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Citation

Barghi, Ameen, John Grabbe, and Arundhati Ghosh. 2018. "Goblet cell carcinoid of the appendix: Case report of a high grade tumor in a 20-year-old." *International Journal of Surgery Case Reports* 46 (1): 69-73. doi:10.1016/j.ijscr.2018.04.011.
<http://dx.doi.org/10.1016/j.ijscr.2018.04.011>.

Published version

<https://doi.org/10.1016/j.ijscr.2018.04.011>

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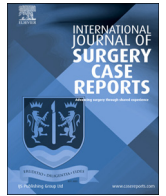
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International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Goblet cell carcinoid of the appendix: Case report of a high grade tumor in a 20-year-old

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ARTICLE INFO

Article history:

Received 17 March 2018
 Received in revised form 10 April 2018
 Accepted 11 April 2018
 Available online 16 April 2018

Keywords:

Goblet cell carcinoid
 Appendix
 Appendectomy
 Pediatric
 Young
 Surgery

ABSTRACT

INTRODUCTION: Goblet cell carcinoid (GCC) is an extraordinarily rare appendiceal tumor that is usually an incidental diagnosis on post-operative histology. It typically presents in the fifth or sixth decade of life. Our patient is the only reported case study of GCC in a pediatric-young adult. Due to its potentially poor prognosis, GCC is surgically treated as an adenocarcinoma, with right hemicolectomy as the mainstay of treatment.

PRESENTATION OF CASE: The patient was a 20-year-old male who presented with a history, physical exam, and work up consistent with acute appendicitis. He underwent an uneventful laparoscopic appendectomy and was diagnosed with a high grade GCC post-operatively.

DISCUSSION: GCC is a rare tumor of the appendix with unique histological features including small rosettes with crescentic nuclei distended with mucin. It is often retroactively diagnosed with histology after a majority of patients present with acute appendicitis symptoms. The behavior of this tumor in pediatric-young adults is very poorly understood.

CONCLUSION: We review the literature for GCC of the appendix and illustrate a case report of a young, otherwise healthy 20-year-old who presented as appendicitis. Although rare, neoplasm must be kept in mind while offering non-operative management for acute appendicitis.

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1. Introduction

Initially described in 1969 by Gagne et al. [1] and later named by Subbuswamy et al. [2] Goblet cell carcinoid (GCC) is a rare primary neoplasm of neuroendocrine origin found in the vermiform appendix. While the molecular aspects of GCC have been described extensively since the 1970s [3], the most-appropriate management is still debatable. GCC shares histologic features with adenocarcinomas and carcinoid tumors, but is distinct from both. GCC is treated like an adenocarcinoma, rather than a carcinoid tumor, with appendectomy for Stage I tumors and right hemicolectomy for higher stages. Most GCCs present in the 5th and 6th decade of life [4]. This case report concerns a 20-year-old, the youngest GCC case report published. We discuss the clinical presentation, the histological findings, and surgical management of a goblet cell carcinoid of the appendix in a young adult. This work is in compliance with SCARE criteria [5].

2. Presentation of case

A 20-year-old male presented to the Emergency Department with a 2-day history of abdominal pain, initially in the periumbilical area subsequently moving to the right lower quadrant. The pain was initially associated with nausea and vomiting. There was no diarrhea, constipation, bloody stools, fevers, or chills. The patient had been diagnosed with mumps two weeks prior and quarantined to his dormitory until two days prior to presentation.

The patient was afebrile, nontoxic in appearance, and with stable vital signs. His abdomen was non-distended, tender to deep palpation in the right lower quadrant, without rebound or guarding. Rovsing's sign was negative. Complete blood count demonstrated a hemoglobin of 14.2, hematocrit of 41.4, white blood cell count of $5.1 \times 10^9/L$ with neutrophil percentage of 30.1%, and platelet count of $133 \times 10^9/L$. Biochemistries and liver function tests were within normal limits. An abdominal/pelvic Computed Tomography (CT) scan with contrast demonstrated a 1.4 cm in diameter appendix with marked mural thickening and mild fat stranding typical of acute appendicitis (Fig. 1). The patient underwent a laparoscopic appendectomy. Intraoperative findings were consistent with an inflamed appendix. Postoperative recovery was uncomplicated.

Pathology confirmed acute appendicitis. In addition, a Grade 3, poorly differentiated, goblet cell carcinoid diffusely involved the

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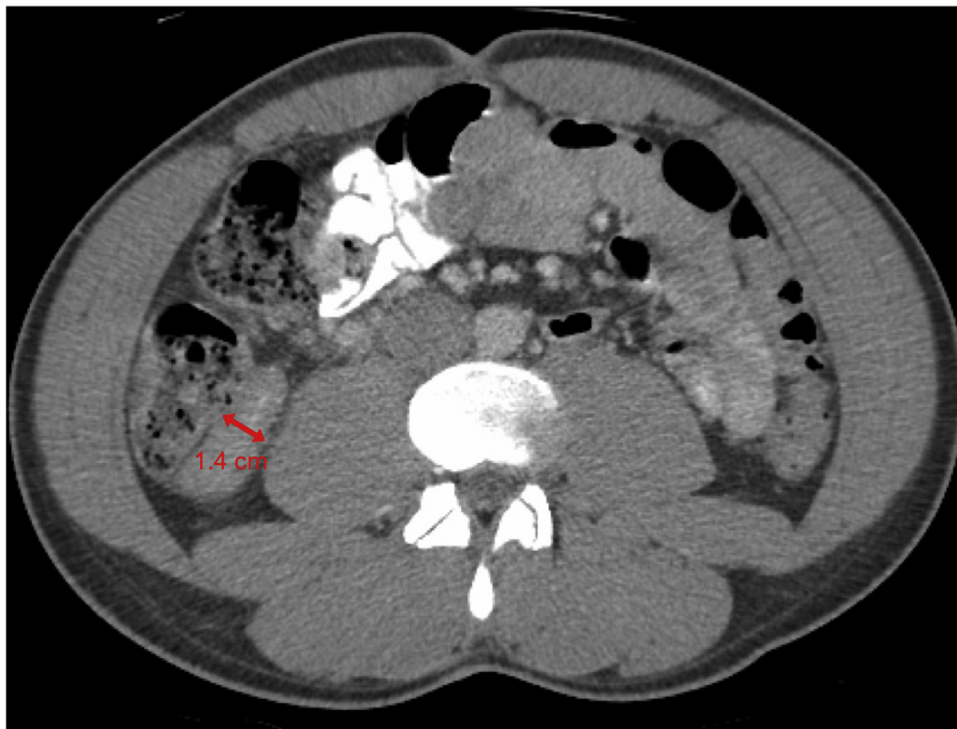


Fig. 1. Abdominal CT performed with oral and IV contrast. Appendix is dilated to 1.4 cm in diameter with marked mural thickening and mild adjacent fat stranding, typical of acute appendicitis.

appendix, from the appendiceal base to 1 cm from the tip (4.5 cm). Tumor invaded the muscularis propria into the subserosa, but did not extend to the serosal surface (pT3NX staging). There was no lymphatic or vascular invasion. Perineural invasion in the periappendiceal fat was present. Regional lymph nodes were not available in the appendectomy specimen.

Immunohistochemically (Figs. 2 and 3), the tumor cells stained positive for CDX-2, synaptophysin, chromogranin and CK20. The tumor was focally positive for CK7. A Ki-67 stain showed a variable proliferative index, ranging from 50% to 80%. The tumor cells also stained positive for mucicarmine. There was no deficiency of mismatch repair proteins tested, as MLH1, MSH2, MSH6, and PMS2 all had preserved expression in tumor cells. These results were compatible with an appendiceal primary, specifically a GCC involving the entire appendix. Patient subsequently underwent right hemicolectomy. Fifty-three lymph nodes were resected and negative for tumor. Colectomy specimen and peritoneal biopsy showed no evidence of malignancy.

3. Discussion

While the incidence of all carcinoid tumors has been rising, GCC of the appendix remains a rare tumor. The age-adjusted annual incidence of all appendiceal tumors is 0.12 cases per 1,000,000 [6]. When classifying epithelial appendiceal tumors, the World Health Organization accepts the term “goblet cell carcinoid” as a form of tumor distinct from both carcinoids and adenocarcinoids (International Classification of Disease, code 8243/3). GCC has peritoneal and lymph node metastatic potential and is treated and staged per American Joint Committee on Cancer, as an adenocarcinoma [7].

In 600 cases reviewed by Pahlavan and Kanthan between 1966 and 2004 the mean age of the patients was 58.89 years [4]. Upon extensive review of the literature, we believe there is no case study documenting GCC in a pediatric-young adult patient. McCusker et al. analyzed the National Cancer Institute’s Surveillance, Epidemiology and End-Results (SEER) program between the years of

1973 and 1998 and documented one 18 year-old in their reported range of the mean age of diagnosis for GCC [6]. We extended that analysis to the years of 1998 and 2014 and identified a total of four patients, all male, ≤ 20 years-old (one 18-year-old, two 19-year-olds, and one 20-year-old). This report is the first case study of a 20-year old with GCC.

Unlike traditional carcinoids that present with focal, apical tumors, GCCs may involve the entire length of the appendix. Acute appendicitis is the most common clinical presentation of GCC [4]. Other presentations include abdominal mass (advanced disease), abdominal pain, and gastrointestinal bleeding. GCCs are most often incidentally diagnosed postoperatively via histology [8].

GCC cells are derived from pluripotent stem cells of intestinal APUD origin with eventual neuroendocrine and mucinous differentiation. The microscopic hallmark of GCC are the small rosettes with crescentic nuclei distended with mucin, as originally described by Subbuswamy [2]. Cells strongly stain positive for mucicarmine, periodic acid-Schiff diastase [9]. Given its crypt cell origin, GCC immunohistochemically stains positive for CDX2, CK20, CK7 [10], NSE, chromogranin A, serotonin, lysozyme, PGP 9.5, IgA and vimentin [11]. The cytoplasmic nature of some neuroendocrine granules results in reactivity for chromogranin A, synaptophysin, Grimelius stain, Fontana-Masson stain, serotonin, substance P, peptide YY, glucagon alpha-chain and S-100 protein [4,12]. Mitotic activity is measured by proliferation index marker Ki-67, which generally serves as prognostic value in pancreatic and gastric neuroendocrine tumors [8,9]. Li et al. reported a Ki-67 greater than 10% in a GCC with a Dukes Stage D (small intestinal metastasis) [13]. Our patient’s Ki-67 index (50%–80%) is potentially poorly prognostic. Microsatellite instability due to loss of expression of mismatch repair proteins MLH1, MSH2, MSH6, and PMS2 is responsible for many gastrointestinal and other carcinomas [14,15]. However, no association has been made with mismatch repair dysfunctionality and neuroendocrine tumors [16]. The molecular pathogenesis of GCC is not understood and only allelic loss of chromosomes 11q, 16q, and 18q have been implicated [17].

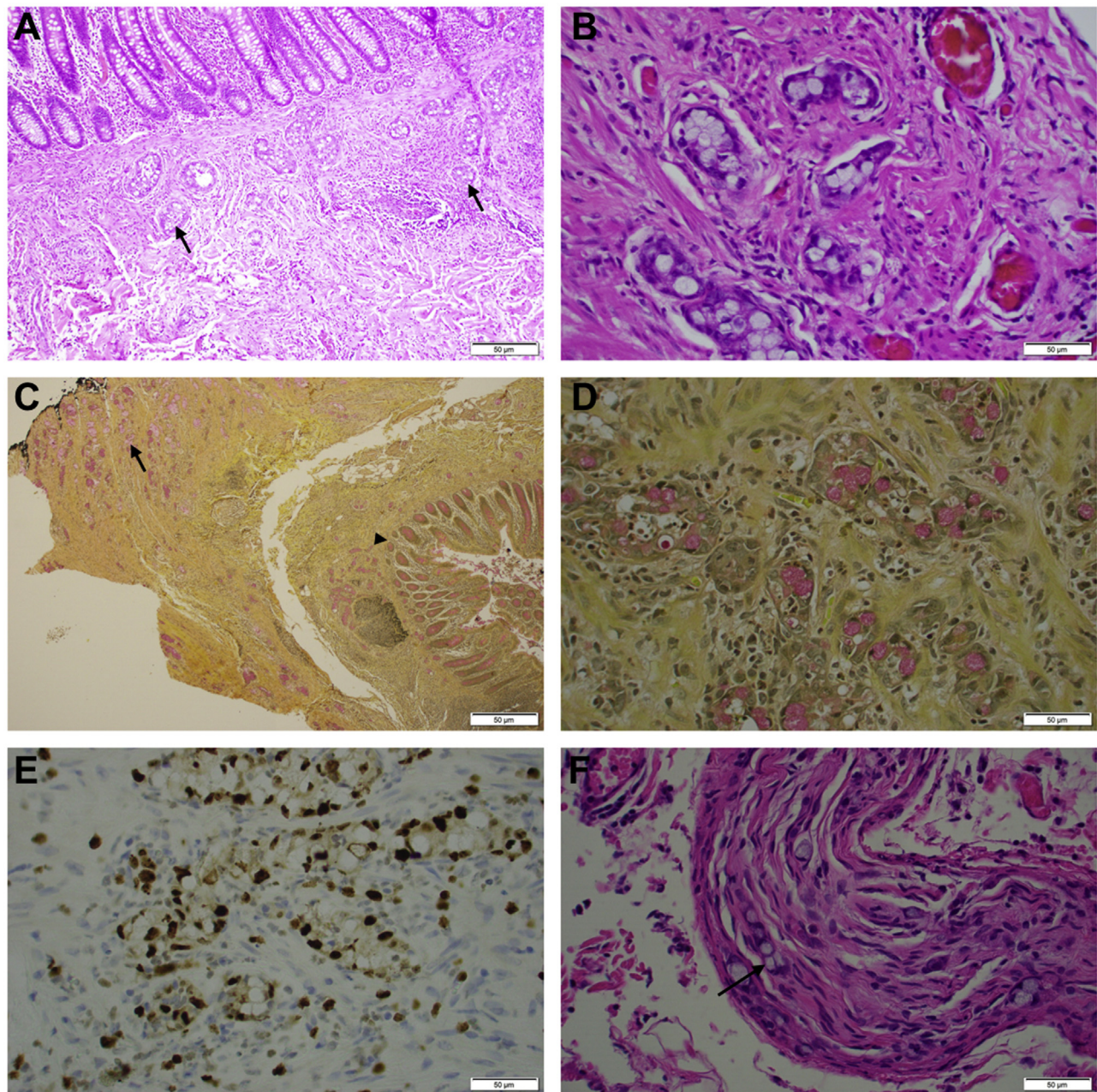


Fig. 2. A: H&E stain highlighting small rosettes (arrows) arranged in clumps, the hallmark of GCC; B: Magnified GCC clusters; C: Mucicarmin stain illustrating extent of GCC infiltration (arrow) into subserosa using basement membrane (arrowhead) as guide; D: Magnified mucicarmin stain displaying mucin distended goblet cells; E: Ki-67 stain with high proliferative index (50–80%); F: Perineural invasion (arrow).

Localized GCC of <1 cm spread, without serosal, mesoappendiceal, or cecal invasion, has a low risk of metastasis and may be managed with appendectomy alone [18]. Diffuse appendiceal involvement, as in our patient, requires right hemicolectomy. Pahlavan and Kanthan present five criteria for advanced surgical management via right hemicolectomy: 1) cellular undifferentiation; 2) increased mitotic activity; 3) involvement of the base of the appendix with caecal wall infiltration; 4) lymph node metastasis; and 5) tumor size greater than 2 cm. Our patient met four of the five criteria.

Metastasis in GCC is between 8 and 50% [19] and most commonly via lymphatics and intraperitoneal invasion, including the ovaries in women. Solid organ metastasis, as to the lungs or liver, is uncommon. The overall five-year survival prognosis for GCC ranges from 40 to 75% but is favorable when disease is appendix lim-

ited [20]. Cytotoxic anti-proliferative adjuvant chemotherapies are similar to those of gastric cancer.

4. Conclusion

GCC of the appendix is an extreme rare tumor that most frequently presents with symptoms of acute appendicitis. Though GCC is typically associated with patients in their fifth or sixth decade of life, we present a case of a 20 year-old, the youngest case report to date. Most GCC of the appendix are low grade and respond well to appendectomy. Our patient had a high grade tumor involving the entire appendix. When offering non-operative management for acute appendicitis, incidental malignancy must be kept in mind, even in young, seemingly health patients as ours.

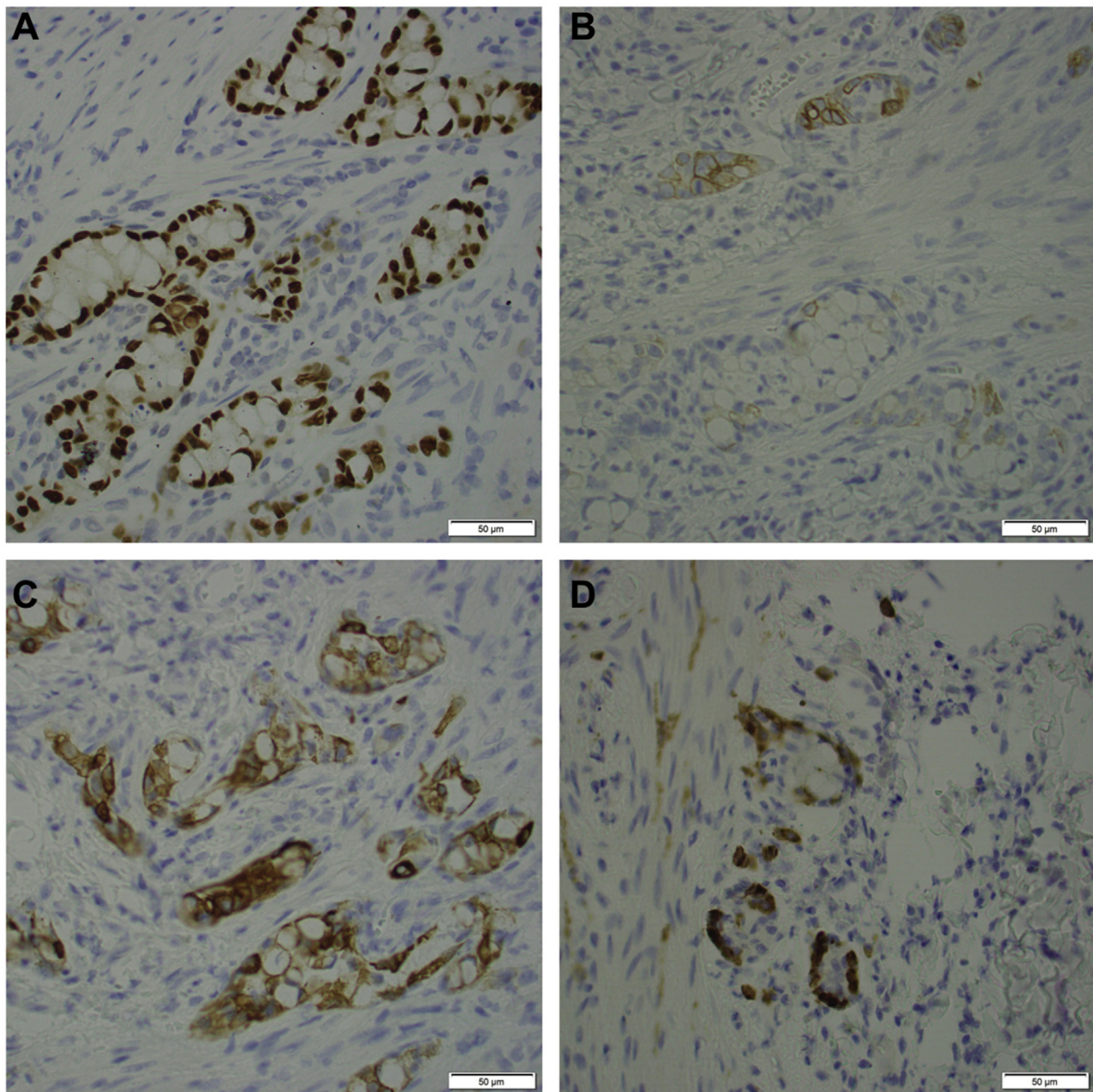


Fig. 3. CDX2 (A), CK7 (B), CK20 (C), and synaptophysin (C) stain indicating crypt cell origin and cytoplasmic characteristic of GCC.

Conflicts of interest

None.

Funding

None.

Ethical approval

This study is exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy

of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ameen Barghi – study concept, design, interpretation, write up.
John Grabbe – study concept, design.
Arundhati Ghosh – study concept, design, interpretation, write up.

Registration of research studies

Case Report

Guarantor

Arundhati Ghosh

References

- [1] F. Gagne, P. Fortin, V. Dufour, C. Delage, Tumors of the appendix associating histologic features of carcinoid and adenocarcinoma, *Ann. Anat. Pathol.* 14 (4) (1969) 393–406 (Paris) <http://europepmc.org/abstract/med/5378353>.
- [2] S. Subbuswamy, N. Gibbs, C. Ross, B. Morson, Goblet cell carcinoid of the appendix, *Cancer* 34 (1974) 338–344.
- [3] P. Roy, R. Chetty, Goblet cell carcinoid tumors of the appendix: an overview, *World J. Gastrointest. Oncol.* 2 (2010) 251.
- [4] P.S. Pahlavan, R. Kanthan, Goblet cell carcinoid of the appendix, *World J. Surg. Oncol.* 3 (2005) 36.
- [5] R.A. Agha, A.J. Fowler, A. Saeta, et al., The SCARE statement: consensus-based surgical case report guidelines, *Int. J. Surg.* 34 (2016) 180–186.
- [6] M.E. McCusker, T.R. Côté, L.X. Clegg, L.H. Sobin, Primary malignant neoplasms of the appendix, *Cancer* 94 (2002) 3307–3312.
- [7] M.B. Amin, S.B. Edge, *AJCC Cancer Staging Manual*, Springer, 2017.
- [8] L.H. Tang, J. Shia, R.A. Soslow, et al., Pathologic classification and clinical behavior of the spectrum of goblet cell carcinoid tumors of the appendix, *Am. J. Surgical Pathology* 32 (2008) 1429–1443.
- [9] R. Kanthan, A. Saxena, S. Kanthan, Goblet cell carcinoids of the appendix: immunophenotype and ultrastructural study, *Arch. Pathol. Lab. Med.* 125 (2001) 386–390.
- [10] S. Van Eeden, G. Offerhaus, A. Hart, et al., Goblet cell carcinoid of the appendix: a specific type of carcinoma, *Histopathology* 51 (2007) 763–773.
- [11] N. Kuroda, S. Mizushima, L. Guo, et al., Goblet cell carcinoid of the appendix: investigation of the expression of β -catenin and E-cadherin, *Pathol. Int.* 51 (2001) 283–287.
- [12] Y. Jiang, H. Long, W. Wang, H. Liu, Y. Tang, X. Zhang, Clinicopathological features and immunoeexpression profiles of goblet cell carcinoid and typical carcinoid of the appendix, *Pathol. Oncol. Res.* 17 (2011) 127–132.
- [13] C.C. Li, M. Hirokawa, Z.R. Qian, B. Xu, T. Sano, Expression of E-cadherin, β -catenin, and Ki-67 in goblet cell carcinoids of the appendix: an immunohistochemical study with clinical correlation, *Endocr. Pathol.* 13 (2002) 47–58.
- [14] C.R. Boland, A. Goel, Microsatellite instability in colorectal cancer, *Gastroenterology* 138 (2010) 2073–2087 (e2073).
- [15] K.B. Geiersbach, W.S. Samowitz, Microsatellite instability and colorectal cancer, *Arch. Pathol. Lab. Med.* 135 (2011) 1269–1277.
- [16] M. Kidd, G. Eick, M.D. Shapiro, R.L. Camp, S.M. Mane, I.M. Modlin, Microsatellite instability and gene mutations in transforming growth factor- β type II receptor are absent in small bowel carcinoid tumors, *Cancer* 103 (2005) 229–236.
- [17] M. Stancu, T.-T. Wu, C. Wallace, P.S. Houlihan, S.R. Hamilton, A. Rashid, Genetic alterations in goblet cell carcinoids of the vermiform appendix and comparison with gastrointestinal carcinoid tumors, *Mod. Pathol.* 16 (2003) 1189–1198.
- [18] T.H. Pham, B. Wolff, S.C. Abraham, E. Drelichman, Surgical and chemotherapy treatment outcomes of goblet cell carcinoid: a tertiary cancer center experience, *Ann. Surg. Oncol.* 13 (2006) 370–376.
- [19] R.L. Warkel, P.H. Cooper, E.B. Helwig, Adenocarcinoid, a mucin-producing carcinoid tumor of the appendix. A study of 39 cases, *Cancer* 42 (1978) 2781–2793.
- [20] S. Shenoy, Goblet cell carcinoids of the appendix: tumor biology, mutations and management strategies, *World J. Gastrointest. Surg.* 8 (2016) 660.

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