Oxford Medical Case Reports, 2024, **5**, 225–228
https://doi.org/10.1093/omcr/omae052
Case Report

Apocrine and clear cell metaplasia in the gallbladder: the first finding in the medical literature

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Abstract

Apocrine metaplasia, specifically, involves the development of cells resembling those in apocrine glands, characterized by their distinctive cytoplasmic features. Apocrine metaplasia in the gallbladder represents a new and intriguing discovery, marking a significant milestone in medical literature. Furthermore, clear cell metaplasia is often observed in other organs like the cervix and has never been documented in the gallbladder. The coexistence of apocrine and clear metaplasia challenges existing paradigms surrounding gallbladder pathology, prompting a reevaluation of the underlying mechanisms that drive these cellular transformations.

Keywords: apocrine, metaplasia, clear cell, acute, cholecystitis, gallbladder

INTRODUCTION

Apocrine metaplasia involves the development of cells resembling those found in apocrine glands, exhibiting distinct cytoplasmic characteristics. These apocrine-like cells typically present a cuboidal or columnar shape, often accompanied by frequent apical blebs or snouts. This type of metaplasia is commonly observed in breast lesions [1]. Likewise, clear cell metaplasia, which describes a condition when cells undergo a transformation causing them to lose their typical staining properties, is frequently noted in various organs such as the cervix and lungs [2–4]. Both apocrine and clear metaplasia in the gallbladder remain largely unexplored.

This case involves a 55-year-old man with a history of autoimmune hemolytic anemia (AIHA) who presented with symptoms suggestive of acute cholecystitis. Following diagnosis and subsequent laparoscopic cholecystectomy, histopathological examination revealed the presence of apocrine metaplasia with foci of clear metaplasia, alongside acute inflammatory changes and biliary pigment deposition.

Figure 1. Gross image displaying multiple fragments of the excised gallbladder. The average wall thickness measures 10 mm, and the mucosa appears dark green and velvety.

CASE PRESENTATION

A 55-year-old man presented to the emergency department with severe abdominal pain persisting for a day, unresponsive to analgesics. The pain, located in the right upper quadrant and radiating to the right shoulder, was accompanied by nausea, vomiting, and fever. His past medical history includes autoimmune hemolytic anemia (AIHA), diagnosed one year prior. He has maintained stability on chronic prednisone (20 mg daily) for one year with no flares of anemia. There is no family medical history. He is a non-alcoholic smoker. Physical examination indicated tenderness in the right iliac fossa, and Murphy's sign was positive. Laboratory investigation revealed a hemoglobin of 11.9 g/dl, blood white cell count of 11.3 × 10^9/l, and glucose of 134 mg/dl. The liver function tests revealed the following: total bilirubin of 3.7 mg/dl, direct bilirubin of 2.9 mg/dl, indirect bilirubin of 0.8 mg/dl, ALT of 143 U/l, AST 76 U/l, and alkaline phosphatase 155 U/l. The rest of the laboratories were within normal limits. Abdominal

Received: December 11, 2023. **Revised:** March 24, 2024. **Accepted:** April 10, 2024

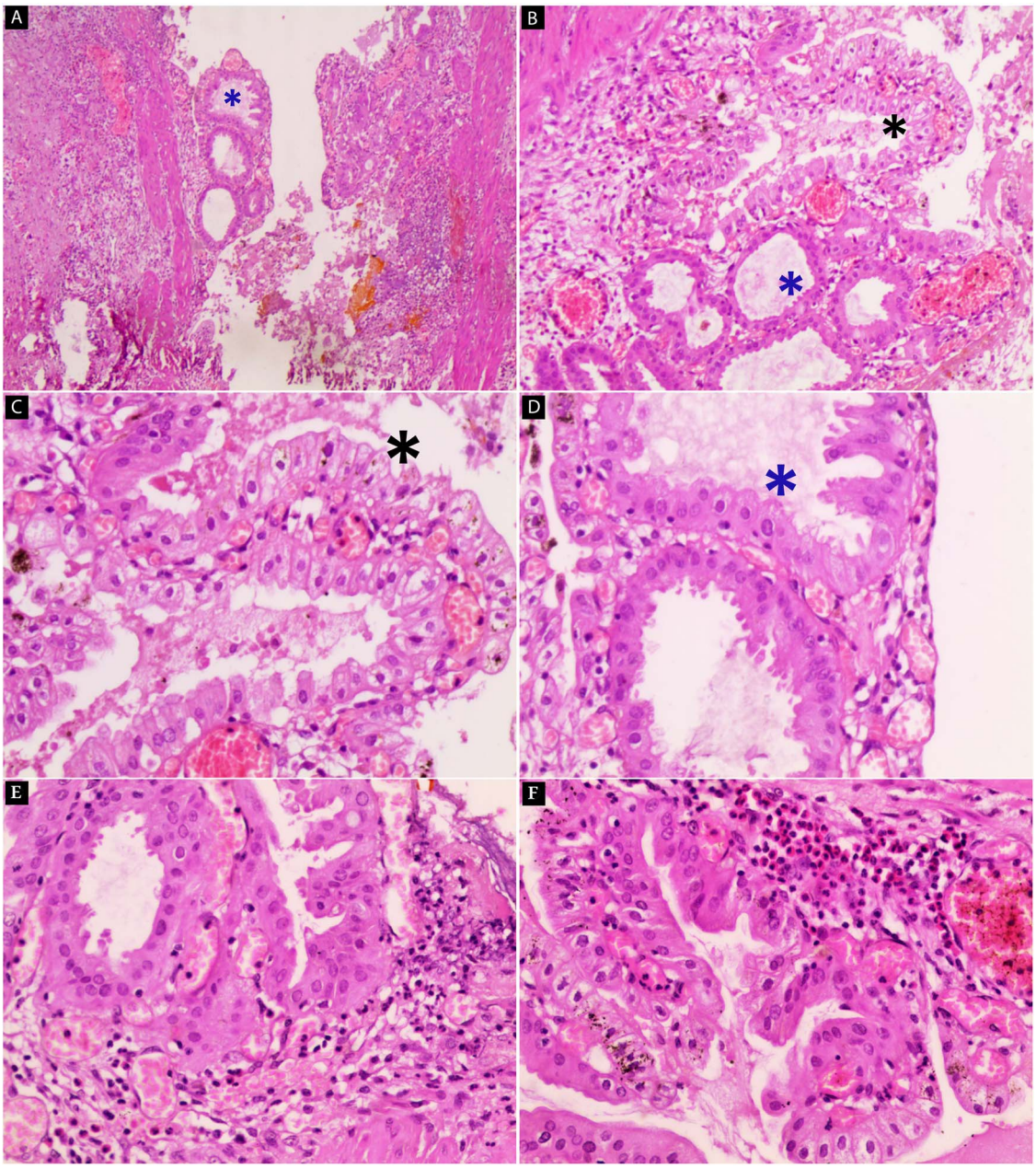

Figure 2. (**A**–**F**) Microscopic images of the gallbladder reveal the presence of apocrine metaplasia (blue asterisk), accompanied by foci of clear cell metaplasia (black asterisk). Infiltration of acute inflammatory cells, including neutrophils and eosinophils, is observed. Additional features include mucosal erosion, congestion, activated fibroblasts, and the presence of biliary pigment (40×,100×,200× magnifications, H&E stain).

ultrasound displayed small stones in the gallbladder, along with wall thickening of approximately 2.5 mm, and pericholecystic fluid. The common bile duct was not dilated. The diagnosis was acute cholecystitis, and the patient underwent laparoscopic cholecystectomy. The specimen was divided by the surgeon, extracted stones, and sent to the pathology department. On gross examination, the excised gallbladder was received in two fragments, opened, and measured 80 mm in length with a 35 mm average diameter. The average wall thickness was 10 mm. The mucosa is dark green and velvety (Fig. 1), and no gallstones were noted. Multiple sections were submitted. Microscopically, apocrine metaplasia with foci of clear metaplasia are identified, particularly in specific regions of the body and fundus. The examined tissue revealed the presence of acute inflammatory cells, including neutrophils and eosinophils (exceeding 15 eosinophils per high-power field), along with mucosal erosion, edema, congestion, activated fibroblasts, and the existence of biliary pigment in the examined tissue (Fig. 2). Apocrine cells exhibited periodic acid-Schiff (PAS) positivity (Fig. 3). The postoperative course was uneventful, and he was discharged the first day after the operation. His condition remained stable after three months of follow-up.

DISCUSSION

Apocrine metaplasia, specifically, involves the development of cells resembling those in apocrine glands, characterized by their distinctive cytoplasmic features [1]. Moreover, these apocrine cells usually assume a cuboidal or columnar appearance with frequent apical blebs or snouts [1]. Apocrine metaplasia is most commonly

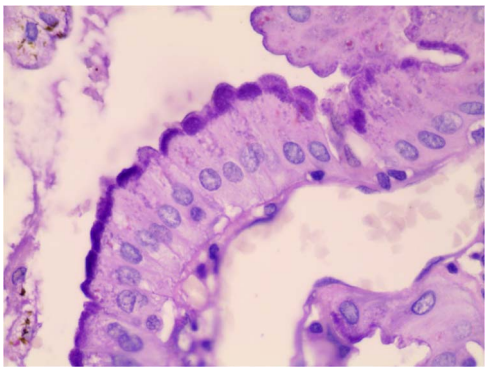

Figure 3. The periodic acid-Schiff reagent (PAS) staining image reveals the presence of glycolipid granules predominantly located in subapical regions within apocrine cells (400× magnification, PAS stain).

found in fibrocystic breast changes [1]. Nevertheless, its presence in the gallbladder has never been reported in the existing medical literature, marking a significant milestone in our understanding of gallbladder pathology.

The gallbladder, typically associated with bile storage and release, is not commonly linked with apocrine metaplasia, rendering this discovery particularly noteworthy.

Similarly, the presence of clear metaplasia, also known as clear cell change, a phenomenon where cells lose their usual staining characteristics, adds further complexity to the narrative [2, 3]. Clear cell change, often observed in other organs like the cervix and lungs [3, 4], has never been documented in the gallbladder.

Transitioning to the discussion of metaplasia within the biliary tract, two primary types are observed: gastric (pyloric) and intestinal. Pyloric gland metaplasia, resembling gastric pyloric-type glands, is the most prevalent, while intestinal metaplasia, characterized by the presence of goblet cells without a clear brush border, hence termed as 'incomplete' metaplasia, is less frequently encountered in gallbladder specimens. Notably, this form of metaplasia is believed to have a closer association with gallbladder carcinogenesis [5, 6].

The development of both pyloric gland metaplasia and intestinal metaplasia is attributed to prolonged inflammation and the presence of gallstones [5]. However, in our case, apocrine and clear metaplasia occur during acute inflammation alongside gallstones.

Moreover, recent research has recognized foveolar metaplasia as another notable addition to the spectrum of metaplastic changes, characterized by the replacement of acidophilic cytoplasm with a voluminous mucinous appearance reminiscent of gastric/foveolar epithelium. Additionally, squamous metaplasia is observed infrequently within the biliary tract [6].

The coexistence of apocrine and clear metaplasia in the gallbladder challenges existing paradigms, suggesting potential factors like inflammation or hormonal influences. Although the direct association with acute cholecystitis remains unclear, the uniqueness of these findings demands further investigation into their implications and mechanisms.

While uncertainties persist in understanding gallbladder malignancies, particularly regarding metaplastic changes as potential precursors [7], it is crucial to recognize that the rarity of this condition may have limited comprehensive reporting within the gallbladder field. However, numerous cases of gallbladder clear cell carcinoma have been documented [7]. The possibility that this case's pathological result represents a precancerous lesion can be explored by drawing parallels with similar occurrences in other organs [3]. Although the specific link remains uncertain, acknowledging reports from other organs provides valuable context to the discussion.

Consequently, further studies and comprehensive investigations into similar cases are necessary to elucidate potential connections and determine the clinical significance of such histopathological variations in gallbladder pathology.

CONCLUSION

In conclusion, our case report documents the first occurrence of apocrine and clear cell metaplasia in the gallbladder, representing a groundbreaking contribution to the field of gallbladder pathology. This unprecedented finding challenges conventional understanding and underscores the need for further research to explore the potential implications and underlying mechanisms of these extraordinary cellular transformations. Our work paves the way for a deeper understanding of gallbladder pathology and may inspire future investigations into the clinical significance of apocrine and clear metaplasia in this organ.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST STATEMENT

No conflict of interest.

FUNDING

There was no funding for this publication.

ETHICAL APPROVAL

No ethical approval was required for this publication.

CONSENT

Informed and written consent from the patient was taken prior to publication.

GUARANTOR

Moatasem Hussein Al-janabi.

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