



MedPharmRes

Journal of University of Medicine and Pharmacy at Ho Chi Minh City
 homepage: <http://www.medpharmres.vn/> and <http://www.medpharmres.com/>



Case report

Gastric adenocarcinoma mimicking a submucosal tumor- a diagnostic pitfall in the pediatric population: report of two cases

Thu Dang Anh Phan^a, Nhu Thi Quynh Nguyen^b and Quynh Phuong Bui^{a*}

^aDepartment of Pathology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam;

^bDepartment Department of Hemato-Oncology, Children's Hospital 2, Ho Chi Minh City, Vietnam.

Received October 5, 2021; Revised November 15, 2021; Accepted July 12, 2022

Abstract: Introduction: Pediatric gastric adenocarcinoma (GAC) is sporadic with limited relevant data, and gastric adenocarcinoma, which presents as submucosal, has seldom been reported. The clinical presentation and outcome have not yet been thoroughly understood. **Case presentation:** Two boys (10 and 14-year-old) were admitted to the hospital with severe malnutrition. Abdominal CT demonstrated the tumor protruding into the stomach, irregular border, and peritoneal metastasis. Gastric biopsies showed pleomorphic cells, variable size, and increased N/C ratio. These cells were arranged into sheet growth patterns, clusters of cells or incomplete tubules with neutrophils infiltrating. The malignant cells showed strong expression of CK, negativity for CD99, NSE, myogenin, CD3, CD20, ALK, and CD30. Both cases were consistent with poorly differentiated gastric adenocarcinomas, diffuse type with lymphovascular invasion. **Discussion and Conclusion:** Pediatric GAC presented with a more advanced stage and poor differentiation. However, the clinical presentation is similar to adult GAC. Because of data limitations, the diagnosis and treatment of pediatric GAC remain a significant challenge. GAC should be kept in mind, especially when a submucosal tumor-like lesion appears in the stomach. Additional molecular investigations, including E-cadherin or HER2 testing of the tumor samples, may offer more treatment choices for these patients.

Keywords: Gastric Adenocarcinomas; gastric cancer; pediatric; case report; submucosal tumor.

1. INTRODUCTION

Pediatric gastric adenocarcinoma (GAC) is extremely rare and generates 0.05% of all gastrointestinal malignancies, the great majority of which are lymphomas and sarcomas [1,2]. Although children are less frequently affected by gastric adenocarcinoma, GAC is still challenging because of its highly aggressive growth pattern and more advanced stage in the diagnosis [3]. Additionally, adenocarcinoma having characteristics of a submucosal tumor (SMT) is uncommon, accounting for 0.2%-0.62% [4]. As its rarity, carcinogens, clinical features, treatment, prognosis, and prevention remain

questionable, we describe two cases in children with some features similar to GAC in adults.

2. CASE PRESENTATION

2.1. Case 1

A 14-year-old boy presented on 16 July 2021 with complaints of progressive increasing abdominal distension, flat stool, severe malnutrition, and no treatment before. He had lost 4kg in 5 months. His father died 11 months ago because of gastric carcinoma.

*Address correspondence to Quynh Phuong Bui at the Department of Pathology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam. E-mail: phuonquynh0201@gmail.com

The patient was pale. Abdominal distension was attributable to massive ascites rather than hepatosplenomegaly. No cervical, inguinal, or axillary adenopathy was palpable.

Hemoglobin was decreased. Biochemistry analysis study of the ascites showed yellow, 12 cells/mm³, scattered mature lymphoid cells, lacking malignant cells, glucose 6.0mmol/L, protein 33.5g/L.

Abdominal ultrasound demonstrated abundant fluid, diffusely thick gastric wall d#12mm. The upper abdominal peritoneum was infiltrated, focally thickened, had an irregular border, and was surrounded by many large lymph nodes d#20-30mm. Computed tomography of the abdomen revealed a tumor protruding into the stomach with an irregular border associated with peritoneal metastasis and thickened gastrointestinal wall (Fig 1). Upper gastrointestinal endoscopies were performed, and gastric biopsies were taken.

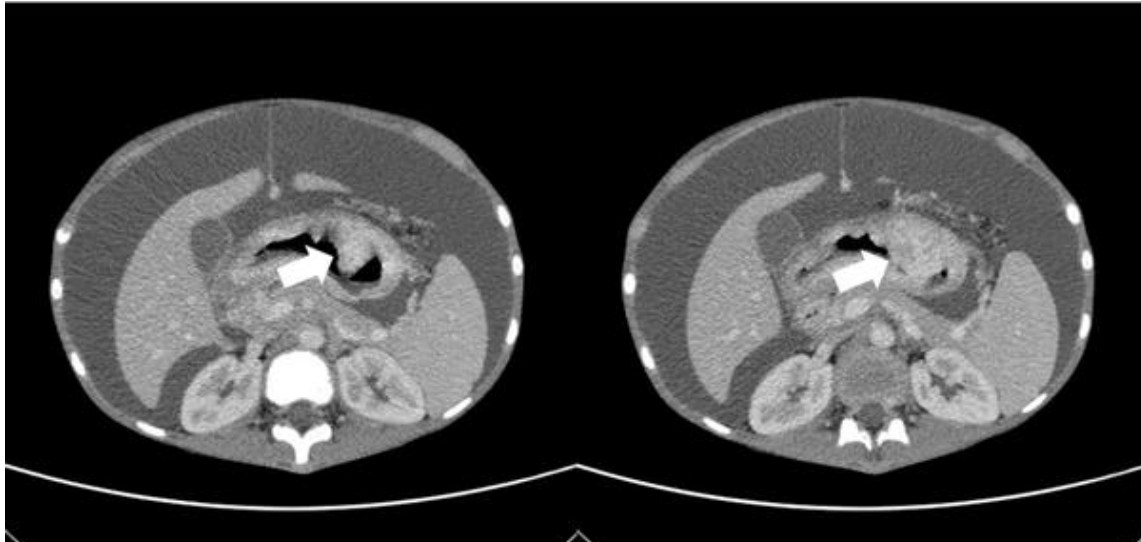


Figure 1. Abdominal CT scan reveals the tumor protruding into the stomach (arrow)

Histopathologic examination of biopsies revealed pleomorphic cells with variable sizes and increased N/C ratio (Fig 2). These cells were arranged into sheet growth patterns, clusters of cells or incomplete tubules with neutrophils infiltrating. The malignant cells showed strong expression of CK (Fig 2), negativity for CD99, NSE, Myogenin, CD3, CD20, ALK, and CD30.

His diagnosis was poorly differentiated gastric adenocarcinoma, a diffuse type.

His treatment information was missing because he had moved to another hospital for treatment.

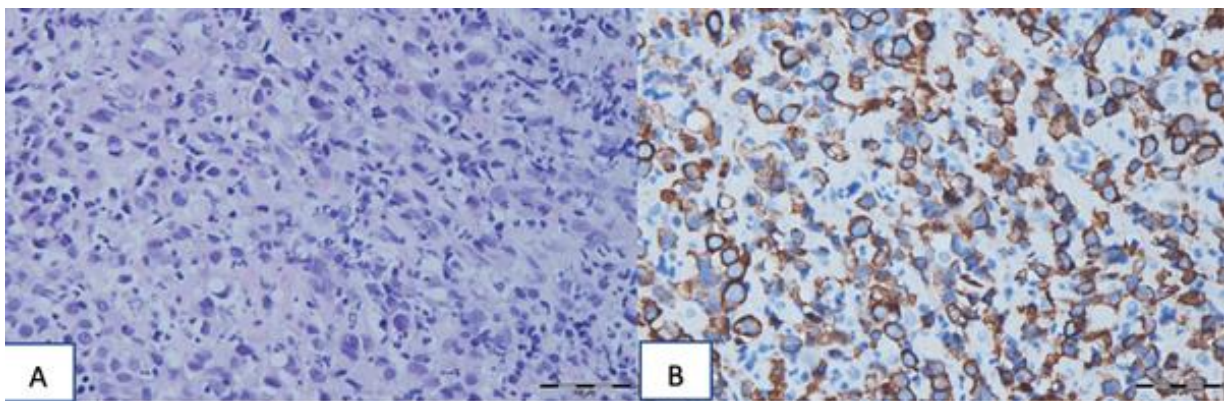


Figure 2. Pathological findings: The pleomorphic cells are arranged into sheet growth patterns, clusters of cells, or uncomplete tubules (A), (H&E staining, 40X). Immunohistochemical staining with CK (B)

and circumscribed cut-surface, hemorrhage in the center, and infiltrating beyond the serosa (Fig 3).

2.2. Case 2

A 10-year-old boy was admitted to the hospital with abdominal pain. He had poor appetite and weight loss. His family history was unknown. Physical examination found abdominal tenderness and no cervical; inguinal adenopathy was palpable. A large tumor in the submucosa of the stomach and an abnormal node in the liver was found on CT scans. The gastric resection was taken, and perigastric lymphadenopathy was noted. The tumor was in the submucosa with white, firm,

Microscopic findings showed pleomorphic cells with variable sizes and increased N/C ratio. The malignant cells are arranged discohesively with a few signet-ring cells (Fig 4). The bizarre nuclei were vesicular with prominent nucleoli. These cells were metastatic to the liver and lymph node (Fig 4). The malignant cells were strongly expressed with CK (Fig 5).

His diagnosis was poorly differentiated gastric adenocarcinoma, a diffuse type with lymphovascular invasion and liver metastasis.

His treatment information was missing because he had moved to another hospital for treatment



Figure 3. Macroscopic finding: the tumor showed no marked ulceration or raised margins (A), and on the cut surface, it showed white, firm, circumscribed hemorrhage in the center and infiltrating beyond the serosa (B)

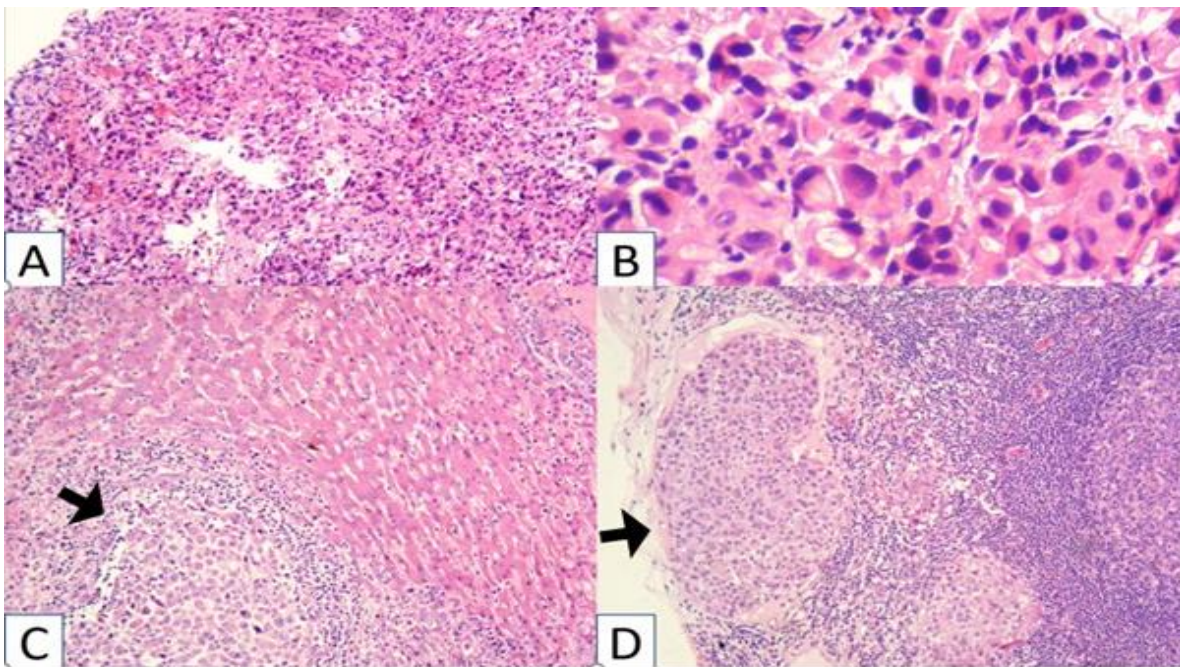


Figure 4. Microscopic findings: the cells are arranged discohesively (A) (H&E staining, 10X) with a few signet-ring cells (B) (H&E staining, 40X). The malignant cells were metastasized to the liver (C) and lymph node (D) (arrow), (H&E staining, 10X).

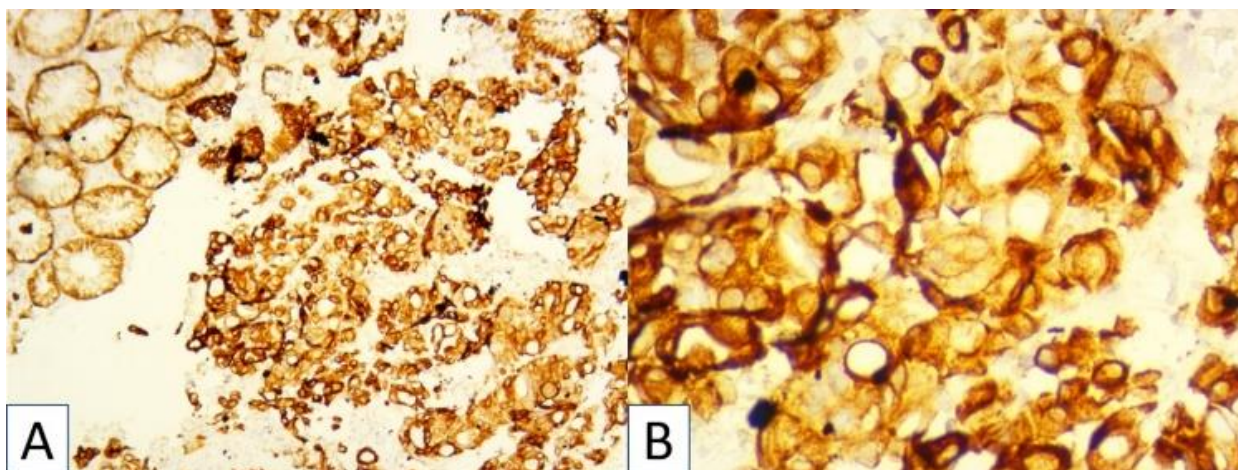


Figure 5. Immunohistochemical staining with CK (A&B)

3. DISCUSSION

Almost all patients diagnosed with GAC are older than 50 years [5]. Less than 5% of all new cases are diagnosed in younger patients [6]. Most gastric malignancies in children are lymphomas and sarcomas [1]. Early-onset GAC is extremely rare; only 0.05% of gastric malignancies in childhood [1,5]. Therefore, there are no criteria for diagnosing GAC in children; most cases are still based on data from adults.

At early stages, gastric carcinoma may have no symptoms; however, at advanced disease stages, it has noticeable symptoms, such as dysphagia, asthenia, indigestion, vomiting, weight loss, early satisfaction of appetite, and anemia. In case 1, the patient presented with progressive increasing abdominal distension, and the boy in case 2 was admitted to the hospital with abdominal pain. The onset of these symptoms commonly indicates advanced disease and a poor prognosis [2].

The standard gold method of diagnosing GAC is the endoscopic examination and forceps biopsies [7]. Besides, contrast-enhanced CT, MRI, EUS, or FOG PET-CT are also used for more advanced staging, notably excluding the peritoneal disease [7].

In both cases, the CT scan showed a tumor protruding into the stomach with an irregular border, especially in case 2, the cancer was located in the submucosal. Imaging examination revealed the possibility of a submucosal tumor (SMT). SMTs are non-epithelial tumors and are frequently covered with intact mucosa [4,8,9]. When SMT presents, it could be a non-neoplastic SMT, compressed by extra-gastrointestinal tumors, or a neoplastic SMT [8]. And in neoplastic SMT, there are non-epithelial and epithelial tumors [8]. Non-epithelial tumors are composed of mesenchymal tumors and lymphomas, which were frequently in children [1,8]. Epithelial tumors comprised neuroendocrine tumors and gastric carcinoma [8]. The tumor's location plays an essential role in clinical diagnosis, and the most common tumor in the stomach is GIST [4,8]. The majority of SMT have no symptoms [8]; however, in these cases, the patients had abdominal pain and lost weight, which favors malignancy. Based on clinical signs and incidence rate, the first diagnosis of these cases was lymphoma. Although GAC in childhood is rare, this different diagnosis cannot be excluded. Therefore, pathology is essential for diagnosis.

In case 1, the boy had metastatic GAC based on a CT scan, although there was no malignant cell in the ascites because the sensitivity of this test is 56.7% [10]. Additionally, Dewitt et al (2007) revealed that 5% of patients with negative cytology were diagnosed with metastatic disease [11]. Therefore, a biopsy was taken from this patient.

Gastric carcinoma usually has poorly differentiated morphology; it is too difficult to distinguish from neuroendocrine tumors, sarcomas, or lymphomas, which are more frequent in children. In case 1, because the tumor was located under mucosa and showed no marked ulceration or raised margins, the clinician can misdiagnose the tumor as GIST, leiomyoma, or lymphoma without pathological evidence. Therefore, immunohistochemistry is critical to confirm the diagnosis, especially in these cases; CK is a valuable marker for confirmation.

In our report, both cases presented with advanced stages with peritoneal carcinomatosis (in case 1) or liver metastasis (in case 2). In case 2, on his CT scan and histology, the boy was diagnosed metastatic to the liver and lymph node. Other reports also showed that pediatric gastric carcinomas presented with metastatic diseases such as peritoneal carcinomatosis, liver metastases, and lung metastases [12]. Histopathologic characteristics of young gastric carcinoma patients are more aggressive, and most patients were metastatic at the time of diagnosis [3]. Our cases were metastatic at the diagnosis with poorly differentiated gastric adenocarcinomas, diffuse type with lymphovascular invasion.

Gastric carcinoma is a disease that has multiple causative factors [7]. About 90% of cases appear sporadically, whereas there is only 10% accompanied by inherited familial genetic components [7,13]. Patients associated with hereditary and environmental factors are at risk of developing gastric carcinoma approximately threefold [6,13]. In our case, the 14-year-old boy's father died of gastric carcinoma; his family history played a crucial role in pathogenesis. Similarly, in Subbiah's report, in 5 pediatric patients with GAC treated at The University of Texas M. D. Anderson Cancer Center, one patient had a family history of GAC, and another with a family history of colorectal carcinoma [5].

Additionally, pediatric cases in GAC are limited, and treatment in children, such as chemotherapy, radiotherapy, and radical surgery, remains the mimic in adults [1,14]. Besides, HER2 and E-cadherin testing give more choices for

clinical application. For example, the patient with overexpressed HER2 can choose trastuzumab, targeted therapy with the anti-HER2 antibody [15]. In addition, E-cadherin is a tumor suppressor, and its expression may affect treatment and prognosis [16].

Based on reported cases of pediatric GAC, the patients in childhood may live five months after diagnosis, whereas the prognosis in adults is better; as their 5-year survival rate is 15% [2].

The children with gastric cancer were detected with advanced disease. GAC mimicking a submucosal tumor is often difficult to be diagnosed, even misdiagnosed with other tumors of these kinds.

Conclusion

Pediatric GAC presents with a more advanced stage and poor differentiation. However, the clinical presentation is like adult GAC. Because of data limitations, the diagnosis and treatment of pediatric GAC remain a significant challenge. Its presentation on CT scan is similar to SMT, such as mesenchymal tumors or lymphomas. It is essential to combine pathological and clinical examination to diagnose. In children older than ten years old who have malnutrition, gastric tumor, or multiple lymph nodes, carcinoma should be considered despite its rarity. Interestingly, choosing appropriate markers is essential in detecting this disease.

ETHICAL STATEMENT

Written informed consent was obtained from the patient to publish these case reports and any accompanying images. Copies of the written permissions from the patients are available for review by the Editor of the journal.

FUNDING

The authors received no financial support for the research, authorship, and/or publication of this article.

CONFLICT OF INTEREST

The authors declare that they have no potential conflicts of interest.

ACKNOWLEDGEMENTS

All contributors to the manuscript other than co-authorships should be acknowledged.

AUTHORS' CONTRIBUTION

Conceptualization and investigation: QPB.
 Visualization: NTQN.
 Writing—original draft: QPB.
 Writing—review & editing: TDAP, QPB.


CONFLICT OF INTEREST

The authors declare that they have no potential conflicts of interest.

FUNDING

No funding to declare.

ORCID ID

Quynh Phuong Bui  <https://orcid.org/0000-0001-9778-7169>

Thu Dang Anh Phan  <https://orcid.org/0000-0002-4062-0904>

Nhu Thi Quynh Nguyen  <https://orcid.org/0000-0003-3439-3044>

REFERENCES

- [1] Öncel S. A case report: gastric adenocarcinoma in childhood. [cited 2021 Sep 16]; Available from: https://www.academia.edu/11404789/A_case_report_gastric_adenocarcinoma_in_childhood.
- [2] Harting MT, Blakely ML, Herzog CE, et al. Treatment issues in pediatric gastric adenocarcinoma. *Journal of Pediatric Surgery*. 2004;39:e8–e10.
- [3] Tessler RA, Dellinger M, Richards MK, et al. Pediatric gastric adenocarcinoma: A National Cancer Data Base review. *Journal of Pediatric Surgery*. 2019;54:1029–1034.
- [4] Cheng X-L, Liu H. Gastric adenocarcinoma mimicking a submucosal tumor: A case report. *World J Clin Cases*. 2019;7:3138–3144.
- [5] Subbiah V, Varadhachary G, Herzog CE, et al. Gastric adenocarcinoma in children and adolescents: Pediatric Gastric Adenocarcinoma. *Pediatr Blood Cancer*. 2011;57:524–527.
- [6] Li J. Gastric Cancer in Young Adults: A Different Clinical Entity from Carcinogenesis to Prognosis. *Gastroenterology Research and Practice*. 2020;2020:1–13.
- [7] Carneiro F, Fukayama M, Grabsch HI, et al. WHO Classification of Tumours - Digestive System Tumours 5th ed 2019.
- [8] Nishida T, Kawai N, Yamaguchi S, et al. Submucosal tumors: Comprehensive guide for the diagnosis and therapy of gastrointestinal submucosal tumors: Submucosal tumors. *Digestive Endoscopy*. 2013;25:479–489.
- [9] Kobara H, Mori H, Rafiq K, et al. Evaluation of gastric submucosal tumors using endoscopically visualized features with submucosal endoscopy. *Oncol Lett*. 2014;8:161–168.
- [10] Jha R, Shrestha H, Sayami G, et al. Study of effusion cytology in patients with simultaneous malignancy and ascites. *Kathmandu University medical journal (KUMJ)*. 2006;4:483–487.
- [11] Desai AP, Gress FG. Extraintestinal Endosonography. *Clinical Gastrointestinal Endoscopy [Internet]*. Elsevier; 2019 [cited 2022 Feb 19]. p. 517-531.e4. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9780323415095000475>.
- [12] Seker M, Aksoy S, Ozdemir N, et al. Clinicopathologic features of gastric cancer in young patients. *Saudi J Gastroenterol*. 2013;19:258.
- [13] Carl-McGrath S, Ebert M, Röcken C. Gastric adenocarcinoma: epidemiology, pathology and pathogenesis. :18.
- [14] Ladd AP, Grosfeld JL. Gastrointestinal tumors in children and adolescents. *Seminars in Pediatric Surgery*. 2006;15:37–47.
- [15] Hechtman JF, Polydorides AD. HER2/neu Gene Amplification and Protein Overexpression in Gastric and Gastroesophageal Junction Adenocarcinoma: A Review of Histopathology, Diagnostic Testing, and Clinical Implications. *Archives of Pathology & Laboratory Medicine*. 2012;136:691–697.
- [16] Liu X, Chu K-M. E-Cadherin and Gastric Cancer: Cause, Consequence, and Applications. *BioMed Research International*. 2014;2014:1–9.