

## CASE REPORT

# Progression of a Cystic Pancreatic Lesion During Pregnancy

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### ABSTRACT

**Context** Mucinous cystic neoplasms are cystic lesions of the pancreas with a relevant risk to progress to invasive cancer. Mucinous cystic neoplasms are characterized by the presence of an ovarian-like stroma and its almost exclusive occurrence in women. **Case report** Here we report the case of a 41-year old patient with a known cystic lesion that became symptomatic briefly after pregnancy. A pancreatic left resection was carried out and histopathology revealed mucinous cystic neoplasms with expression of estrogen, progesterone, and luteinized hormone receptors in the stromal compartment. **Conclusion** Together with the documented growth during pregnancy, it suggests a hormonal influence on the tumor biological of mucinous cystic neoplasms. Cystic lesions in women of childbearing age require therefore special attention.

### INTRODUCTION

Cystic lesions of the pancreas pose a challenge for diagnosis and management. Most of these lesions are neoplastic with a varying malignant potential. The spectrum of lesions comprises almost always benign serous cystic neoplasm as well as those with a relevant malignant potential such as intraductal papillary mucinous neoplasia (IPMN) and mucinous cystic neoplasia (MCN). The differential diagnosis of mostly benign lesions and those with a relevant malignant potential is often difficult, as is the estimate of the risk of progression.

### CASE REPORT

A forty-one-year-old woman presented with abdominal pain and a cystic lesion in the pancreatic tail measuring approximately 6x7 cm. The patient history was remarkable for the diagnosis of a 3x4 cm pancreatic cyst (without symptoms or worrisome features [1]) 3 years earlier (Figure 1a), childbirth (primipara) 3 months earlier and attacks of acute pancreatitis at the 24<sup>th</sup> gestational week and 2 weeks prior to hospital admission. Routine lab values were all in the normal range, except for an alkaline phosphatase of 300 U/L (norm 35-104 U/L), ALAT of 92 U/L (norm 10-35 U/L) and hemoglobin of 10.2 g/dL (norm 12-16 g/dl). MR imaging (Figure 1b) revealed a cystic lesion

of the body of the pancreas, which showed a markedly heterogeneous signal with cystic components and foci of hyperintensity on a native T1-weighted sequence, highly suggestive of a status post hemorrhage. In addition, several thin septations with faint enhancement of contrast material were seen. The differential diagnosis included hemorrhagic pseudocyst or hemorrhagic cystic neoplasia. Although part of the increase in cyst size might have been due to hemorrhage, the appearance of septations with contrast enhancement (that were not visible on the first MRI), suggests that the increase was also due to growth of neoplastic and/or mesenchymal cells.

Due to the symptoms and the suspicion of a neoplastic lesion, the interdisciplinary decision was to resect the lesion. An oncological pancreatic left resection with lymphadenectomy and splenectomy was carried out (Figure 2). The postoperative course was uneventful and the patient was discharged on the 8<sup>th</sup> postoperative day. The final histopathological analysis revealed a mucinous cystic neoplasia (MCN) of the pancreas with moderate dysplasia (Figure 3a). There were marked regressive changes with old and fresh hemorrhages, and partially acute, partially chronic inflammatory changes (Figure 3a). Immunohistochemistry revealed co-expression of CK7 and CK20 and focal positivity for MUC5, whereas MUC2 was positive only in goblet cells and MUC1 was completely absent. The stromal compartment displayed positivity for estrogen and progesterone receptors (Figure 3b). The luteinized hormone receptor (LHR) was present both in the epithelial cells and in the stromal component (Figure 3c), whereas no expression of the prolactin receptor was found.

### DISCUSSION

MCN is a cystic neoplasm of the pancreas that is characterized by the presence of a dense, ovarian-like

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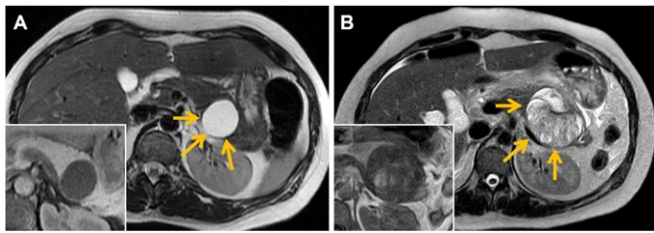
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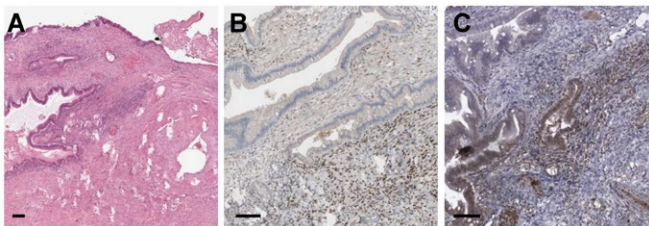
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**Figure 1.** MRI scan showing the cystic lesion in the (a.) pancreatic tail at presentation and (b.) three years earlier.



**Figure 2.** Resected specimen; scale 1cm



**Figure 3.** Histopathology of the tumor, (a.) hematoxylin-eosin staining, (b.) progesterone receptor staining, (c.) luteinized hormone receptor staining; scale 100 µm

stroma and its almost exclusive occurrence in the body-tail of the organ in women aged 40-60 years. The risk for invasive cancer is less than 15% in small lesions without mural nodules but increases with size and the presence of these nodules [1]. Irrespective, current guidelines recommend surgical resection for all fit patients, since the individual risk of progression to invasive cancer is not predictable [1]. The exclusive occurrence in women and the expression of estrogen and progesterone receptors in the stromal compartment of MCN is a peculiar observation. It has been speculated that during development primitive ovarian cells/yolk sac cells are incorporated into the developing pancreas (when the dorsal pancreatic anlage is close to the left primordial gonad) [2]. Alternatively, it has been suggested that the ovarian stroma, which is similar to the stroma in the fetal pancreas, is induced by the neoplastic epithelial cells of the lesion [3].

Irrespective of the etiology, the expression of sex hormone receptors in the stroma of MCN suggests that this tumor could respond to hormonal changes. Not surprisingly, there have been several reports of MCN diagnosed and/

or becoming symptomatic during pregnancy including benign MCN and invasive carcinomas associate with MCN (to the best of our knowledge 15 cases) [4-18].

As in our case and in other described cases [7, 12], the sometimes rapid growth during pregnancy suggests a possible relationship to female sex hormones. How sex hormones influence MCN growth and development is currently not known. Specifically, it is not clear whether high levels of estrogen and progesterone during pregnancy induce proliferation of the stromal compartment, or result in changes in the stromal cells that indirectly stimulate the growth of the neoplastic epithelial cells. Further, it is also not known whether these hormonal changes increase the rate of transformation of a benign tumor into a malignant one.

Not only do estrogen and progesterone levels change during pregnancy, striking changes also occur in prolactin and chorionic gonadotropin (hCG) levels. Here we show that the LH receptor, which also binds hCG, is expressed in the epithelial and the stromal compartments of MCN, whereas no expression of the prolactin receptor was detected. However, whether this is a common observation for MCN and how hormonal changes during pregnancy effect the neoplastic and/or stromal compartment of MCN is currently not known.

In conclusion, cystic lesions of the pancreas detected before or during pregnancy require special attention. A thorough diagnostic work-up should rule out MCN or other premalignant/malignant cystic lesions. In case of detection during pregnancy, timing of resection has to be individualized depending on symptoms and size of the lesion.

### Conflicting Interest

The authors had no conflicts of interest.

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