



## Case Report

### **Inflammatory myofibroblastic tumor causes formation of an ileal conglomerate in a patient previously treated for Wilms' tumor [version 2; referees: 1 not approved]**

Leganger, Julie; Soerensen, Rikke Raagaard; Rosenberg, Jacob; Burcharth, Jakob

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CASE REPORT

**REVISED** Case Report: Inflammatory myofibroblastic tumor causes formation of an ileal conglomerate in a patient previously treated for Wilms' tumor [version 2; referees: 1 not approved]

Julie Leganger <sup>1</sup>, Rikke Raagaard Soerensen<sup>2</sup>, Jacob Rosenberg<sup>1</sup>, Jakob Burcharth<sup>3</sup>

<sup>1</sup>Center for Perioperative Optimization, Department of Surgery D-113, Herlev Hospital, University of Copenhagen, Herlev, Copenhagen, Denmark

<sup>2</sup>Department of Pathology, Herlev Hospital, University of Copenhagen, Herlev, Copenhagen, Denmark

<sup>3</sup>Department of Surgery, Zealand University Hospital, University of Copenhagen, Copenhagen, Denmark

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**Abstract**

Introduction: Inflammatory myofibroblastic tumors (IMTs) are uncommon mesenchymal lesions classified by WHO as neoplasms of uncertain behavior. Morphologically, IMTs are composed of proliferating spindled myofibroblastic cells accompanied by a marked - usually chronic - inflammatory infiltrate. The etiology is unknown, but several theories have been suggested, including an association with Wilms' tumor. IMTs are rarely diagnosed in adults and have been reported in various organs. IMTs are considered benign but with a potential to recur at their primary site.

Case report: A 44-year-old female experienced intermittent severe abdominal pain, loose stools and a visible abdominal bulge. In early childhood the patient had been treated for a Wilms' tumor. At admission Meckel's diverticulitis was suspected, but during surgery a tumor in the terminal ileum, creating a conglomerate of small intestinal loops, was observed and completely resected. The pathology report characterized the tumor as a histologically benign inflammatory myofibroblastic tumor. Postoperatively, the patient experienced several complications including an anastomotic leakage and subsequent formation of an abscess and transcutaneous fistula.

Discussion: IMTs rarely arise in the small intestine, and to our knowledge the manifestation of a small intestine conglomerate has not been described previously. Making the diagnosis is difficult, and numerous differential diagnoses were possible in this case. Approximately 8-25% of IMTs in the gastrointestinal tract recur locally. Complete surgical resection is the treatment of choice, and re-excision is the preferred therapy for local recurrence. To our knowledge, no guidelines concerning follow-ups are available.

Conclusion: IMTs in the terminal ileum can mimic Meckel's diverticulitis and present with symptoms of obstructive ileus due to the formation of a conglomerate of small intestinal loops. Furthermore, IMTs should be considered as a diagnostic possibility in patients with a past medical history of Wilms' tumor.

**Open Peer Review**

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	1	2
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- 1 **Jiaqi Shi** , University of Michigan, USA
- 2 **Jasmine Kamboj**, Sanford Health, USA  
**Komal Arora**, UHS Hospital, USA

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**Corresponding author:** Julie Leganger ([julieleganger@gmail.com](mailto:julieleganger@gmail.com))

**Author roles:** **Leganger J:** Conceptualization, Methodology, Resources, Visualization, Writing – Original Draft Preparation; **Raagaard Soerensen R:** Conceptualization, Resources, Visualization, Writing – Original Draft Preparation; **Rosenberg J:** Conceptualization, Methodology, Supervision, Writing – Original Draft Preparation; **Burcharth J:** Conceptualization, Methodology, Supervision, Writing – Original Draft Preparation

**Competing interests:** No competing interests were disclosed.

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**REVISED Amendments from Version 1**

The author information of Rikke Raagaard Soerensen is changed to Department of Pathology, Herlev Hospital, University of Copenhagen, Herlev, Copenhagen, Denmark instead of Department of Pathology, Hvidovre Hospital, University of Copenhagen, Hvidovre, Copenhagen, Denmark. Rikke Raagaard Soerensen was during this work employed at Herlev Hospital.

See referee reports

**Introduction**

Inflammatory myofibroblastic tumors (IMTs) are rare mesenchymal neoplasms composed of proliferating myofibroblastic spindle cells, and an accompanying inflammatory - usually chronic - infiltrate<sup>1</sup>. The etiology of IMTs is unknown, but an association with Wilms' tumor, the most common primary renal malignancy in children, has been suggested<sup>2,3</sup>. Furthermore, theories suggesting a link to infectious agents, tumor associated factors, and cytokines have been proposed<sup>4</sup>. IMTs are most commonly seen in children and young adults<sup>1</sup>. IMTs were initially considered a pulmonary tumor<sup>2</sup>, but the lesions have subsequently been reported in various extrapulmonary organs including the mesentery and gastrointestinal tract<sup>4</sup>.

This report presents a case of an IMT in the terminal ileum in a female adult, treated for Wilms' tumor in childhood. The tumor caused a conglomerate of small bowel and mimicked Meckel's diverticulitis, which to our knowledge has not previously been described. We reported this case according to the CARE guidelines<sup>5</sup>.

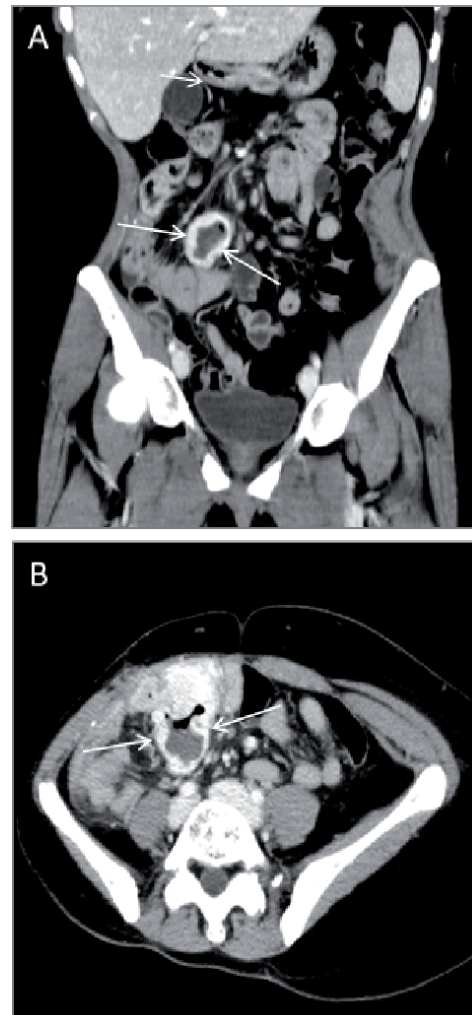
**Case report****Clinical data**

A 44-year-old woman was admitted to the hospital due to intermittent severe abdominal pain, during which a visible bulge appeared in the right lower abdominal quadrant. Furthermore, the patient had experienced loose stools over a two year period. The initial blood tests were inconspicuous, with the exception of a slight neutrophilia. The past medical history included treatment for a Wilms' tumor at the age of one with a right-sided nephrectomy and subsequent radiochemotherapy.

Ileus was initially suspected, and an abdominal CT scan was performed, showing a 3 × 5 × 4 cm mass in the small intestine. The imaging report described, that the lesion was composed of a solid and a necrotic portion plus an air-filled space (Figure 1), which lead to the tentative diagnosis of an underlying Meckel's diverticulitis. A diagnostic laparoscopy was initiated, but converted to an open ileocecal resection with a primary anastomosis, as a tumor in the terminal ileum was discovered. There was no sign of intestinal perforation.

**Histopathologic findings**

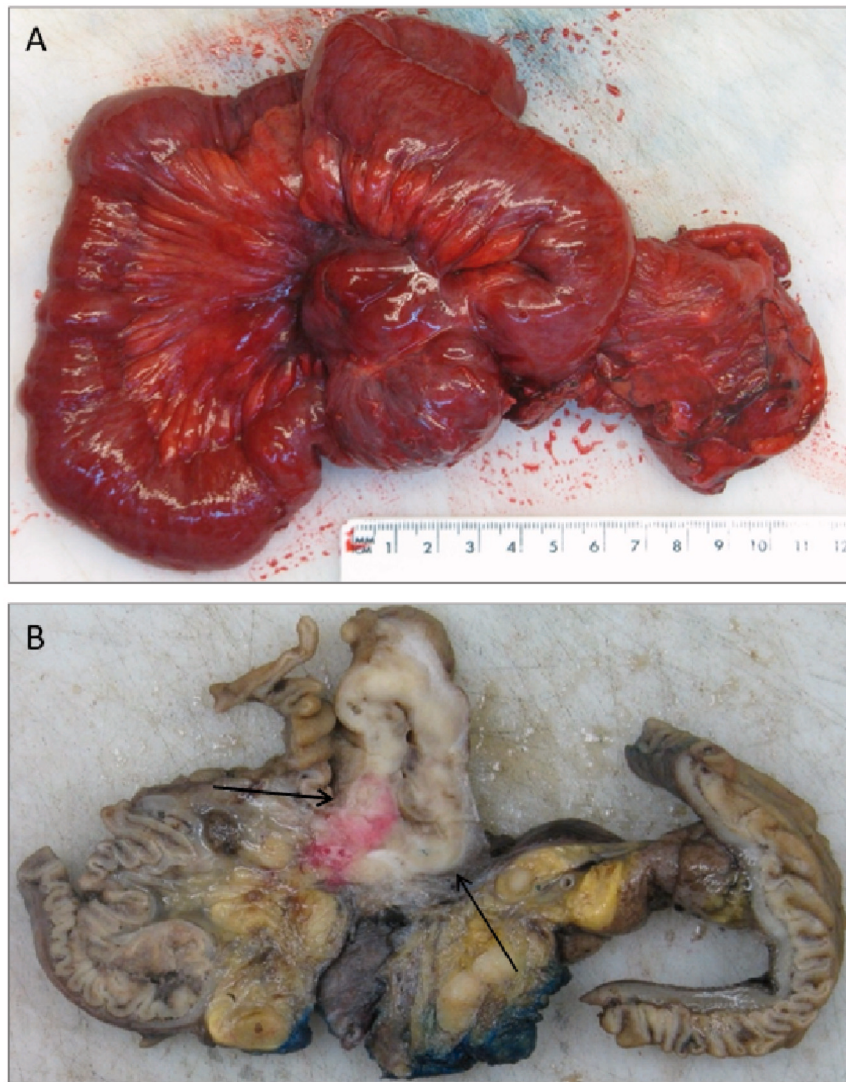
Grossly, the specimen consisted of a cecal pole that included the appendix and the distal 40 cm of the terminal ileum bound



**Figure 1. Abdominal CT performed pre-operatively.** Coronal (A) and horizontal (B) planes of the abdominal CT scan performed pre-operatively revealed a mass in relation to the small bowel (indicated by arrows).

together in a conglomerate (Figure 2). 10 cm from the proximal resection margin a diverticulum-like pouch arising from the ileal wall was identified. The lesion contained a solid tumor of firm consistency, that measured 3 (depth) × 5 (width) cm. The cut surface of the tumor elicited heterogeneity with white/grayish areas and focal haemorrhage. The tumor was totally embedded.

Microscopy revealed a mesenchymal tumor infiltrating the ileal wall, the submucosa and adjacent mesentery. No true diverticulum was found. The tumor was composed of a dense proliferation of spindle-shaped cells primarily arranged in a fascicular growth pattern, focally also exhibiting a storiform architecture, admixed with a marked chronic inflammatory infiltrate and discrete areas of neutrophilic granulocytes (Figure 3). Immunohistochemically, the tumor cells were positive for actin, vimentin, desmin,



**Figure 2.** The gross appearance of the tumor before (A) and after (B) formalin fixation. The tumor (indicated by arrows) infiltrated the wall of the small intestine and the adjacent mesoileum (B), creating a conglomerate of dilated small bowel (A).

and h-caldesmon, focally positive for factor 13A and CD68, and had a negative reaction for ALK1, CD34, CD117, DOG1, S100, AE1/AE3, CK18, CK7, CK19, beta-catenin and MDM2. Ki-67 staining showed a low proliferative rate. Although h-caldesmon reactivity was considered atypical for the tumor, the pathology report characterized the tumor as an IMT based on morphology and additional staining properties.

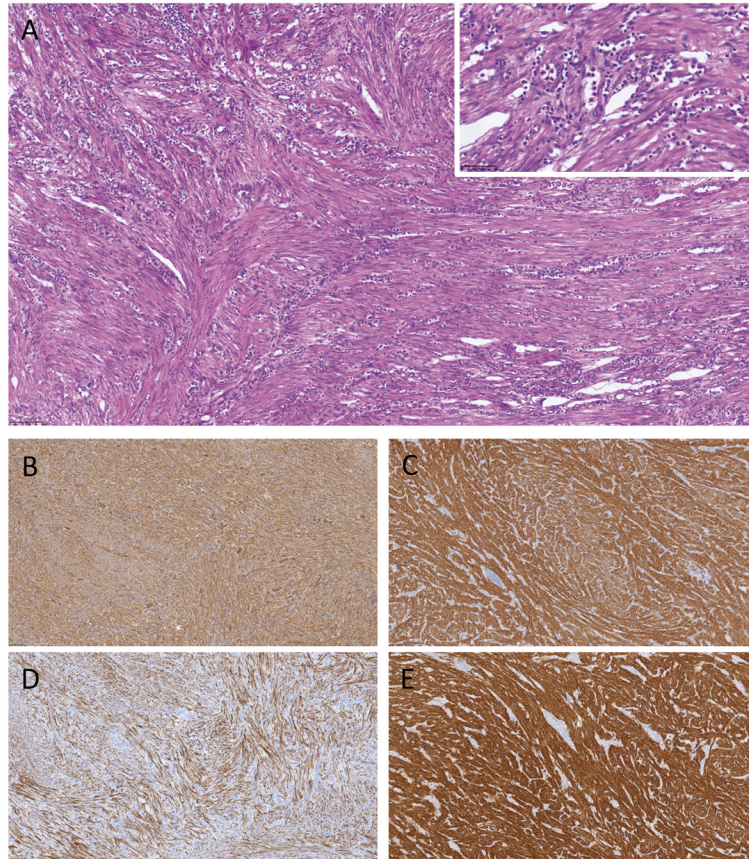
#### Postoperative care and follow-up

Postoperatively, the patient suffered several complications including an intraabdominal abscess caused by a small anastomotic leakage. Subsequent percutaneous drainage of the abscess led to a phlegmone involving the abdominal wall, complicated by the development of a transcutaneous fistula with connection

to the peritoneum. Six months after surgery the patient was still having symptoms from the transcutaneous fistula but was otherwise well. She was advised to have a control abdominal magnetic resonance imaging (MRI) after one year.

#### Discussion

We reported a case of an adult female patient presenting with an IMT in the terminal ileum causing a conglomerate of small intestinal loops leading to obstructive ileus. A previous study has reported that only 1.2% of IMTs arise from the small intestine<sup>3</sup>. It has been described that IMTs in the small bowel can cause intestinal obstruction due to intussusception<sup>1</sup>. However, in our case a conglomerate of small bowel was the cause of ileus, which to our knowledge has not been presented previously in the literature. In



**Figure 3. Histopathology of the tumor.** The tumor mass was built from bundles of spindled myofibroblastic cells with a low proliferative rate arranged in a crossing manner, accompanied by a pronounced lymphocytic infiltrate. Focally, infiltration with polynuclear granulocytes was observed (A, shown in the insert). Immunohistochemically, the tumor cells were positive for vimentin (B), actin (C), desmin (D) and h-caldesmon (E).

general, patients suffering from IMTs may clinically present with an abdominal mass or non-specific symptoms including abdominal pain<sup>6</sup>. In approximately 15–30% of cases the patients present with a constitutional syndrome of fever, weight loss, malaise and a variety of laboratory abnormalities such as anemia, thrombocytosis, leukocytosis, polyclonal hyperglobulinemia, or elevated erythrocyte sedimentation rate<sup>3</sup>. In this case the subject only presented with a few of these features.

Macroscopically, IMTs in the gastrointestinal tract are most often characterized as solid, sessile, and solitary lesions, although cases with multiple lesions have been described<sup>4</sup>. In this case the tumor mimicked a diverticulum and based on the clinical presentation, numerous differential diagnoses were possible including Meckel's diverticulitis. The histological differential diagnoses of IMTs depend on the dominant basic histological patterns, which involve the extent of proliferation and sclerosing, and the extent to which the IMT is fibromyxoid/vascular<sup>3</sup>. It is important to distinguish IMTs from other lesions in the family of inflammatory pseudotumors, as well as from non-neoplastic fibrosclerosing processes and malignant neoplasms with a prominent inflammatory infiltrate, e.g. fibromatosis, sarcoma,

gastrointestinal stromal tumor, and mesenteric panniculitis<sup>6</sup>. Immunohistochemically, the spindle cells in consideration in the diagnostic process of IMT are presented in Table 1. The tumor is reactive to antibodies directed against vimentin, smooth muscle actin, and muscle specific actin in the majority of cases. Anaplastic lymphoma kinase expression is detected in approximately 50% of cases<sup>2,4,6</sup>. The frequency of this finding decreases with age.

A possible association with Wilms' tumor has previously been suggested and different theories have been proposed. One theory is a shared genetic predisposition; another theory is that the treatment of Wilms' tumor involving radiation and chemotherapy may damage the tissue and predispose the patient to development of IMTs. Notable that the latency time in this case is remarkable longer from the other reported cases<sup>2</sup>. The IMTs were at first considered a postinflammatory condition but is now acknowledge as a distinct neoplasm based on clonal rearrangements involving chromosome 2p<sup>6</sup>. The IMTs have been classified by WHO as a neoplasm of uncertain behavior<sup>2</sup>. The tumors are widely acknowledged as benign but with a potential to recur at the primary site. Approximately 8–25% recurs locally<sup>1,4</sup>. Rare examples

**Table 1. Clinical and pathological features characteristic for inflammatory myofibroblastic tumors (IMTs).** Adapted from 6, to consider in the diagnostic process of IMT.

Features that favour IMT diagnosis	Features that discourage IMT diagnosis
<ul style="list-style-type: none"> <li>• Child or young adult</li> <li>• Mass in lung or soft tissue of abdomen, pelvis, or retroperitoneum</li> <li>• Diffuse inflammatory infiltrate with prominent plasma cells</li> <li>• Mild nuclear atypia including scattered ganglion-like cells</li> <li>• Low mitotic rate without atypical forms</li> <li>• Anaplastic lymphoma kinase positivity by immunohistochemistry or anaplastic lymphoma kinase gene</li> <li>• Wilms' tumor</li> </ul>	<ul style="list-style-type: none"> <li>• Middle-aged or older adult</li> <li>• Mass in skin or subcutis, lymph node, spleen, or bladder</li> <li>• Patchy, predominantly lymphocytic inflammatory infiltrate</li> <li>• Moderate to severe nuclear atypia with hyperchromasia</li> <li>• Atypical mitoses</li> <li>• Necrosis</li> </ul>

are described with tumors undergoing malignant transformation<sup>2</sup> and/or with metastasis<sup>4</sup>. Several studies have attempted to find predictors of aggressive behavior in IMTs without success<sup>6</sup>. However, it has been suggested that IMTs with a proliferating pattern, a multinodular presentation, or a manifest myofibroblastic or fibroblastic phenotype are more likely to recur<sup>4</sup>. Furthermore, IMTs arising in the gastrointestinal tract are more likely to recur compared with similar tumors arising elsewhere<sup>7</sup>. Anaplastic lymphoma kinase expression is associated with a lower risk of metastasis<sup>6,7</sup>. Complete surgical resection is the treatment of choice, and re-excision is the preferred therapy for local recurrence<sup>7</sup>. To our knowledge no guideline on IMT follow-up is available.

## Conclusion

An IMT in the terminal ileum can mimic Meckel's diverticulitis and the clinical manifestations can include intestinal obstruction due to the formation of a conglomerate of small intestinal loops. Furthermore, IMTs should be considered as a diagnostic possibility in patients with a past medical history of Wilms' tumor<sup>2</sup>.

## Consent

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

## Author contributions

JR contributed to the conception of the article. JL, RSS, JR, and JB contributed to the design of the work. JL contributed to the acquisition of data and prepared the first draft of the manuscript. RSS provided expertise in pathology and acquisition of clinical photographs. JL, RSS, JR, and JB were involved in the revision of the draft manuscript and have agreed to the final content.

## Competing interests

No competing interests were disclosed.

## Grant information

The author(s) declared that no grants were involved in supporting this work.

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# Open Peer Review

Current Referee Status: 

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## Version 2

Referee Report 08 January 2018

doi:10.5256/f1000research.13499.r29440



**Jasmine Kamboj**<sup>1</sup>, **Komal Arora**<sup>2</sup>

<sup>1</sup> Sanford Health, Bemidji, MI, USA

<sup>2</sup> Anatomic and Clinical Pathologist, UHS Hospital, Johnson City, NY, USA

Doubt the diagnosis of IMT in absence of Alk positivity and positivity for h-caldesmon. Otherwise the case report is well written. Authors should consider an alternate diagnosis of a smooth muscle neoplasm also. The discussion section lacks detailed description of the differential diagnosis. Other spindle cell tumors should also be excluded by describing their histologic and immunohistochemical features.

**Is the background of the case's history and progression described in sufficient detail?**

Yes

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Partly

**Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?**

Partly

**Is the case presented with sufficient detail to be useful for other practitioners?**

Partly

**Competing Interests:** No competing interests were disclosed.

**We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.**

Referee Report 26 September 2017

doi:10.5256/f1000research.13499.r26317



**Jiaqi Shi** 

Department of Pathology, University of Michigan, Ann Arbor, MI, USA



This case report described a presumable rare inflammatory myofibroblastic tumor (IMT) in the terminal ileum leading to an ileal conglomerate in a patient previously treated for Wilms' tumor. Overall the case was well-presented with adequate discussion. However, the diagnosis of the tumor and the conclusion are not supported by the histology or immunohistochemical staining pattern, and therefore further studies are necessary in order to reach a definitive diagnosis. Detailed comments are listed below:

1. The findings are not diagnostic of IMT in this case based on the morphology of the tumor, lack of ALK1 expression, and diffuse h-caldesmon staining which is more typical for a smooth muscle tumor such as a leiomyoma or leiomyosarcoma. The rich lymphocytic infiltrate also raised the possibility of an EBV-associated smooth muscle tumor if the patient is immunocompromised. An EBER in-situ hybridization would be helpful to further evaluate for this possibility.
2. Again, the diffuse and strong h-caldesmon staining of this tumor is very unusual for IMT, and is not supportive of this diagnosis. All of the reported h-caldesmon positive IMT cases have only focal positivity. In my opinion, a FISH analysis for ALK1 translocation is necessary to reach the diagnosis of IMT in this case.
3. In Figure 1A, there are 3 arrows and it is not clear what one of the arrows is pointing to. Please clarify.
4. In Figure 2A, please add an arrow to indicate the mass. For both A and B, please modify the background so that it is a solid color without blood or other materials.
5. Please provide a 3 dimensional measurement of the tumor in gross description.
6. More discussion on the differential diagnosis of IMT based on histology and immunohistochemical profile is recommended.

**Is the background of the case's history and progression described in sufficient detail?**

Yes

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Partly

**Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?**

Partly

**Is the case presented with sufficient detail to be useful for other practitioners?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Referee Expertise:** Gastrointestinal, hepatobiliary, pancreatic pathology

**I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.**

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