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JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 6

Heterotopic respiratory mucosa in the rectum: Case report and review of the literature

Marina Cipullo[1]; Rossella D'Onofrio[1]; Mimma Bonomo[1]; Cristiana Laudi[1]; Gianluca Witel[2]; Paola Campisi[3]; Giovanni De Rosa[3]; Anna Sapino[2,4]; Teresa Staiano[1]*

[1]Digestive Endoscopy Unit, Candiolo Cancer Institute, FPO - IRCCS, Str. Prov. 142, km 3.95 – CANDIOLO (TO), Italy.

[2]Department of Pathology, Candiolo Cancer Institute, FPO - IRCCS, Str. Prov. 142, km 3.95 – CANDIOLO (TO), Italy.

[3]Pathology Unit, Mauriziano Hospital, Turin, Italy.

[4]Department of Medical Sciences, University of Torino, Italy.

***Corresponding Author: Teresa Staiano**

Diagnostic and Interventional Digestive Endoscopy, FPO-IRCCS Candiolo Cancer Institute, Str. Provinciale 142 km 3,95 10060 Candiolo (TO), Italy.

Tel: +0119933027; Email: teresa.staiano@ircc.it

Received: Jun 06, 2025

Accepted: Jun 25, 2025

Published: Jul 02, 2025

Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/3661

Abstract

Background: Heterotopic tissue in the gastrointestinal tract is rare, with pancreatic and gastric heterotopia being the most reported types [1]. Heterotopic respiratory mucosa (HRM), particularly in the rectum, is exceedingly rare, with only three cases documented in the literature [2-4].

Case report: We present a case of rectal HRM, observed in a 70-year-old male who underwent colonoscopy for a positive fecal occult blood test (FOBT). Histology confirmed the presence of ectopic respiratory bronchial tissue, with ciliated epithelium and seromucinous glands. Its endoscopic resection led to symptom resolution.

Discussion: Rectal HRM is extremely rare and can be mistaken for other conditions. The pathogenesis of HRM is unclear, although it may result from embryological misdevelopment. The present case adds to the limited literature on HRM.

Conclusion: This case highlights the importance of recognizing HRM in the differential diagnosis of other rectal lesions. Long-term follow-up is essential due to the potential malignant transformation, and further studies are needed.

Keywords: Heterotopic respiratory mucosa; Rectal ectopia; Submucosal lesion.

Introduction

Heterotopia, the presence of histologically normal tissue in an anatomically abnormal location, is an intriguing phenomenon. The gastrointestinal tract is the most frequent site of heterotopic tissue, with gastric and pancreatic heterotopia being the most common forms [1]. While such cases are usually asymptomatic and discovered incidentally, they may occasionally cause symptoms or mimic neoplasms, leading to diagnostic uncertainty [5]. Heterotopic respiratory mucosa (HRM) is a rare subtype, typically identified in the upper gastrointestinal tract, such as the esophagus or stomach. Its presence in the rectum is exceptionally rare, with only three cases described in the literature [2-4]. We here describe a case of HRM, its clinical presentation, histopathological and immunohistochemical findings, and the patient's post-treatment outcome, along with a review of the literature.

Case report

The patient, a 70-year-old male smoker, presented with significant comorbidities, including hypertension, infrarenal abdominal aortic aneurysm, dyslipidemia, Leriche syndrome, and stage IIIb chronic kidney disease secondary to cholesterol embolization-related glomerulosclerosis. Additional medical history included recurrent pleuropericarditis and erectile dysfunction with a vascular component. The patient was receiving aspirin, irbesartan/hydrochlorothiazide, febuxostat, pantoprazole, ezetimibe and vitamin D treatment.

In 2020, following a positive fecal occult blood test (FOBT), he underwent his first colonoscopy. The examination revealed a small ulceration at the ileocecal valve and terminal ileum and a 10 mm submucosal lesion in the proximal rectum, described as roundish, mobile, elastic, and covered by normal-appearing mucosa. Histopathological examination of biopsies reported a rectal cystic lesion lined by ciliated columnar epithelium, consistent with a hamartomatous lesion / tailgut cyst type (Figure 1a, 1b).

The patient was subsequently lost to follow-up, and no further investigations were performed. Several years later, following an episode of acute diarrhea, the patient presented for gastroenterological evaluation. A colonoscopy was recommended and then performed, confirming aphthous ulcers in the terminal ileum and a rectal submucosal lesion of 12 mm which reproduced the same features described in the previous endoscopic examination. The lesion was resected en bloc using a diathermic loop (Figure 2a, 2b).

Histological examination confirmed in the rectal submucosa the presence of ectopic bronchial-type tissue (Figure 1c), as well as seromucinous, PAS positive peribronchial-type glands (Figure 1d). The bronchial ciliated cells were surrounded by a single layer or multiple layers of basal cells (Figure 3a). Immunohistochemical analysis revealed strong positivity for p40 (Figure 3b), consistent with respiratory differentiation, and rare endocrine cells identified by synaptophysin staining (Figure 3c).

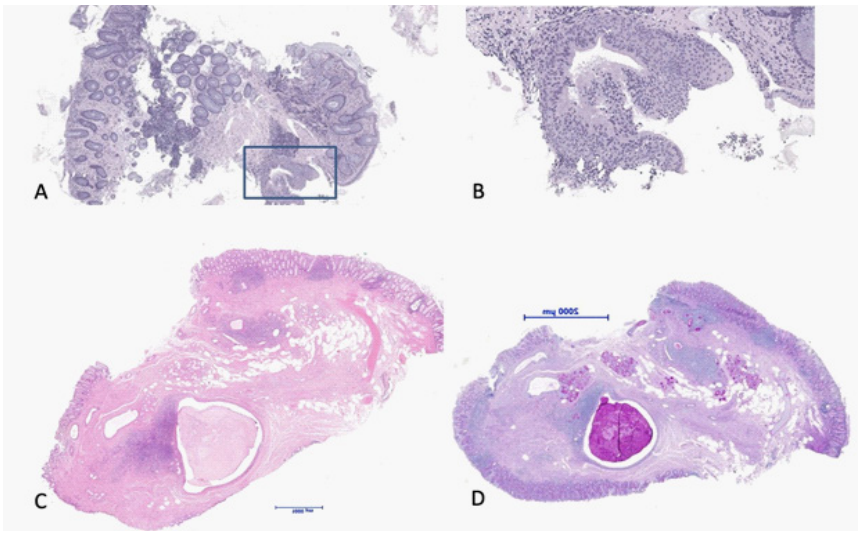

Figure 1: Histopathological findings.
(A,B) First biopsy, hematoxylin and eosin (H&E) staining, showing the cystic structure and the presence of ciliated columnar epithelium.
(C) Second biopsy, H&E staining, demonstrating the characteristic bronchial tissue with seromucinous glands.
(D) Second biopsy, Periodic acid-Schiff (PAS) staining, highlighting seromucinous peribronchial glands with PAS-positive mucin.

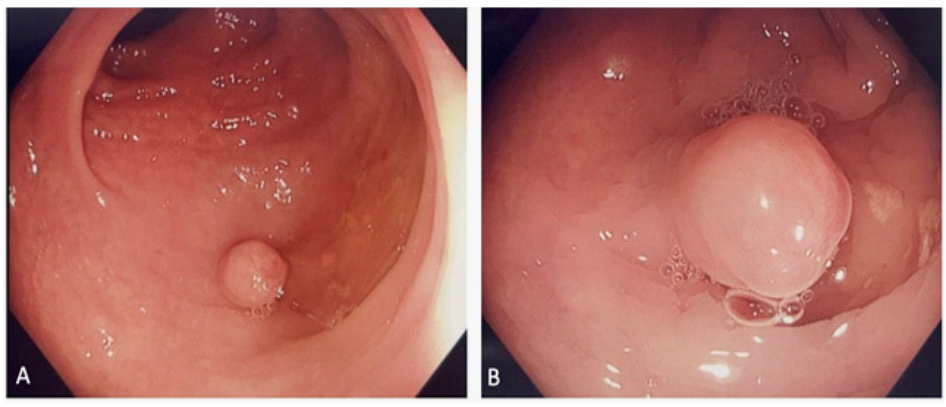

Figure 2: **(A)** Endoscopic findings. **(B)** Endoscopic view of the rectal submucosal lesion.

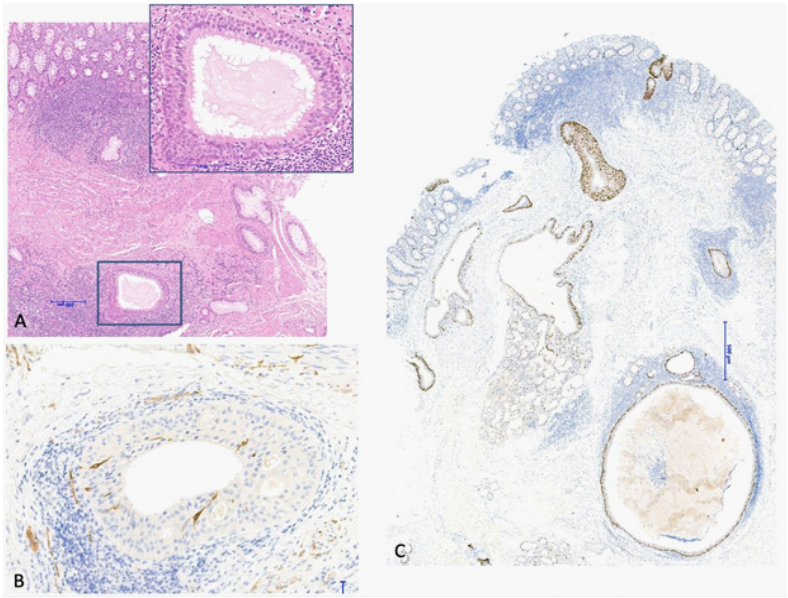

Figure 3: Histopathological findings.
(A) Ciliated bronchial epithelium (inset).
(B) Synaptophysin-positive neuroendocrine cells are scattered between ciliated epithelial cells.
(A) p40 positive cells at the base of the gland structures.

Discussion

Ectopic tissue on the rectum is very rare, with gastric and pancreatic mucosa being the most commonly reported [1]. Rectal ectopy of salivary gland tissue has also been reported together with three cases of respiratory mucosa [6]. The first case of rectal HRM was reported in 2007 by Kawahara et al., who described a submucosal lesion surrounding a rectal mucinous adenocarcinoma in a 43-year-old man. Histological analysis revealed ciliated airway epithelium and seromucinous glands with associated goblet cells, consistent with airway mucosa [2]. A subsequent case, reported in 2014, described a similar lesion in a 38-year-old man who presented with rectal discomfort without tumor lesions. Notably, this case was unique in having only a ciliated bronchial epithelial component, representing the first case of ectopic bronchial epithelium without a seromucinous component in the rectum [3]. Finally, the most recent case, presented in 2019, described a rectal lesion in a 50-year-old male with a history of chronic diarrhea, histologically characterized by pseudostratified ciliated epithelium [4].

In our case, a 70-year-old male patient was incidentally diagnosed with a 10 mm submucosal mass in the rectum during a routine colonoscopy. The lesion was consistent with HRM and showed ciliated columnar epithelium, a hallmark of respiratory mucosa. Following resection, the patient's previous symptoms of acute diarrhoea resolved, highlighting a functional aspect of HRM that may not have been fully appreciated in previous reports. The initial misinterpretation of the lesion as a "tailgut cyst" emphasizes the challenges in diagnosing HRM. Tailgut cysts, a congenital remnant of the embryonic hindgut, can present with similar histological features, including ciliated columnar epithelium, but are localized in the retrorectal or presacral space, with a predominance in females (female to male ratio 5: 1) [7].

Such diagnostic challenges underscore the complexity of the pathogenesis of HRM, which remains largely unknown. It is widely accepted that the occurrence of heterotopic mucosal tissues in the gastrointestinal tract could be related to developmental anomalies during early embryogenesis, but the exact mechanisms are still not fully understood. Indeed, it is known that pluripotent cells in the primitive intestinal tract can differentiate into different epithelial types during embryonic development [8]. However, this theory does not explain ectopic tissues such as salivary glands, which are derived from the oral ectoderm. It has been proposed that salivary gland progenitor cells may migrate aberrantly to the rectum during early embryogenesis, where local stimuli may induce their differentiation. Similarly, a developmental failure mechanism could explain the occurrence of ectopic airway mucosa, although the exact pathophysiology remains unclear [9]. The persistence of tissue that normally regresses or migrates during fetal development has been proposed. Specifically, the gastrointestinal tract and the respiratory system share a common embryological origin, both arising from the endoderm.

During the process of embryonic development, tissues that are destined to form the respiratory tract may, may remain in ectopic locations due to abnormal migration or differentiation. This could result in the presence of respiratory-type mucosa in the gastrointestinal tract, such as in the rectum, as seen in our case. The "foregut heterotopia" hypothesis suggests that ectopic airway mucosa in the rectum may result from incomplete foregut descent or aberrant adhesion of ectodermal cells during early embryogenesis [10]. This explanation may clarify the common histopathological features observed in our case and the three previous Japanese cases. Abnormalities in early development may also contribute to cellular changes that predispose these areas to develop pathological characteristics. Although malignant transformation of ectopic tissues is rare, cases of adenocarcinoma arising from ectopic pancreatic tissue and pyloric adenoma in ectopic gastric mucosa have been documented [11]. This highlights the importance of long-term surveillance of patients with ectopic mucosal lesions, even though malignant transformation is rare.

Finally, our patient also presented with ulcerative lesions in the terminal ileum and at the ileocecal valve during both colonoscopies. These findings were incidental endoscopic discoveries and of non-specific significance on histological evaluation, as the patient had no clinical symptoms, laboratory abnormalities, or fecal markers suggestive of inflammatory bowel disease (IBD). Furthermore, there was no family history of IBD, and the patient has never required treatment for these lesions. To date, there is no evidence in the literature to suggest a correlation between these findings and rectal HRM. Given the rarity of HRM and the limited number of reported cases, it is currently impossible to hypothesize any definitive relationship between these conditions. However, this observation highlights the need for further studies to explore whether such findings represent coincidental occurrences or point to a shared underlying pathophysiological mechanism.

Although HRM is a benign condition, its clinical implications warrant careful consideration. In our case, its resection resulted in symptomatic improvement, notably normalization of bowel habits. Moreover, complete excision eliminates the risk of misdiagnosis during subsequent evaluations and prevents potential complications, including the rare risk of malignant transformation.

Conclusion

This case report documents the occurrence of a rectal HRM, adding to the sparse body of literature on this rare entity. This case emphasizes the need for increased clinical awareness and highlights the necessity of future research to clarify the underlying mechanisms of HRM and to guide the development of effective clinical management strategies. Due to the rarity of this condition and the potential for future complications, including the possibility of malignant transformation, long-term follow-up is essential to ensure optimal management and prevent future risks.

Declarations

Ethical statements: Written informed consent was obtained from the patient for the publication of this case report and accompanying images. The study was conducted in accordance with ethical principles and applicable regulations.

Conflicts of interest: The authors have no conflicts of interest to declare.

Funding:

Italian Ministry of Health: Ricerca Corrente 2025.

FPRC 5x1000 Ministero della Salute 2022 – CARESS.

Author contributions: T.S.: Article conceptualization, methodology, investigation, and writing the original draft; R.D., M.B., M.C.: conceptualization, methodology, investigation, and writing the original draft. G.W., P. C., G. D. R..: investigation, resources, data curation, and visualization; A.S.: conceptualization, data curation, supervision. All authors read and approved the final version of the manuscript.

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