

# Unfused Liver Segments: a Case Report of an Unknown Phenotype of the Conradi-Hünemann-Happle Syndrome

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## ABSTRACT

**Background:** Since its description in 1957, Couinaud's classification of the segmental organization of the liver has remained valid. However, recent investigations by 3-dimensional computed tomography suggest a significant variability of the vascular anatomy and segment volume. Here, we report a surprise finding during the laparoscopic cholecystectomy of a patient with Conradi-Hünemann-Happle syndrome, in whom the liver segments were not fused.

**Case report:** Laparoscopic cholecystectomy was performed because of recurrent biliary pancreatitis in a 47 year-old male patient, who had been diagnosed with Conradi-Hünemann-Happle syndrome. Upon direct view, the liver parenchyma appeared normal, but liver segments were separated and connected by fibrous bridges containing vascular structures, only. Since the hilar anatomy was unclear, an open cholecystectomy was performed without technical difficulties and the postoperative course was uneventful. Postoperatively, magnetic resonance imaging was performed, which revealed a trifurcation of the portal vein and a right bile duct draining into the left main duct. Intersegmental signal alterations corresponded to the fibrous bands seen during laparoscopy.

**Conclusions:** The intraoperative findings of this case confirm the segmental organization of hepatic anatomy proposed by Couinaud. The first description of such an unusual anatomical variant in an extremely rare genetic disorder strongly suggests an association with the genetic background of the syndrome. The established abnormalities of cholesterol biosynthesis in patients with Conradi-Hünemann-Happle syndrome may well explain the observed liver anomaly, which is a novel phenotype of this syndrome. Based on this case, we suggest a potential involvement of the mutation in the emopamil-binding protein gene in liver development and regeneration.

**Key words:** segmental liver development – Couinaud's liver segments – chondrodysplasia punctata – unfused liver segments – liver segments.

**Abbreviations:** CDPX2: X-linked dominant chondrodysplasia punctata; EPB: emopamil-binding protein; MRCP: magnetic resonance cholangiopancreatography; MRI: magnetic resonance imaging; RCDP: rhizomelic chondrodysplasia punctata.

## INTRODUCTION

In 1957, Couinaud described eight liver segments of comparable size due to their segmental vascular orientation and supply [1]. This concept of segmental liver anatomy is the basis for the development of liver surgery. More recent investigations by 3-dimensional computed tomography, however,

suggest that the vascular anatomy and segment volume vary and may differ significantly [2]. In particular, the arterial blood supply of the liver varies frequently with aberrant right and left arteries being most common [3]. Also, intrahepatic variations of the biliary tree or separate segmental ducts as well as variations of the portal vein (e.g. trifurcation) may cause serious problems during surgery. These variations do not affect liver function and are not obvious upon direct view of the liver.

We report an incidental finding of unfused liver segments during laparoscopic surgery in a patient with Conradi-Hünemann-Happle syndrome.

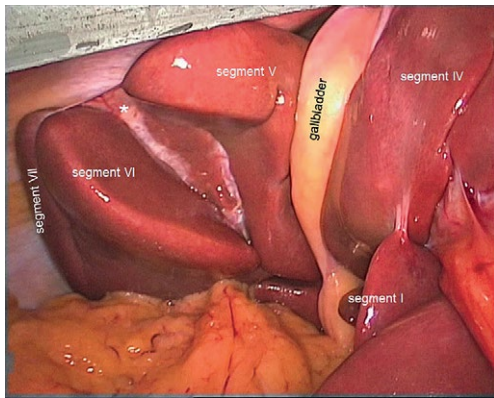
**CASE REPORT**

Laparoscopic cholecystectomy was performed in a 47 year-old male patient with Conradi-Hünemann-Happle syndrome (X-linked dominant chondrodysplasia punctata, CDPX2) for recurrent biliary pancreatitis and elevated transaminases, alkaline phosphatase, gamma-GT and bilirubin due to multiple gallstones, which were preoperatively confirmed by ultrasound. Neither preoperative ultrasound nor endoscopic retrograde cholangiography revealed anatomical abnormalities. The patient suffered from chronic pain due to arthrosis of the hips, knees and lumbar spine.

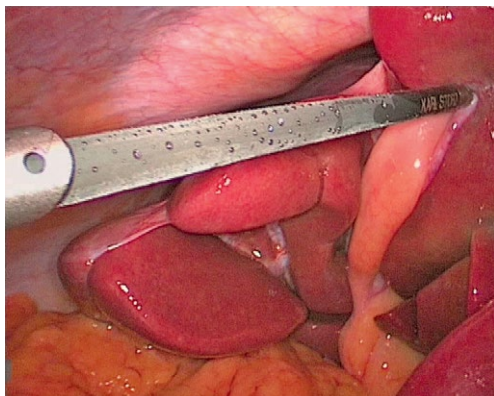
Upon direct view during laparoscopic cholecystectomy, separate liver segments were seen which were only connected by fibrous bridges containing the vascular structures (Figs. 1, 2). Since this surprising discovery hampered liver retraction and intraoperative orientation, a cholecystectomy was performed after conversion to open surgery.

Postoperatively, magnetic resonance imaging (MRI) was performed to explore the intrahepatic anatomy. Corresponding to the intraoperative finding of fibrous bands between the liver segments, signal alterations were found around the intrahepatic vessels (Fig. 3). Furthermore, MRI revealed a trifurcation of the portal vein (Fig. 4a) and a right bile duct draining into the left main duct (Fig. 4b).

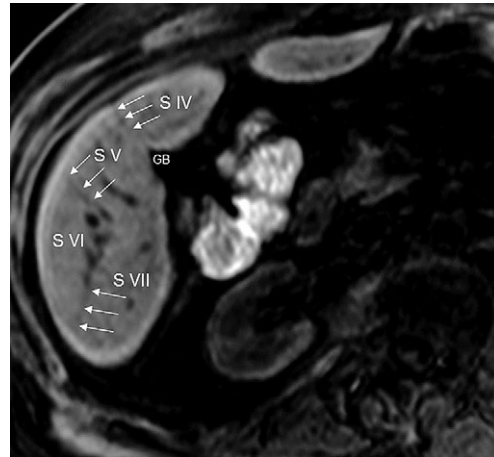
The postoperative course was uneventful and the patient was discharged from hospital on the fifth postoperative day with normal transaminases and bilirubin.



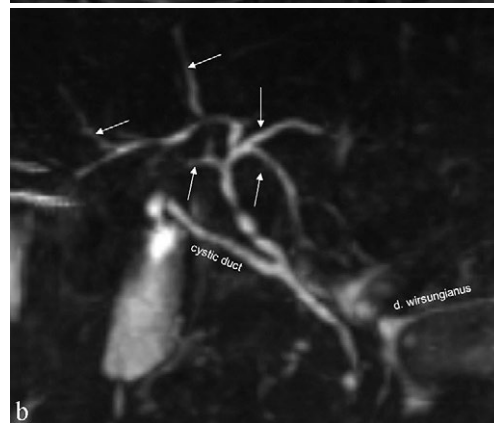
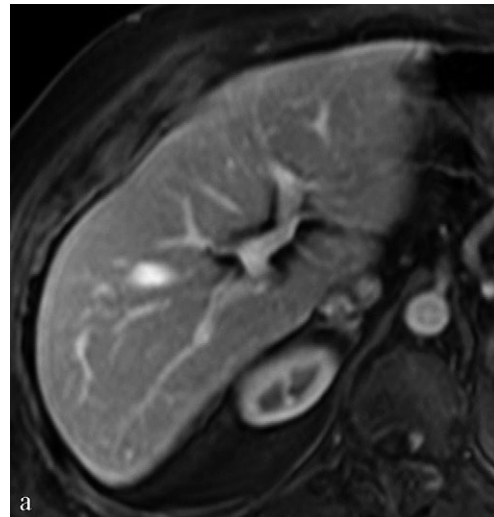
**Fig. 1.** Intraoperative laparoscopic image of the non-fused liver segments and the connecting fibrous bridges (\*) containing the vascular structures.



**Fig. 2.** Another intraoperative laparoscopic view of the non-fused liver segments.



**Fig. 3.** Coronal MRI shows fibrous gaps (arrows) between the liver segments as a sign of the separation.



**Fig. 4.** MRI: trifurcation of the portal vein (a); MRCP image showing the drainage of the right bile duct branch into the left main branch (arrows) (b).

**DISCUSSION**

The Conradi-Hünemann-Happle Syndrome is an X-chromosomal dominant genetic disorder based on a mutation in the emopamil-binding protein (EPB) gene, which is coding for an enzyme of the biosynthesis of

cholesterol. Since Conradi [4] and Hünemann [5] described this syndrome, it is sometimes also known as the Conradi-Hünemann Syndrome. Due to the X-chromosomal dominant inheritance of chondrodysplasia punctata, which was described by Happle in 1979 [6], cases in adult males are very rare since the mutation is lethal for most male embryos. Chondrodysplasia punctata occurs in 1 out of 100,000 live births [7]. The Conradi-Hünemann-Happle Syndrome affects 1/400,000 births and 95% of patients are female with a variable phenotype including nanism, scoliosis and disproportionate shortening of the long bones [8]. Also, craniofacial defects, cataracts and dermatological diseases such as transient ichthyosis and atrophic residua in a mosaic pattern may occur. Huffnagel and colleagues showed in patients with rhizomelic chondrodysplasia punctata (RCDP) that cardiac abnormalities occur more frequently than in the general population [9].

Rakheja and Boriack described an accumulation of precholesterol sterols in lipid rafts of liver tissue of an infant with Conradi-Hünemann-Happle syndrome [10]. The authors assume that this accumulation may disturb embryonic and foetal development, which may also affect the liver. This abnormal sterol metabolism in patients with Conradi-Hünemann-Happle Syndrome is also mentioned by Kelley et al. [11]. Despite these findings, hepatic abnormalities have not been described for this syndrome in the literature.

The intraoperative findings of this case underline the segmental development and resulting anatomical definitions of the liver in a fascinating way. While hepatic biliary and vascular variants are frequent [3], the lack of segmental fusion has not been described in literature.

During embryology, the liver develops from endodermal epithelial cells which move into the transverse septum (mesoderm) and differentiate into hepatocytes as well as cholangiocytes. The so-called liver bud generates the gall bladder first and develops further into the left and right hepatic bud, which later develop into the left and right liver lobes. It is assumed that the liver segments further develop out of these liver buds. According to this theory, the findings of our case may reflect a continuous separation of liver segments as well as a lack of fusion during development.

## CONCLUSION

Considering the low incidence of the Conradi-Hünemann-Happle syndrome and the first description of this unusual intraoperative discovery, the lack of fusion of liver segments is most likely associated with the genetic background of the syndrome. This assumption should be considered for further research in liver development and regeneration.

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**Authors' contributions:** F.B. wrote the report and performed the operation. F.B., S.H.: data acquisition, review of the literature and drafting of the manuscript. M.A. advised and drafted the liver anatomy section. H.L. critically reviewed the report. All authors read and approved the final manuscript.

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