

Biliary microhamartomas (von Meyenburg complexes), liver metastasis simulators: a series of eight cases

Microhamartomas de los conductos biliares (complejos de Von Meyenburg), simuladores de metástasis hepáticas: una serie de ocho casos

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Abstract

Background: Von Meyenburg complexes are benign hamartomatous lesions, they are part of the spectrum of ductal plate malformations. They are rare, reported in 0.35-5.6% of the general population, predominantly in adults, with no clear predilection for sex. **Objective:** To present the clinical characteristics of Von Meyenburg complexes in our region. **Method:** We searched all cases with diagnosis of Von Meyenburg complexes in a period from 2012 to 2022, in our institutions. **Results:** We identified eight cases, with an average age of 59.25 years, with a predominance of females and with one case associated with gastric carcinoma. **Conclusions:** It is important to adequately recognize this entity, since due to its multifocal nature it can easily simulate metastasis, additionally, and its presence does not rule out other synchronous neoplasms.

Keywords: Hamartomas. von-Meyenburg. Bile ducts. Metastasis. Gastric carcinoma.

Resumen

Antecedentes: Los complejos de Von Meyenburg son lesiones hamartomatosas benignas que forman parte del espectro de las malformaciones de la placa ductal. Son poco frecuentes, se reportan en un 0.35-5.6% de la población general, predominantemente en adultos, sin clara predilección por un sexo. **Objetivo:** Presentar las características clínicas de los complejos de Von Meyenburg en nuestro medio. **Método:** Se buscaron todos los casos con diagnóstico de complejos de Von Meyenburg en nuestras instituciones entre 2012 y 2022. **Resultados:** Identificamos ocho casos, con un promedio de edad de 59.25 años, con predominio por el sexo femenino y con un caso asociado a carcinoma gástrico. **Conclusiones:** Es importante reconocer y diagnosticar adecuadamente esta afección, ya que por su naturaleza multifocal fácilmente puede simular metástasis, y además su presencia no descarta otros procesos neoplásicos sincrónicos.

Palabras clave: Hamartomas. Von Meyenburg. Conductos biliares. Metástasis. Carcinoma gástrico.

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Introduction

Bile duct microhamartomas or von Meyenburg complexes were first described in 1918 as benign hepatic malformations of the embryonic ductal plate, placing them within the spectrum of ductal plate lesions (such as congenital hepatic fibrosis and Caroli disease)¹. These are small hamartomatous lesions affecting the smallest intrahepatic bile ducts. They are composed of bile duct elements, often with well-demarcated, open lumens, containing thick bile inside. Although their etiology is unclear, they can be observed in livers with and without cirrhosis, in children and adults. They have occasionally been associated with cirrhosis due to chronic viral hepatitis, alcohol-related liver disease, and adult polycystic liver disease².

They are rare and can be confused with or associated with malignant neoplasms or metastases, making it important to have a good understanding of them.

Method

Cases diagnosed as bile duct microhamartomas or Von Meyenburg complexes were identified from the archives of Hospital General de México Dr. Eduardo Liceaga and the Institute of Medical Biological Research at the Universidad Veracruzana, over a 10-year period (2012-2022). A basic analysis was conducted using descriptive statistics.

Results

We identified a total of 8 cases, with an age range of 21 to 71 years (mean, 59.25 years). 62.5% of the cases occurred in women and 37.5% in men, with a 1.6:1 ratio. In 7 (87.5%) patients, lesions were incidental findings during surgeries for cholecystitis, and 1 (12.5%) was associated with diffuse gastric adenocarcinoma (Table 1). In all cases, a liver biopsy was performed to rule out the presence of metastases, as the lesions were identified as multifocal on the liver surface (Fig. 1). Microscopically, diagnosis was established by observing proliferative lesions in all patients, composed of ducts with cuboidal epithelium, cytologically without atypia, with some bile plugs inside, surrounded by fibrous stroma (Fig. 2).

Discussion and Conclusions

Von Meyenburg complexes have a variable frequency. In series of liver needle biopsies, an incidence of 0.35%³ up to 0.6%⁴ has been reported, and in autopsy series, 0.49%⁵ up to 2.8%⁴, and up to 5.6%, being more common in adults, as in children they only represent 0.9% of total cases⁶.

They do not have a clear gender predilection, and although the age range of presentation is broad, from 17 to 76 years, they are most frequently diagnosed in the fourth and fifth decades of life^{3,4}. In our series, although the age range is similar to that reported in the literature, the mean age is slightly higher, corresponding to the sixth decade of life.

Macroscopically, they appear as small nodules, generally < 1.0 cm, grayish-white in color, usually distributed both in the subcapsular regions and throughout the hepatic parenchyma, making them visible from the liver external surface, as was the case in our patients. Microscopically, they look like well-demarcated lesions composed of bile ducts with dilated, anastomosed lumens with bile plugs. Epithelium is cytologically soft, without atypia or mitosis, and with a very low proliferative rate when marked with Ki-67. They are associated with stroma that can be loose, myxoid, or densely fibrous; most have mild lymphoid infiltrate and are found adjacent to portal tracts^{2,4,7}.

In general, they do not present symptoms or abnormalities in liver function tests, making them incidental findings in most cases, although they have sometimes been associated with abdominal pain, infectious processes such as cholangitis, hepatic abscesses⁸, fatigue, jaundice³, and biliary colic⁹.

Differential diagnoses include bile duct adenomas and, more rarely, cholangiocarcinomas²; sometimes they can be mistaken for hepatic metastases. It is important to emphasize that their diagnosis does not exclude the synchronous presence of malignant neoplastic processes¹⁰, as seen in one of the patients in our series.

Although they generally have a benign clinical course, they can rarely progress to cholangiocarcinomas, as epithelial cells may present mutations in tumor suppressor genes, such as TP53, APC, PTEN, or p16¹¹.

In conclusion, bile duct microhamartomas or Von Meyenburg complexes are rare and generally asymptomatic lesions that are important to recognize, as



Figure 1. A: multiple nodular lesions on the liver surface observed during laparoscopic surgery. B: similarly, diffuse lesions are observed on the liver surface in open surgery. C: Cut surface of a liver biopsy fixed in 10% formalin, showing multiple grayish-white nodular lesions affecting the capsular and subcapsular regions of the liver, as well as deeper areas of the parenchyma.

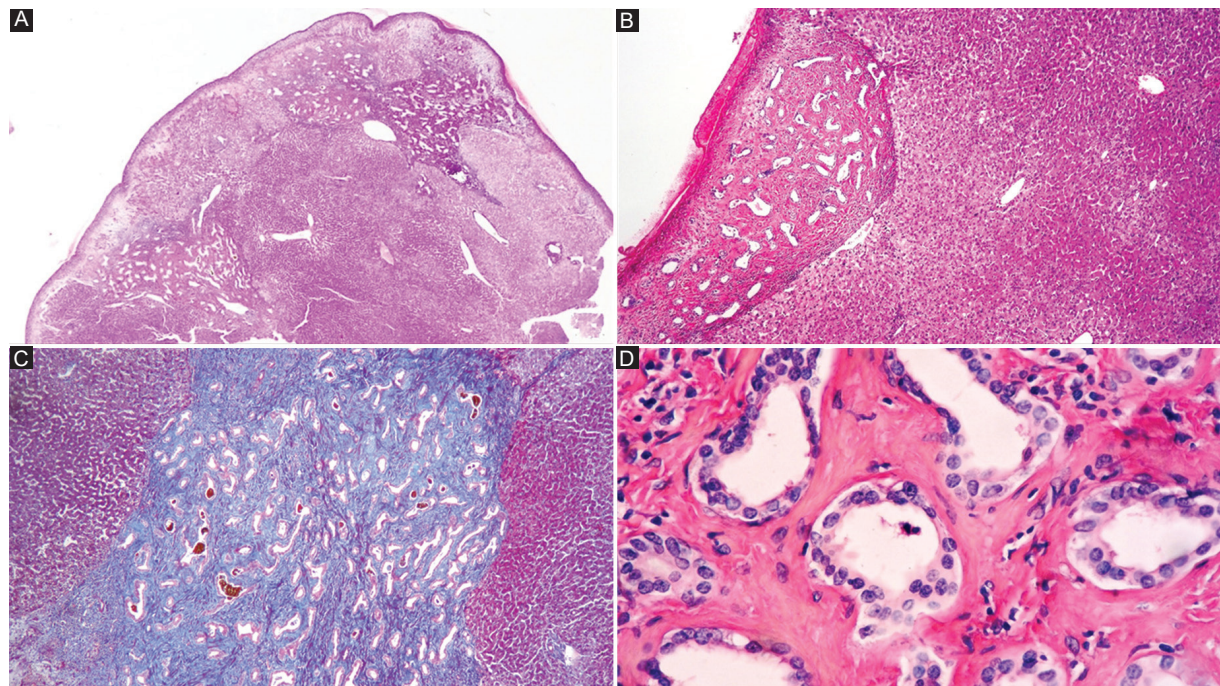


Figure 2. A: at low magnification, the lesions appear multifocal with normal interposed hepatic parenchyma (hematoxylin and eosin, 40 $\times$). B: at medium magnification, the lesions are well-demarcated, composed of ducts embedded in fibrous stroma (hematoxylin and eosin, 100 $\times$). C: the stroma surrounding the ducts consists of collagen fibers stained blue. Bile is also observed in some ducts (Masson's trichrome, 100 $\times$). D: at high magnification, the epithelium lining the ducts is cytologically bland, with no cellular atypia (hematoxylin and eosin, 400 $\times$).

they can mimic metastases, can rarely progress to cholangiocarcinoma (warranting consideration for long-term follow-up), and their presence does not rule

out other synchronous processes (so their diagnosis should not discourage a protocol for investigating a suspected malignant neoplasm).

Table 1. Characteristics of patients with Von Meyenburg complexes

Case No.	Age (years)	Sex	Other Findings
1	21	Female	Microvesicular steatosis, liver regeneration
2	71	Male	Diffuse gastric adenocarcinoma (poorly cohesive), with signet ring cells
3	69	Female	Chronic and acute cholecystitis, hemorrhagic, ulcerated
4	67	Female	Chronic and acute abscessed cholecystitis, cholecystolithiasis
5	68	Male	Chronic cholecystitis, cholecystolithiasis
6	50	Female	Chronic cholecystitis
7	65	Male	Chronic cholecystitis
8	63	Female	Chronic cholecystitis, cholecystolithiasis

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired

clinical data and informed consent was not required for this retrospective observational study.

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