CASE REPORT

Gastroblastoma: An Extremely Rare Biphasic Tumour.

Nurasyikin Hanifah[1,2], Norlisa Khalid[1,2], Amizatul Aini Salleh[2], Noorjehan Omar[2], Pavitratha Puspanathan[3], Razana Mohd Ali[1]

[1] Department of Pathology, Faculty of Medicine and Health Science, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[2] Department of Pathology, Hospital Sultan Idris Shah, 43400 Serdang, Selangor, Malaysia
[3] Department of Pathology, Hospital Pulau Pinang, Jalan Residensi, 10990 Georgetown, Pulau Pinang, Malaysia

ABSTRACT

Gastroblastoma represents an exceedingly rare, low-grade malignant neoplasm of the stomach characterized by biphasic epithelial and mesenchymal components. The pathogenesis of this entity remains inadequately elucidated, while its clinical manifestations are diverse and nonspecific. Definitive diagnosis relies on the identification of specific genetic alterations; however, detailed histopathological examination complemented by comprehensive immunohistochemical analysis remains fundamental to accurate diagnosis. The apparent rarity of this neoplasm may be partially attributed to underdiagnosis resulting from limited recognition among clinicians and pathologists. This case report of a 27-year-old male documents the first case of gastroblastoma encounter among Malaysian population, with emphasis on its clinical presentation and distinctive pathological features, thereby contributing to the existing literature and potentially serving as a reference for future investigations of this uncommon gastric neoplasm.
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Corresponding Author:
Dr. Razana Mohd Ali, MPath
Email: razanamo@upm.edu.my
Tel: +603 97692384

INTRODUCTION

Gastroblastoma is a rare biphasic gastric neoplasm comprising uniform spindle cells admixed with epithelial elements arranged in distinctive nests and glandular formations. The 2019 WHO Classification of Tumours of the Digestive System designates this entity among malignant epithelial tumours [1]. This neoplasm typically originates within the gastric muscularis propria, predominantly affecting the antrum, with a notable predilection for adolescent and young adult males. While detection of the pathognomonic *MALAT1-GLI1* fusion transcript provides definitive diagnosis in combination with histomorphology, the underlying pathogenetic mechanisms remain incompletely characterized.

The clinical manifestations frequently include abdominal discomfort, occasionally presenting as palpable abdominal masses on physical examination. Nonspecific systemic symptoms such as fatigue, anaemia, and weight loss have been documented in some cases [1-3]. The exceedingly low incidence of this neoplasm, coupled with its heterogenous clinical presentation and limited awareness among healthcare professionals, presents substantial diagnostic challenges potentially leading to underrecognition. Current understanding of gastroblastoma derives almost exclusively from individual case reports owing to its exceptional rarity.

Herein, we report the first case of gastroblastoma in Malaysia, documenting its clinical presentation, histomorphological features, immunohistochemical characteristics, differential diagnostic considerations, management approach, and clinical outcome, thereby expanding the existing literature on this uncommon neoplastic entity.

CASE REPORT

A 27-year-old male patient presented with a three-week history of progressive abdominal distension accompanied by abdominal discomfort and painless rectal bleeding with Haemoglobin level of 10.3 g/dL. There was no significant medical history except for a visit to the Hospital Emergency five years prior for fever

and vomiting. Abdominal examination during this visit was unremarkable, however per rectal examination revealed multiple hemorrhoids. He was discharged with a diagnosis of infective acute gastroenteritis and was given a date for endoscopy in which he defaulted.

During the subsequent visit, an initial abdominal ultrasonography identified a large, predominantly cystic intraperitoneal mass. Subsequent computed tomography (CT) imaging of the abdomen demonstrated a large multiloculated cystic intraperitoneal lesion with enhancing soft tissue components, thick septations, and calcification foci, which exerted significant mass effect on adjacent structures (Fig. 1). The mass is extremely large, positioned in the central abdomen and extending inferiorly into the pelvic cavity, with dimensions of 14.3 cm (AP) × 20.8 cm (W) × 23.7 cm (CC). Anterosuperiorly, it reaches the right subhepatic region at the level of inferior border of T11 vertebra. The mass lacks clear separation from adjacent organs and structures, pushing these organs primarily superiorly and toward the superolateral sides. The stomach antrum and pylorus have been displaced superiorly and compressed, causing luminal narrowing. The mass's boundaries are indistinct, thus the difficulty to accurately determine its organ of origin. No tumour markers were done at this stage.

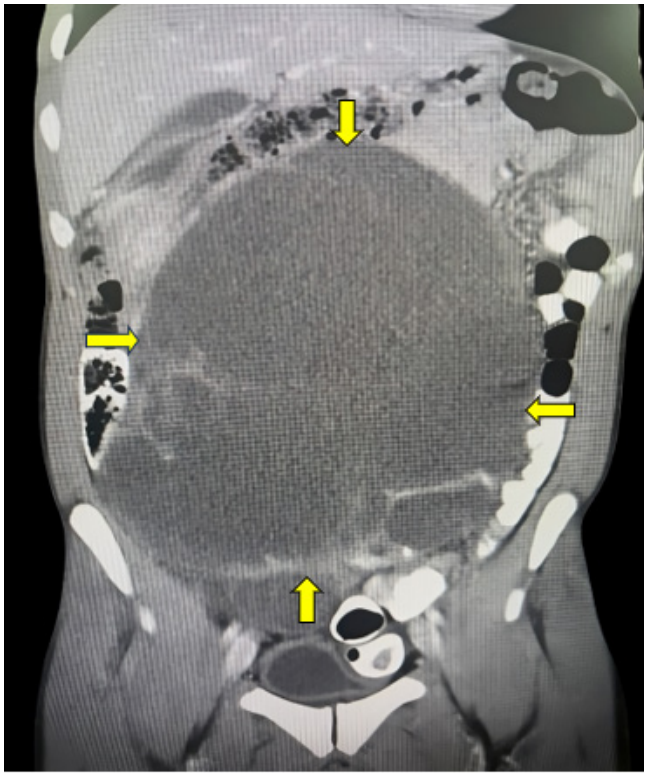

Fig 1: CT Abdomen: Large multiloculated cystic intraperitoneal mass (block arrow) with enhancing soft tissue components, thick septations, and calcification foci displacing the surrounding organs structures.

Exploratory laparotomy demonstrated an exophytic multiloculated cystic mass originating from the greater curvature of the stomach near the pylorus, with adhesions to the left anterior abdominal wall. Intraoperative rupture of several locules released approximately 2 liters of brownish fluid. Multiple enlarged lymph nodes were palpable along the greater curvature while the overlying gastric mucosa appeared macroscopically unremarkable. A wedge resection of the affected gastric segment was performed.

The surgical specimen comprised a well-circumscribed cystic mass measuring 235 × 225 × 110 mm, with a lobulated external surface (Fig. 2). The lesion originated from the submucosal layer of the gastric wall. Sectioning revealed a predominantly multiloculated cystic architecture containing blood clots and necrotic material with focal solid component measuring 30 mm in greatest dimension. Ten lymph nodes ranging from 5 to 20 mm in diameter were isolated from the specimen. Histological assessment revealed a biphasic neoplasm

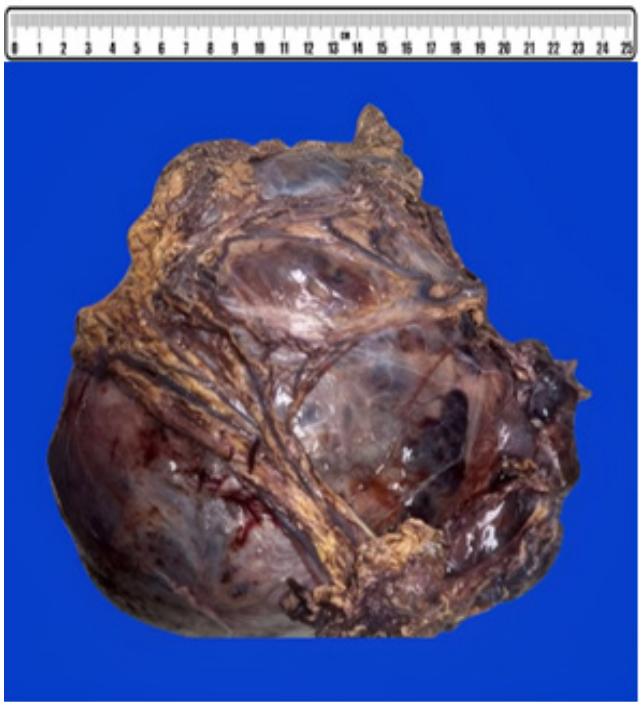

Fig 2: The specimen consists of a well-circumscribed cystic mass measuring 235 × 225 × 110 mm, with lobulated external surface.

extending from the submucosal layer to the gastric muscularis propria with extension into the serosa. The predominant component consisted of relatively bland, monotonous spindle cells arranged in a nodular plexiform pattern embedded within a myxoid stroma (Fig. 3A-B). Hypocellular areas characterized by thin-walled curvilinear blood vessels separated by variably thickened hyalinized septa were observed throughout

the tumour. A less prominent epithelioid component featured glandular and cribriform islands (Fig. 3C). Mitotic activity was minimal, with immunohistochemistry demonstrating a low Ki67 proliferative index (<5%). Histological examination of all ten lymph nodes showed reactive changes without metastatic involvement and all margins were clear of malignancy.

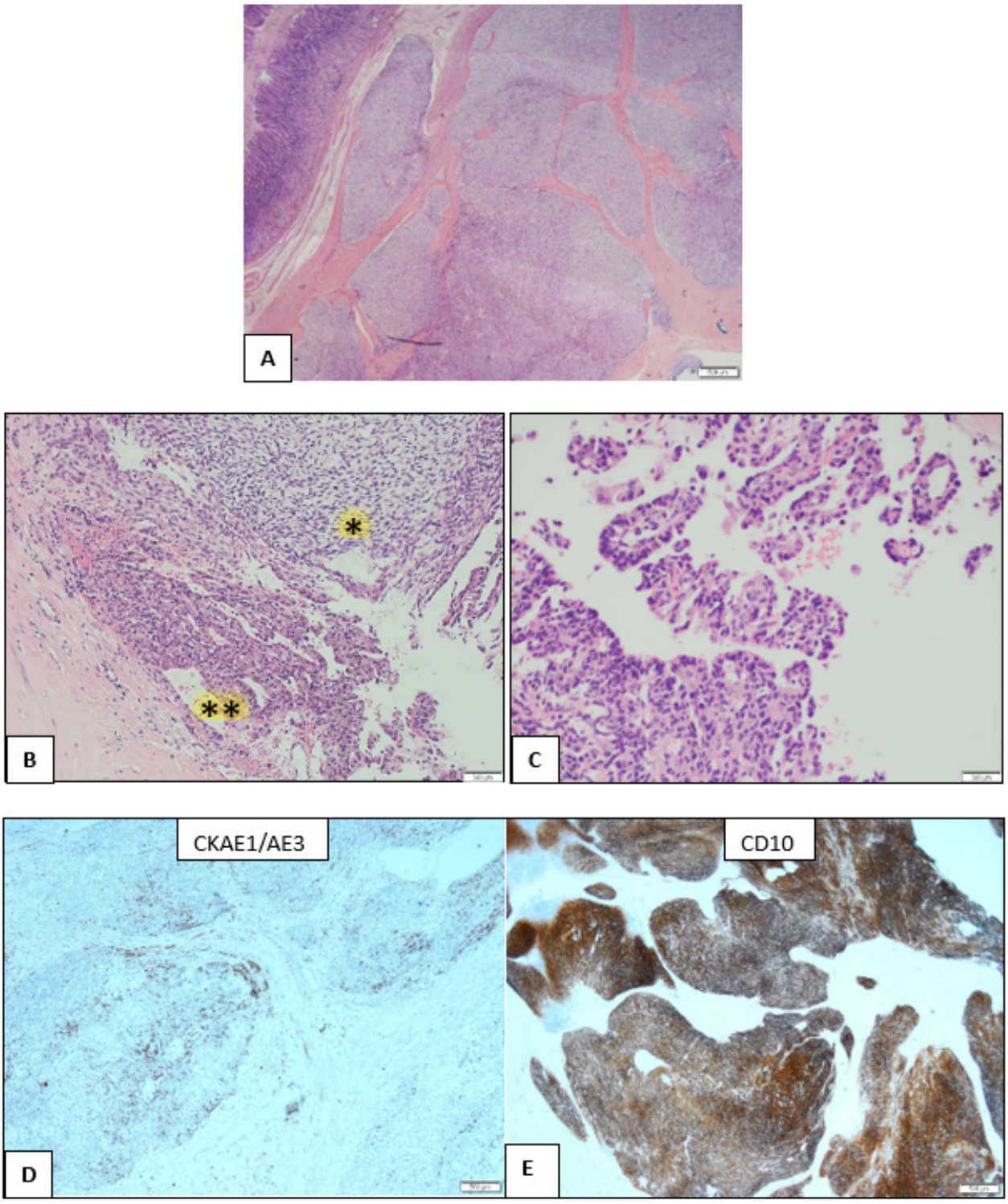

Figure 3: A) Prominent nodular plexiform architecture arising from the muscularis propria, with intervening hyalinised septae. Note: The overlying gastric mucosa was fairly unremarkable (Hematoxylin and Eosin, x20). B) Biphasic histomorphology, mesenchymal spindle cell component (*), glandular epithelial component (**) (Hematoxylin and Eosin, x200). C) The epithelial cells were uniform and appear bland (Hematoxylin and Eosin, x400). Immunohistochemistry. D) Patchy strong cytoplasmic positivity for CK AE1/AE3 (immunohistochemistry, x20). E) Diffuse and strong membranous positivity for CD10 (immunohistochemistry, x20).

Immunohistochemical analysis demonstrated diffuse positive membranous expression of CD10 (Fig. 3E), CD56, CD99, and cytoplasmic vimentin immunoreactivity within the neoplastic cells. Epithelial markers MNF116 and CK AE1/AE3 (Fig. 3D) showed patchy positivity in both spindle and glandular elements. The epithelioid cell population exhibited focal synaptophysin and BER-EP4 immunoreactivity. These neoplastic cells were negative for SMA, TLE-1, S100, β-catenin, CD34, STAT6, HMB45, CD117, DOG1, SATB2, p63, WT1, SALL4, EMA, GFAP, and H-caldesmon immunohistochemistry.

The constellation of morphological features raised differential diagnostic considerations between gastroblastoma and plexiform fibromyxoma, both entities within the spectrum of *GLI-1* rearranged neoplasms. The presence of an epithelial component with strong pan-cytokeratin immunoreactivity supported a diagnosis of gastroblastoma, which was made through consultation with local and overseas gastrointestinal pathologists. Although molecular confirmation of *MALAT1-GLI-1* fusion was not performed due to financial constraints associated with private laboratory testing, the histomorphological and immunohistochemical profile was deemed sufficient for diagnostic classification.

Clinical follow up one year post surgery revealed an uncomplicated recovery with no reported symptoms. Surveillance computed tomography demonstrated no radiographic evidence of local recurrence or distant metastasis.

DISCUSSION

Gastroblastoma constitutes a rare gastric neoplasm initially characterized in 2009 by Miettinen et al., who identified three distinctive biphasic gastric tumours in young adults with morphological features distinct from other known biphasic neoplasms including carcinosarcoma, synovial sarcoma, teratoma, and mixed tumours [1,2]. The designation "gastroblastoma" was adopted based on morphological similarities to other paediatric biphasic blastomatous neoplasms, notably pulmonary blastomas and nephroblastomas. There were only 29 documented cases in the medical literature including the present case, underscoring its rarity [2,3].

This entity predominantly affects young adults with a slight male predominance, though cases in elderly patients have been reported [1-4]. Clinical presentation varies considerably. The tumour typically originates from the gastric muscularis propria and may manifest as an endophytic mass, polypoid lesion, intramural nodule, or exophytic growth with multinodular or lobulated contours. The most frequent anatomical sites, in descending order, include the gastric antrum, greater curvature, lesser curvature, fundus, pylorus, and proximal stomach [2,3].

Histopathologically, gastroblastoma exhibits a characteristic biphasic pattern comprising varying proportions of uniform oval to spindle cells arranged in diffuse sheets, intermingled with uniform epithelial cells forming clusters, cords, and occasionally glandular structures. Mitotic activity is typically sparse, with generally low Ki67 proliferative indices. There is no hallmark immunophenotype discovered from literature. Immunohistochemically, both components commonly express CD10, CD56, and cytokeratins, while lacking expression of DOG1, CD34, calretinin, and chromogranin. In addition, the epithelial component expresses CAM5.2, CK7, EMA and CD99, while the mesenchymal component expresses vimentin [2-5]. The comparison of characteristic immunohistochemical profiles for gastroblastoma and the main differentials in this case is summarised in Table 1.

Table I: Comparison of immunohistochemical studies in gastroblastoma with the main differentials

*Immunohistochemical markers	Gastroblastoma	Plexiform fibromyoma	Carcinosarcoma	Gastrointestinal Stromal Tumour (GIST)	Synovial Sarcoma
	Epithelial component				
CK AE1/AE3	Focal positive	Negative	Positive (epithelial and spindle)	Negative	Positive (epithelial), Focal (spindle)
MNF116	Positive	NA	NA	NA	NA
EMA	Focal positive (weak)	NA	NA	NA	Focal positive
Synaptophysin	Focal positive	NA	Negative	NA	NA
	Spindle component				
Vimentin	Positive (spindle and glandular)	NA	Positive	NA	NA
	Epithelial and Spindle component				
CD10	Positive	Focal positive	NA	NA	NA
CD56	Positive	NA	NA	NA	Positive
SMA	Negative	Diffuse positive	Negative/Positive	Positive/Negative	NA
H caldesmon	Negative	Focal positive	Negative/Positive	Positive/Negative	Negative
Reticulin	Not Done	NA	Positive (surrounds individual cells)	NA	NA
p53	Not Done	NA	Positive	NA	NA
TLE-1	Negative	NA	NA	NA	Positive
β catenin	Negative	NA	NA	NA	Positive
Calretinin	Negative	NA	NA	NA	Positive
CD99	Focal positive	NA	NA	NA	Positive
CD34	Negative	Negative	NA	Positive	Negative
CD117 (C-kit)	Negative	Negative	NA	Positive	Focal positive
DOG 1	Negative	Negative	NA	Positive	Positive/Negative
S100	Negative	Negative	Negative/Positive	Negative/Positive	Negative/Positive
HMB45	Negative	NA	NA	NA	NA
GFAP	Negative	NA	NA	NA	NA
STAT 6	Negative	NA	NA	NA	NA
SATB2	Negative	NA	NA	NA	NA
P63	Negative	NA	NA	NA	NA
WT1	Negative	NA	NA	NA	Negative
SALL 4	Negative	NA	NA	NA	NA
BerEP4	Focal positive	NA	NA	NA	NA
#Molecular mutations (expected outcomes)	MALAT1-GLI1 gene fusion + others	MALAT1-GLI1 gene fusion, GLI1 polysomy	NA	KIT or PDGFRA mutations SDH-deficient	SS18-SSX1/2/4 rearrangement

*The panel of immunohistochemistry were done for the case with the actual result, for the stated differentials, results are based on their expected outcomes (ref. WHO Classification of Tumours Editorial Board. Digestive system tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2019 [cited 2025 September 12]. (WHO classification of tumours series, 5th ed.; vol. 1). Available from: https://tumourclassification.iarc.who.int/chapters/31.)

The molecular testing was not done, expected results were given in the table.

NA – Not applicable.

The molecular signature of gastroblastoma is characterised by the *MALAT1-GLI1* fusion gene, identified in most reported cases. However, this genetic alteration has also been identified in plexiform fibromyxoma, another rare gastric neoplasm. The key distinguishing feature in the latter is that it lacks the biphasic morphology. Additional reported molecular alterations in gastroblastoma also included *EWSR1-CTBP1, PTCH1-GLI2,* and *ACTB-GLI1* fusion genes. Differential diagnosis should encompass other biphasic epitheliomesenchymal neoplasms, particularly carcinosarcoma and synovial sarcoma, which are high-grade malignancies, typically exhibit more aggressive biological behaviour [2,4]. Hence, in combination of its rarity, deceptive appearance, lack of specific diagnostic signs makes gastroblastoma prone to being underdiagnosed. A comprehensive evaluation of both clinical and pathological features is crucial for its accurate diagnosis, along with a high degree of suspicion.

Surgical resection is generally considered curative, as gastroblastoma is regarded as a low-grade malignant tumour with low proliferative activity and typically indolent behaviour. However, owing to the limited number of reported cases, comprehensive understanding of the natural history and biological behaviour of this entity remains incomplete, necessitating long-term follow-up studies to accumulate additional clinical data [5]. A recent case report of gastroblastoma, systematically reviewed previously reported cases and documented metastatic disease in 4 patients during the surveillance period, in which one patient developed locoregional recurrence 51 months postoperatively. Given the potential for late recurrences, long-term surveillance is of paramount importance [2].

According to published reports, long-term surveillance has included clinical evaluation and imaging studies during the initial 2-year period, followed by annual assessment as clinically warranted. Endoscopic surveillance may be particularly valuable for monitoring anastomotic sites and facilitating early detection of local recurrence. Nevertheless, the risk factors that affect the prognosis or grade the malignancy have not been clearly defined due to the limited number of cases [2,5]. The present case had six monthly surveillance CT planned with clinical follow up as the treatment protocol.

CONCLUSION

Gastroblastoma represents an exceptionally rare gastric malignancy, with our report documenting the first case identified in Malaysia. This entity typically demonstrates indolent biological behaviour, and despite occasional documented instances of metastasis and recurrence in the literature, most cases demonstrate favourable clinical outcome. While definitive diagnosis ideally incorporates demonstration of characteristic molecular alterations, in resource-constrained settings, diagnosis primarily depends on recognition of the distinctive biphasic histomorphology, characterised by spindle cell elements and epithelial cell nests, supplemented by confirmatory immunohistochemical profiles. Current evidence, though limited, indicates surgical resection as the preferred treatment approach. The exceptional rarity of gastroblastoma has precluded comprehensive understanding of its clinicopathological characteristics, biological behaviour pattern, and optimal management strategies. Therefore, meticulous documentation of emerging cases and systematic collection of long-term follow-up data remain imperative to enhance our collective understanding of this uncommon gastric malignancy.

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