

# A Case of Tubular Carcinoid of the Appendix: A Rare Entity

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## ABSTRACT

Carcinoid tumours of the appendix are low-grade neoplasms with neuroendocrine differentiation. They are typically found incidentally during appendectomies. Tubular carcinoid is an extremely rare, distinct, and benign form of appendiceal carcinoid. Here, the authors present the case of a 32-year-old male who presented with an abdominal mass and pain radiating to the right iliac fossa. Appendectomy was performed, and the gross examination revealed a congested and exudate-covered appendix. Microscopic analysis showed small tubules infiltrating the appendix wall, along with evidence of acute appendicitis. Differential diagnoses considered included carcinoid tumour with glandular differentiation and metastatic adenocarcinoma. Additional sections were examined, and a final diagnosis of tubular carcinoid was made after conducting a panel of immunohistochemical markers and Alcian blue stain. Since most tubular carcinoids are not identifiable on gross, microscopic assessment and serial sectioning play a crucial role in diagnosing this condition.

## CASE REPORT

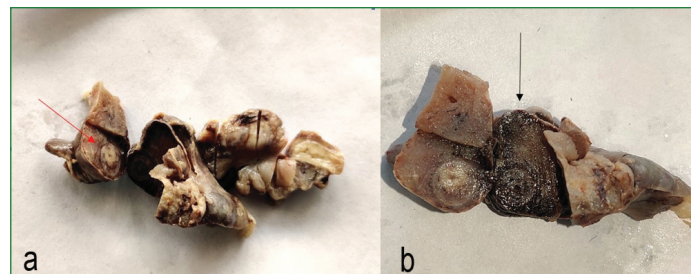
A 32-year-old male presented with dull, constant pain in the central abdomen radiating to the right iliac fossa and diarrhea for two weeks. He had taken luminal antibiotics and antiamebic treatment along with analgesics for symptomatic relief. As he did not recover, he sought emergency medical attention. Upon examination, a firm, non-tender mass measuring 5×4 cm was identified in the right iliac fossa. Contrast-Enhanced Computed Tomography (CECT) revealed a swollen appendix with adhered omentum due to a sealed appendicular perforation, along with a minimal collection in the surrounding area. A provisional diagnosis of an inflamed appendicular mass was made, and he underwent surgery. Intraoperatively, a sealed appendicular perforation with adhered omentum was found, along with a pus pocket containing approximately 250 mL of pus. Appendectomy and adhesiolysis of the adhered omentum were performed, revealing a necrotic appendix with a healthy base.

On gross examination, the appendix measured 6.5 cm in length, was covered with exudate, and appeared congested. On the cut section, the lumen was visible, and a few haemorrhagic areas were observed in the appendiceal wall [Table/Fig-1]. Microscopic examination revealed multiple tiny widely separated tubules dispersed in the muscularis propria of the appendix, involving less than half of the circumference. These tubules were lined by cuboidal cells with uniform round basal nuclei, eosinophilic cytoplasm, and scant luminal mucin. The tubules appeared retracted from the stroma [Table/Fig-2]. The tubules exhibited a low mitotic index ( $\leq 2$  mitoses/10 hpf), and no nuclear atypia was observed. Congested blood vessels and an inflammatory infiltrate rich in neutrophils were also identified transmurally and in the periappendiceal area. The appendiceal mucosa appeared histologically unremarkable. Serial sectioning of the appendix revealed that the tumour measured 6 mm in greatest dimension under the microscope and was located 2.4 cm away from the base of the appendix, which was free of tumour. Differential diagnoses of carcinoid tumour with glandular differentiation and metastatic adenocarcinoma were considered.

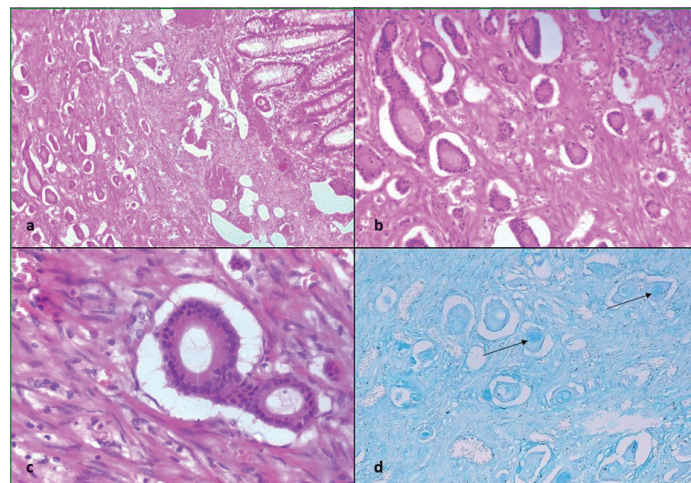
A panel of immunohistochemical markers (synaptophysin, chromogranin, Ki-67, and pan-cytokeratin) and Alcian blue staining were performed to confirm the diagnosis. Alcian blue staining

**Keywords:** Alcian blue, Appendicitis, Right iliac fossa

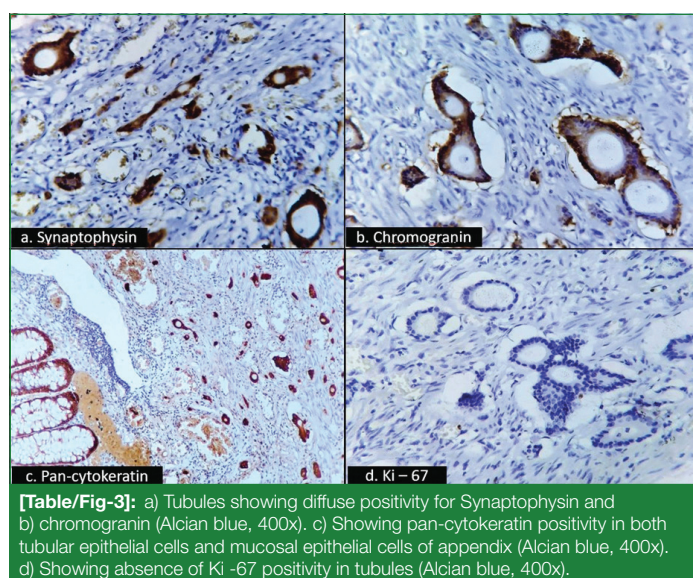
showed positivity in the luminal secretions of the tumour tubules, while the lining cells of these tubules did not take up the stain [Table/Fig-2]. The appendiceal mucosal epithelial cells exhibited positivity for Alcian blue and served as a positive internal control. The tubules in the appendicular wall showed positivity for synaptophysin, chromogranin, and pan-cytokeratin, and Ki-67 expression was  $<2/10$  hpf [Table/Fig-3].



**[Table/Fig-1]:** a) Gross image of the resected appendix. Lumen identified (red arrow); b) Haemorrhagic area noted in the wall (black arrow).



**[Table/Fig-2]:** a) Tubules infiltrating the wall of the appendix with histologically unremarkable appendiceal mucosa (H&E, 100x); b) Tumour tubules displaying retraction from the surrounding smooth muscle and stroma (H&E, 200x); c) Tumour tubules with uniform nuclei, intra-luminal mucin and retraction from the stroma (H&E, 400x); d) Mucin within the tumour tubules staining positive with Alcian blue (arrows). No Alcian blue positivity in the lining cells of the tubules (Alcian Blue, 200x).



Histomorphological findings and ancillary test results favoured the diagnosis of tubular carcinoid with evidence of acute appendicitis and periappendicitis. Up till the writing of the present case report, the patient has been on follow-up for six months and is doing well.

## DISCUSSION

Carcinoids are tumours with neuroendocrine differentiation, accounting for more than 50% of appendiceal neoplasms, and approximately 90% of these tumours are low-grade and confined to the appendix [1-4]. The majority of carcinoids are incidentally discovered during appendectomies performed for acute appendicitis [2]. While most of them occur in the distal portion of the appendix, a small percentage has been reported in other parts [5,6], as in the present case where the tumour was located in the proximal portion.

Tubular carcinoids are a biologically distinct form of appendiceal carcinoids, usually considered benign and proposed to represent L-cell carcinoids [3,5-9]. The size of tubular carcinoids typically ranges between 3-10 mm [6]. In the present case, no tumour was identified grossly, and the estimated size under microscopy was 6 mm [Table/Fig-1]. Tubular carcinoids are composed of tubules lined by cuboidal cells, containing minimal mucin in their lumen, and appearing retracted from the surrounding stroma and smooth muscle [Table/Fig-2]. The luminal mucin stains positive with Periodic Acid Schiff and Alcian blue [5-7,10]. Similarly, in the present case, Alcian blue showed positivity for mucin in the tubular lumina, while the lining cells of the tubules were negative [Table/Fig-2].

Appendiceal carcinoids with glandular differentiation often pose a diagnostic challenge. The differential diagnoses include goblet cell carcinoids, tubular carcinoids, and mixed carcinoid adenocarcinomas [1,4,6,9,10]. It is important to differentiate between these three carcinoids with glandular differentiation and metastatic adenocarcinomas, as tubular carcinoids are benign with an excellent prognosis, and appendectomy alone is sufficient as a treatment modality [9]. However, goblet cell carcinoid is a tumour with uncertain malignant potential and may require hemicolectomy if margins are involved [1]. Additionally, mixed carcinoid adenocarcinoma and metastatic adenocarcinoma have a poor prognosis.

Goblet cell carcinoids, like tubular carcinoids, are often only identified on microscopy. They are typically larger and circumferential compared to tubular carcinoids. Goblet cell carcinoids are characterised by the presence of discrete glands lined by goblet cells, which are separated by smooth muscle or stroma. Unlike

tubular carcinoids, which only have intraluminal mucin, goblet cell carcinoids have both intraluminal mucin and intracytoplasmic mucin in the lining cells [1,4,6,7]. Mucin lakes around the glandular structures may also be observed. Therefore, they exhibit a different pattern of Alcian blue and Periodic Acid Schiff positivity compared to tubular carcinoids. Goblet cell carcinoid was not considered as a differential diagnosis in the present case since the tubules were not lined by goblet cells. Additionally, no intracytoplasmic Alcian blue positivity for mucin was found in the cells lining the tubules [Table/Fig-2].

Mixed carcinoid adenocarcinomas are grossly apparent with involvement of the adjacent bowel. In these cases, the appendix is usually obliterated or fibrotic. Microscopically, these tumours present with areas of endocrine islands along with compressed goblet cell nests infiltrating the submucosa and muscularis propria, resembling a typical carcinoid. The mitotic rate is around 10/10 hpf. They show focal staining with neuroendocrine markers and diffuse positivity with Carcinoembryonic Antigen (CEA) [1]. In the present case, however, there was no bowel involvement peroperatively. Microscopically, the mucosa and submucosa were unremarkable, no endocrine islands were seen, and no mitotic figures were identified. Therefore, mixed carcinoid adenocarcinoma was not considered in the present case.

The possibility of metastatic carcinoma in the present case was ruled out based on the absence of nuclear pleomorphism, absence of mitotic figures, and a Ki-67 index of less than 2% [Table/Fig-3]. Similar findings have been reported by Burke AP et al., [1].

Ancillary tests such as synaptophysin, chromogranin, and pan-cytokeratin immunohistochemistry can also be used to confirm the diagnosis. Synaptophysin and chromogranin positivity have been reported in tubular carcinoids [1,6]. In the present case, the tumour cells showed strong diffuse positivity for synaptophysin, chromogranin, and pan-cytokeratin [Table/Fig-3].

## CONCLUSION(S)

Tubular carcinoid is an extremely rare form of appendiceal carcinoid, usually detected incidentally during microscopy. It is essential to perform thorough sampling of the appendectomy specimen when suspicious foci of tubular carcinoid are identified, to determine the size of the tumour and its extent. Moreover, it is crucial to differentiate this benign entity from morphological mimics due to their relatively aggressive biological behaviour.

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