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Early gastric cancer with diffuse heterotopic gastric glands and granular cell tumors mimicking advanced gastric cancer

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ABSTRACT

INTRODUCTION: Heterotopic gastric grands (HGGs) are gastric grands that are observed in the submucosa and are considered to be paracancerous lesions or precursors of gastric cancer (GC). Granular cell tumors (GCTs) are benign neural origin tumors. Gastrointestinal GCTs are rare and gastric GCTs are seldom seen. We report the case of a patient who was diagnosed with early GC with diffuse HGGs affecting the whole stomach and two GCTs mimicking advanced GC.

PRESENTATION OF CASE: The patient is a 71-year-old male with epigastric discomfort. Gastrointestinal endoscopy revealed an ulcerated lesion at the mid-gastric body. A biopsy specimen indicated adenocarcinoma. Moreover, gastrointestinal endoscopy revealed a submucosal tumor at the posterior wall and multiple transparent protuberances across the entire stomach. Computed tomography demonstrated diffuse gastric wall thickening with lymphadenopathies. Total gastrectomy was performed under the preoperative diagnosis of advanced GC with lymph node metastases. The pathological diagnosis was adenocarcinoma invading submucosal stroma without lymph node metastasis, two GCTs, and diffuse HGGs affecting whole stomach.

DISCUSSION: Preoperative diagnosis of GC depth or range associated with HGGs is often difficult. Although diffuse HGGs are sometimes observed, there is no previous report of a case of HGGs with whole gastric wall thickening observed by computed tomography. As a result, this case was overdiagnosed as advanced GC. Although the relationship between GCTs and HGGs or GC is unclear, there is no case report of GCTs accompanied by HGGs or GC.

CONCLUSION: This case report suggested that cautious preoperative assessment for GC co-occurring with HGGs is required.

1. Introduction

Heterotopic gastric glands (HGGs) are gastric glands that are observed in the submucosa. The incidence of HGGs is 4.0% to 20.1% among surgical specimens resected for gastric cancer (GC) or gastric ulcers, and an association between HGGs and GC has been reported [1–3]. Preoperative diagnosis of GC depth or range associated with HGGs is often difficult [4]. Granular cell tumors (GCTs) are benign, mesenchymal tumors that originate from Schwann cells [5]. GCTs may occur at many sites, the most frequent being the tongue, skin, and subcutaneous tissue [5,6]. GCTs in the gastrointestinal tract are extremely rare, with only approximately 4% to 6% of all GCTs occurring in this location [6]. The esophagus is the most common location of GCTs in the gastrointestinal tract, followed by the colon, and gastric GCTs are seldom seen [6–8]. Here we report the case of a patient who was diagnosed with early GC with diffuse HGGs affecting the whole stomach and two GCTs mimicking advanced GC. This case report has been prepared in line with the SCARE criteria [9].

2. Presentation of case

A 71-year-old male was admitted to his family doctor with epigastric discomfort. Upper gastrointestinal endoscopy was performed and revealed an ulcerated lesion at the mid-gastric body. A biopsy specimen taken from the ulcerated lesion revealed moder-

Abbreviations: HGGs, heterotopic gastric grands; GC, gastric cancer; GCTs, granular cell tumors.

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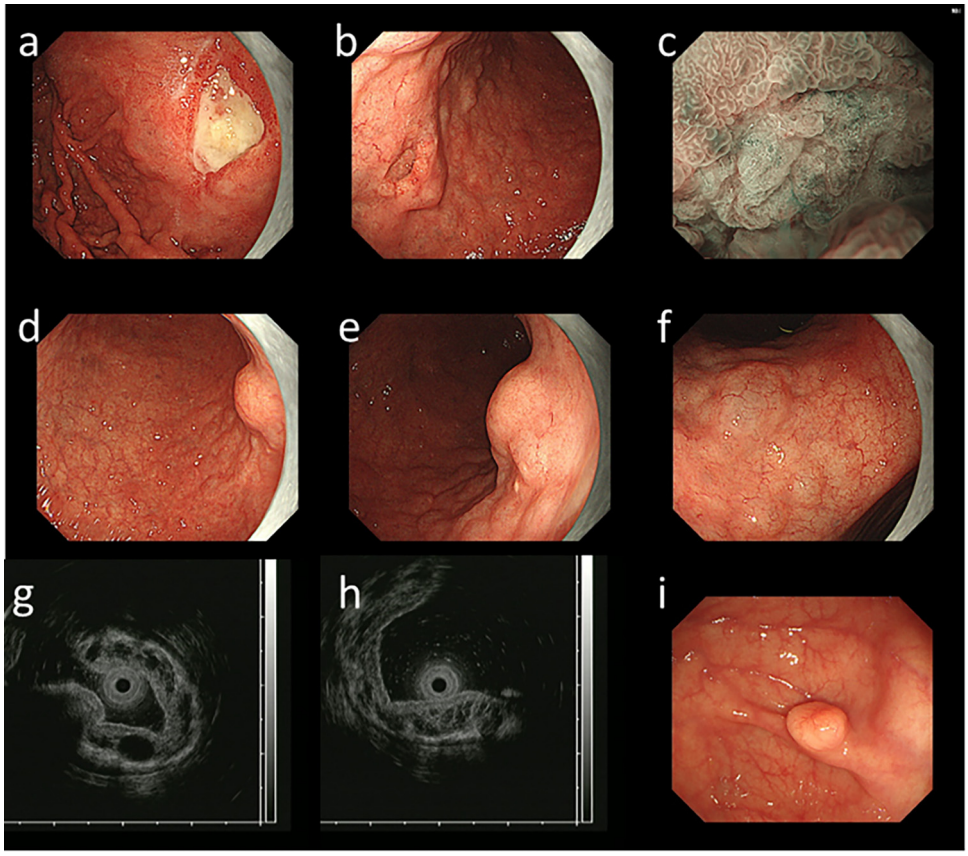

Fig. 1. Findings of gastroduodenal endoscopy and colonoscopy. (a) A 30 mm ulcerated lesion covered by regenerative epithelium with a smooth margin at the anterior wall of the upper-gastric body. This lesion suggested a benign ulcer. (b) An ulcerated lesion at the mid-gastric body. The biopsy specimen from this lesion revealed moderately differentiated adenocarcinoma. Multiple diffuse protuberances such as submucosal tumors were observed around the lesion. (c) Irregular ductal structures with deposition of white opaque substance at cancer lesion. (d) A 30 mm submucosal tumor at the posterior wall of the gastric angle. (e) Multiple protuberances around the submucosal lesion. (f) Multiple protuberances such as submucosal tumors were observed across almost the whole stomach. (g) Endoscopic ultrasonography of submucosal tumor. Circular low echoic lesion was observed. (h) Endoscopic ultrasonography of multiple diffuse protuberances. Multiple cystic low echoic lesions throughout almost the entire stomach were observed. These findings suggested heterotopic gastric glands. (i) Colonoscopy revealed an 8 mm submucosal tumor in the cecum. The biopsy specimen from this lesion revealed a granular cell tumor.

ately differentiated tubular adenocarcinoma. Thus, the patient was referred to our department. The patient was a smoker, had a history of habitual alcohol consumption, and reported a medical history of hypertension and hyperlipidemia. Regarding family history, his mother had GC.

Laboratory data indicated an elevated carcinoembryonic antigen level of 7.9 ng/ml. The remaining laboratory data were within normal limits. A repeat upper gastrointestinal endoscopy was performed (Fig. 1). In addition to the known GC lesion, a 30 mm ulcerated lesion covered by regenerative epithelium with a smooth margin at the anterior wall of the upper-gastric body was observed. The findings of this lesion suggested a benign peptic ulcer. Moreover, a submucosal tumor was detected at the posterior wall of the gastric angle. Endoscopic ultrasonography of the submucosal tumor revealed a circular low echoic lesion. Furthermore, multiple transparent protuberances such as submucosal tumors were observed across almost the entire stomach. Endoscopic ultrasonography of these lesions revealed multiple cystic low echoic lesions mainly at the second to third layer, and these findings suggested diffuse HGGs. Contrast study demonstrated an irregular ulcerated lesion surrounded by submucosal tuber at the anterior wall of the mid-gastric body (Fig. 2). This lesion seemed to spread under the submucosal layer. Although the range of the lesion was indefinite, this lesion was suspected to be invading to deeper submucosal stroma or the muscle layer. Gastric wall stiffening such as scirrhous GC was not observed. Colonoscopy revealed an 8 mm yellowish submucosal tumor in the cecum (Fig. 1). Histological analysis of a biopsy specimen taken from this lesion revealed a GCT. Computed tomography demonstrated diffuse gastric wall thickening (Fig. 3). Lymphadenopathies around the cardia and lesser curvature were observed and lymph node metastases were suspected. The gastric wall thickening was observed close to the liver and direct invasion to the liver was suspected. In this case, the depth of GC invasion and the range of the lesion were indeterminate. Moreover, the etiology of diffuse gastric thickening was unknown, although involvement of HGGs was suspected. Therefore, total gastrectomy with D2 lymphadenectomy, omentectomy, and splenectomy was performed under the preoperative diagnosis of advanced GC with lymph node metastases.

Macroscopic findings of the resected specimen revealed diffuse gastric wall thickening of approximately 10 mm (Fig. 4). A GC lesion existed at the anterior wall of the mid-gastric body and gastric ulcer scarring was present at the anterior wall of the upper-gastric wall. Moreover, two yellowish submucosal tumors were detected at the posterior wall of the gastric angle and at the lesser curvature of the gastric body. Submucosal cystic changes were observed in the whole stomach. The pathological diagnosis was a moderately differentiated tubular adenocarcinoma invading submucosal stroma without lymph node metastasis, two GCTs, and diffuse HGGs affecting the whole stomach (Fig. 5).

Postoperatively, the patient recovered uneventfully and was discharged on postoperative day 14. At the time of writing this

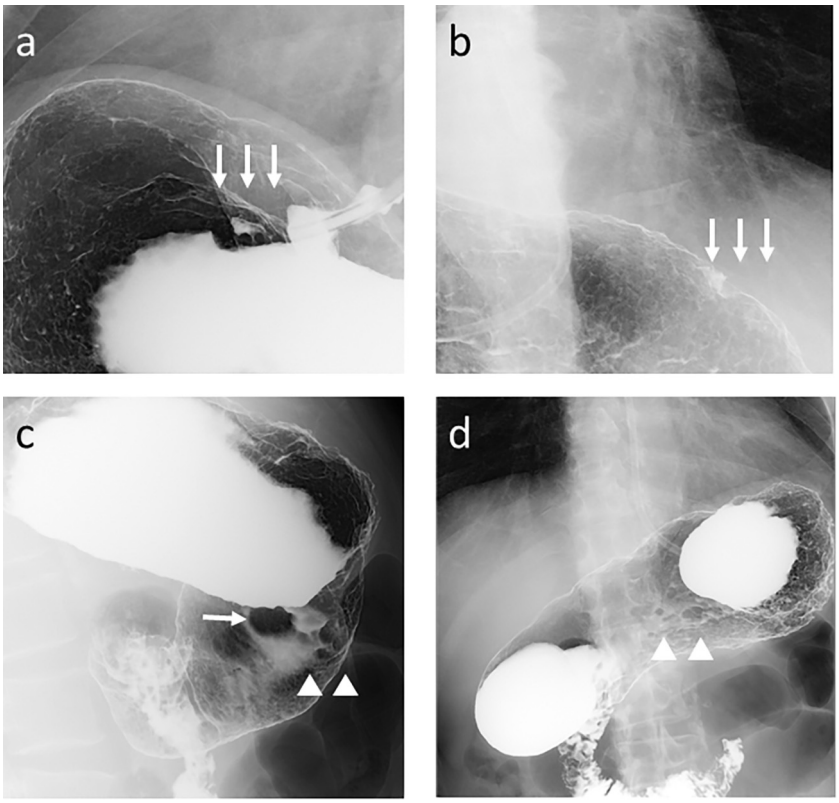

Fig. 2. Contrast study of the stomach. (a, b) An irregular ulcerated lesion surrounded by submucosal tuber at the anterior wall of the mid-gastric body (arrows). This lesion seemed to spread under the submucosal layer. Although the range of the lesion was indeterminate, it was suspected to be invading to a deeper submucosal layer or muscle layer. (c) An 18 mm submucosal tumor was observed at the posterior wall of the lower-gastric body (arrow). Multiple small polypoid lesions were observed near the submucosal lesion (arrow heads). (d) Multiple small polypoid lesions (arrow heads).

report, 20 months have passed and the patient has experienced no recurrence.

3. Discussion

This case was found to be early submucosal GC, which was overdiagnosed as advanced GC because diffuse HGGs existed in the whole gastric wall and diffuse gastric wall thickening was observed by computed tomography. Moreover, this lesion was accompanied with two GCTs, an extremely rare condition.

HGGs are gastric glands that are observed in the submucosa, and are naturally seen in the lamina propria of mucus membranes. Although the etiology of HGGs is not well clarified, they are considered to be congenital or acquired [1,3,10]. Most cases are considered to be the latter, and HGGs are regarded to be an aberration of the epithelium into the submucosa as a result of repeated erosion and regeneration of the mucosa [1,3]. Our patient had gastric ulcer scarring as well as a GC lesion. His gastric mucosa may have undergone repeated ulceration and regeneration, thus possibly accounting for the occurrence of diffuse HGGs. Moreover, HGGs penetrating into the submucosal layer through the muscularis mucosae were microscopically observed. Therefore, this case was also considered to be acquired diffuse HGGs. Although diffuse HGGs are sometimes observed [1], there was no previous report of a case of HGGs with whole gastric wall thickening observed by computed tomography. As a result, this case was overdiagnosed as advanced GC.

The association between HGGs and GC has been reported [1–4]. One hypothesis is that both HGGs and GC develop as a result of repeated erosion and regeneration of the mucosa, suggesting that HGGs are paracancerous lesions [3]. Another hypothesis is that HGGs themselves have the potential to develop into GC, and a few case of multiple GC associated with HGGs have been reported [4,11]. Because HGGs are considered to be a precursor of GC, total gastrectomy is an acceptable procedure for this patient.

Although the role of splenectomy for complete resection of splenic hilar and peri-splenic artery lymph nodes has been controversial, Japanese GC treatment guidelines recommend complete clearance of splenic hilar lymph nodes by splenectomy for potentially curable advanced GC invading the greater curvature of the upper stomach [12]. Moreover, removal of the greater omentum is usually integrated within the standard gastrectomy for GC invading the subserosa or deeper [12]. Therefore, our patient underwent splenectomy and omentectomy; however, these procedures were subsequently determined to be unnecessary. Lymphadenopathies around the cardia and the lesser curvature were considered to be inflammatory changes and D2 nodal dissection was also unnecessary.

Accurate preoperative diagnosis of GC depth or range associated with HGGs is often difficult [4]. In this case, GC accompanied with diffuse HGGs was suggested preoperatively by endoscopic ultrasonography. However, computed tomography showed diffuse gastric wall thickening with lymphadenopathies. Because we could not rule out advanced GC affecting the whole stomach with lymph node metastases, we performed total gastrectomy with D2 lymphadenectomy, omentectomy, and splenectomy. However, a preoperative contrast study did not show gastric wall stiffening as is present in scirrhous GC. This finding was discrepant from the computed tomography findings. This patients had lymphadenopathies detected by computed tomography, we were not able to avoid overtreatment. However, this case suggested the possibility of an early disease stage in GC with diffuse HGGs even if computed tomography demonstrates diffuse gastric wall thickening. Because

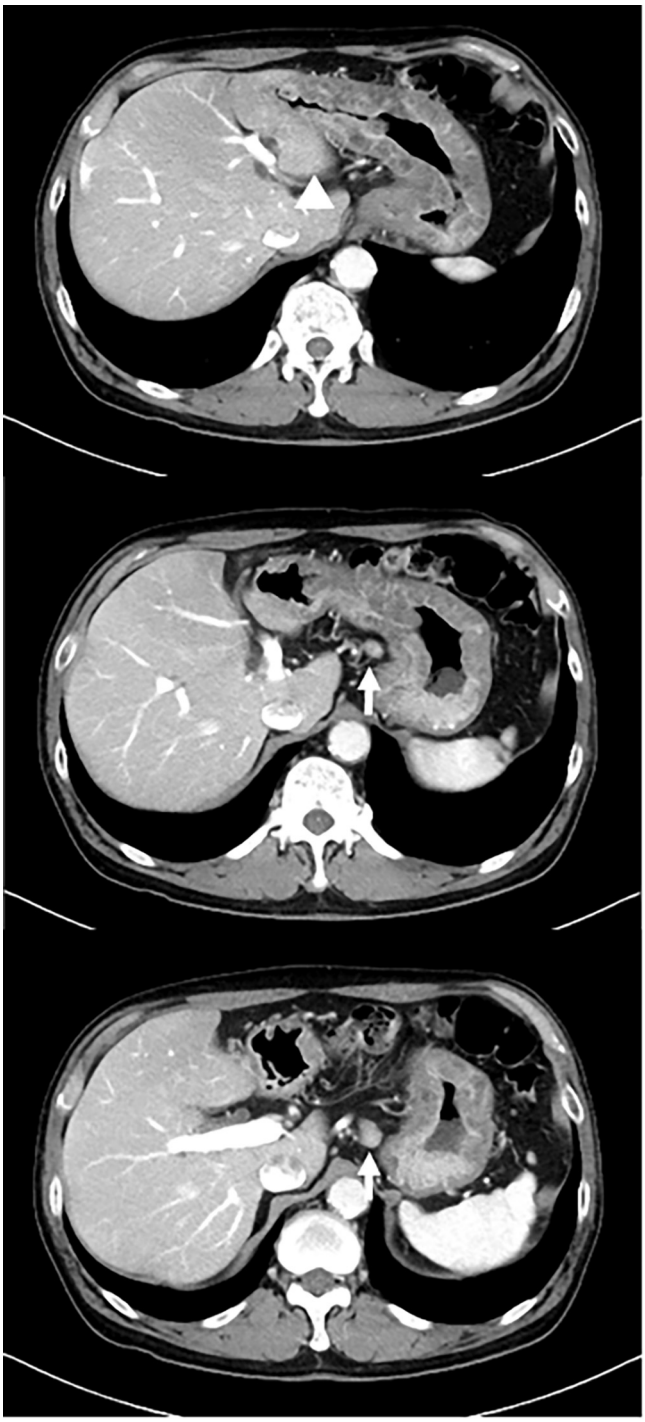

Fig. 3. Findings of abdominal computed tomography. Thickening of the whole gastric wall was observed. Lymphadenopathies around the cardia and lesser curvature were observed and lymph node metastases were suspected (arrows).Thickening of the gastric wall was close to the liver and direct invasion to the liver was suspected (arrow head).

diffuse HGGs may be the cause of overdiagnosis of GC depth or range, cautious preoperative assessment to avoid overtreatment for GC concomitant with HGGs is required.

GCTs are rare neural origin tumors. Immunohistochemical staining for S-100 protein supports the proposed origin of the tumor to be Schwann cells [13]. Although the natural history of GCTs is unclear, most are considered to be benign tumors. GCTs may occur at many sites, however, the most common sites are the skin and soft tissue, and GCTs in the gastrointestinal tract are extremely rare. Of these rare gastrointestinal GCTs, gastric GCTs account for only 4% of cases [14]. Most GCTs occur as solitary lesions [8], and there is no report of multiple gastric GCTs. Moreover, this patient had a colonic GCT in the cecum as well as two gastric GCTs. An et al. [6] reported that GCT locations are confined within the same organs in patients with multiple GCTs. Although the relationship between GCTs and HGGs or GC is unclear, there is no case report of a GCT accompanied by HGGs or GC to date.

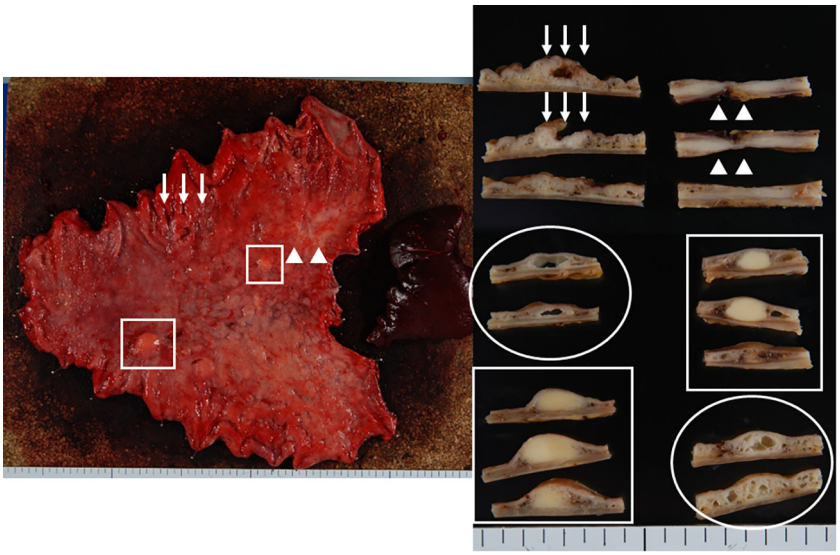

Fig. 4. Macroscopic findings of the resected specimen and its cut surfaces. Gastric wall was thickened diffusely to aproximately 10 mm. Gastric cancer lesion at the anterior wall of the mid-gastric body (arrows). Gastric ulcer scarring (arrow heads). Two yellowish submucosal tumors (surrounded by squares). Submucosal cystic changes were observed in the whole gastric wall (surrounded by circles).

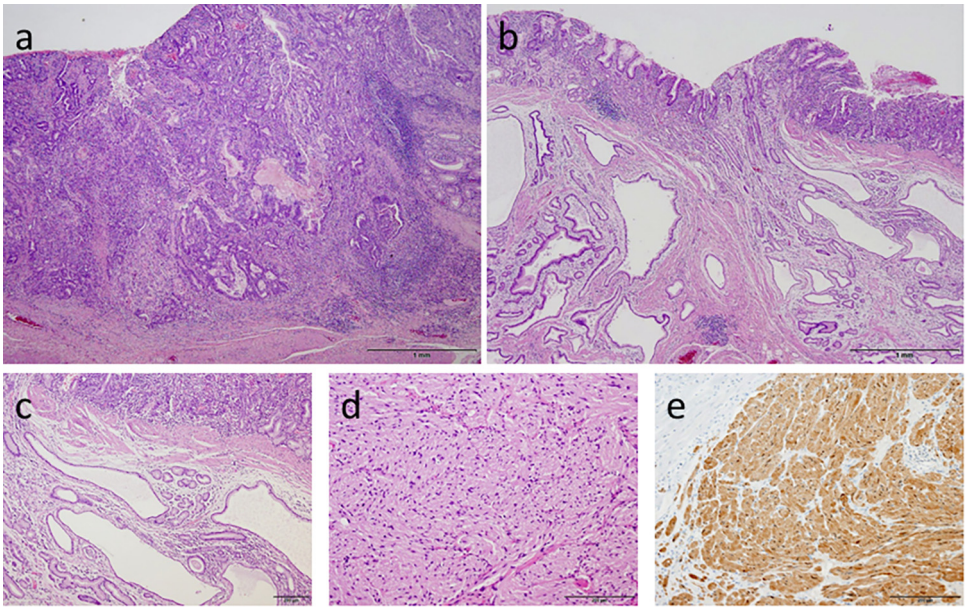

Fig. 5. Microscopic findings of the resected specimen. (a) Moderately differentiated adenocarcinoma invading submucosal stroma (×100). (b) Heterotopic gastric glands penetrating into the submucosal layer through the muscularis mucosae (×100). (c) Submucosal heterotopic gastric glands were observed in the whole gastric wall (×200). (d) Microscopic findings of the submucosal tumor. Sheet of large and polygonal cells with round to oval, eccentrically located nuclei and eosinophilic granular cytoplasm with lower mitotic activity. This finding suggests a granular cell tumor (×200). (e) Immunohistochemical staining for S-100 protein in the submucosal tumor. Diffuse and strong expression of S-100 protein was observed.

4. Conclusion

We reported a patient with GC with diffuse HGGs and two GCTs. Because diffuse HGGs existed in the whole gastric wall, and diffuse gastric wall thickening was observed by computed tomography, an early submucosal GC was consequently overdiagnosed as advanced GC. Although the relationship between GCTs and HGGs or GC is unclear, the patient exhibited two gastric GCTs, which is rare. Because diffuse HGGs may be the cause of overdiagnosis of GC depth or range, cautious preoperative assessment to avoid overtreatment for GC concurrent with HGGs is required.

Conflict of interest

The authors have no disclosure or conflict of interest related to this manuscript.

Funding

None.

Ethical approval

This is not a research study which requires ethical approval. So, there is no ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Yusuke Watanabe drafted the manuscript, performed surgery, and followed-up the patient.

Masato Watanabe, Nobuhiro Suehara, and Nami Ishikawa participated in the surgery and supervised the writing of the manuscript.

Tomohiko Shinkawa contributed the data extraction and post-operative management.

Taizo Hosokawa and Hirotada Akiho contributed to preoperative assessment.

Mari Mine and Sadafumi Tamiya contributed to the pathological diagnosis.

Kazuyoshi Nishihara and Toru Nakano contributed to the revision of the manuscript.

All authors read and approved the final manuscript.

Toru Nakano gave final approval of this manuscript.

Registration of research studies

This is not a research study involving human participants. Therefore, this manuscript is not applicable in this section.

Guarantor

Yusuke Watanabe.

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