen BJ, Parker JJ. Diagnosis of Caroli's disease by computed tomography : report of two cases. *Radiology* 1979 Sep; 132(3) : 661-4
24. Musante F, Derchi LE, Bonati P. CT cholangiography in suspected Caroli's disease. *Comput Assist Tomogr* 1982 Jun; 6 (3) : 482-5
25. Sorensen KW, Glazer GM, Francis IR. Diagnosis of cystic ectasia of intrahepatic bile ducts by computed tomography. *Comput Assist Tomogr* 1982 Jun; 6(3) : 486-9
26. Inciardi M, Leonard JC. Role of hepatobiliary scintigraphy in the diagnosis of Caroli's disease. *Clin Pediatrics* 1982 Dec; 21(12) : 738-40