CASE REPORT

Extragonadal Germ Cell Tumor of Oesophagus in a Young Female Patient: A Case Report

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Background: This case report describes an exceptionally rare instance of a mixed germ cell tumor located in the esophagus of a young female patient.

Case Report: A 21-year-old woman without a family history of cancer presented with dysphagia and hepatomegaly. Histopathological and immunohistochemical findings of the esophageal mass were consistent with a mixed germ cell tumor, predominantly yolk sac tumor with minor choriocarcinoma-like differentiation. Despite extensive liver metastasis, the patient responded well to a modified BEP chemotherapy regimen.

Conclusion: This case highlights the aggressive nature of extragonadal germ cell tumors and the importance of the correct diagnosis and prompt initiation of chemotherapy.

Keywords: Extragonadal germ cell tumor; Esophagus; Mixed germ cell tumor; Yolk sac tumor; Chemotherapy; BEP regimen; Rare malignancy

Received 26 December 2024 | Revised 14 May 2025 | Accepted 14 May 2025

J Med Assoc Thai 2025;108(Suppl. 2):S164-167

Website: http://www.jmatonline.com

Extragonadal germ cell tumors (EGGCTs) are rare malignancies that account for a small fraction of all germ cell tumors, with most cases occurring in males[1,2]. EGGCTs can arise in various anatomical locations, such as the mediastinum, retroperitoneum, and brain, but cases in the esophagus are extremely uncommon, especially in women[2,3]. This case report highlights an exceptionally rare occurrence of a mixed germ cell tumor in the esophagus of a young female, adding to the very limited literature on EGGCTs in females, particularly in such an unusual location.

In women, extragonadal germ cell tumors are significantly less common than in men. Most EGGCTs in females have been reported in the mediastinum or the retroperitoneum, and they are often associated with other conditions, such as elevated tumor markers and distant metastases[3,4]. The median age at diagnosis in women tends to be in the 20s to 30s, similar to that observed in male patients[3]. However, the primary sites of EGGCTs in females are rarely the esophagus, making this case even more unique. The esophagus is an extremely rare site for these tumors, with only a few cases reported in the literature.

EGGCTs are often curable with chemotherapy, and early detection is crucial for improving patient outcomes. Here, we report a rare case of an esophageal mixed germ cell tumor in a 21-year-old female, with a focus on the diagnostic challenges and management strategies.

Case Report

A 21-year-old woman, without family history of cancer, presented with dysphagia and hepatomegaly. Initial laboratory revealed anemia and hepatitis (AST 114 U/L, ALT 44 U/L, TB 1.6 g/dl, DB 1.3 mg/dl). Esophagogastroduodenoscopy showed distal esophageal mass, and the biopsy revealed undifferentiated high-grade neoplasm (Figure 1A). The immunohistochemistry results were positive for SALL4, AFP, beta-hCG, and AE1/AE3 but negative for PLAP, OCT3/4, CD30, and CD117 (Figure 1B). Overall findings were consistent with mixed germ cell tumor, with predominant yolk sac tumor component and suspected minor choriocarcinoma-like differentiation. Patient's serum tumor markers were elevated: AFP 111775 IU/ml, Beta-HCG 91.1 mIU/ml, LDH 1396 U/L. The chest

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How to cite this article:

Siriboonpipattana W, Wirasorn K, Watcharenwong P, Charoenthanadhol T, Putraveephong S, Chaisuriya N, Chindaprasirt J. Extragonadal Germ Cell Tumor of Oesophagus in a Young Female Patient: A Case Report. J Med Assoc Thai 2025;108(Suppl. 2):S164-167.

DOI: 10.35755/jmedassocthai.2025.S02.S164-S167

and abdominal CT showed 2.6x2.8x5.2 cm distal esophageal mass and innumerable liver metastases (Figure 2A).

Shortly after diagnosis of extragonadal germ cell tumor, her liver function was deteriorated (AST 319 U/L, ALT 126 U/L, TB 4.8 g/dl, DB 4.5 mg/dl). The authors decided to start the first cycle of cisplatin and bleomycin in June 2023. Due to severely impaired liver function, etoposide was not started at that time. After 1st cycle of chemotherapy, her liver function was improved, and tumor markers were all decreased. Thus, she started on BEP regimen and continued up to 4 cycles.

After completing the four cycles of chemotherapy, the patient showed a marked reduction in tumor size (Figure 2B) and normalization of her serum tumor markers. Her liver function continued to improve, and she was discharged in stable condition. Unfortunately, after three cycles of chemotherapy, the disease progressed rapidly and her functional status was declined.

Discussion

Extragonadal germ cell tumors are rare malignancies, and the esophagus is an extraordinarily uncommon site for their development[1,5]. These tumors can present with a variety of symptoms depending on their location, and they often require a combination of imaging studies, biopsy, and immunohistochemical analysis for accurate diagnosis[4,6].

Gastrointestinal tract is not a typical site for germ cell tumors. Most of the reported cases were metastasis from primary testicular tumors[7-9]. The esophagus is even more unusual than other gastrointestinal organs, and the rarity of this occurrence makes this case particularly exceptional. As esophageal malignancies are more commonly associated with squamous cell carcinoma or adenocarcinoma, identifying a germ cell tumor in this location presents a unique diagnostic challenge. This case adds to the very limited body of literature regarding EGGCTs in the esophagus, offering new insight into their clinical presentation and management.

In one of the few documented cases of EGGCT in the esophagus, a 62-year-old male presented with difficulty in swallowing, and imaging revealed an abnormal thickening in the distal esophagus[10]. Histological diagnosis showed poorly differentiated carcinoma with yolk-sac tumor, confirmed by positive isochromosome 12p, and the patient had elevated AFP and beta-hCG levels. This case shares similarities with our patient, as both had liver metastasis at

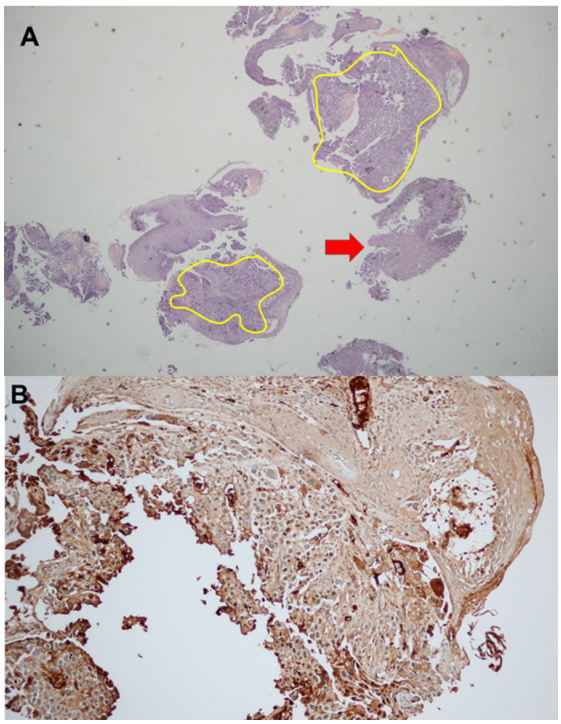

Figure 1. A) Fragments of esophageal mucosa containing sheets of atypical cells in the submucosal area (Area) associated with necrosis (Arrow), B) Expression of hepatocytic-like differentiation markers, increasing expression of AFP that associated with high AFP level in the serum.

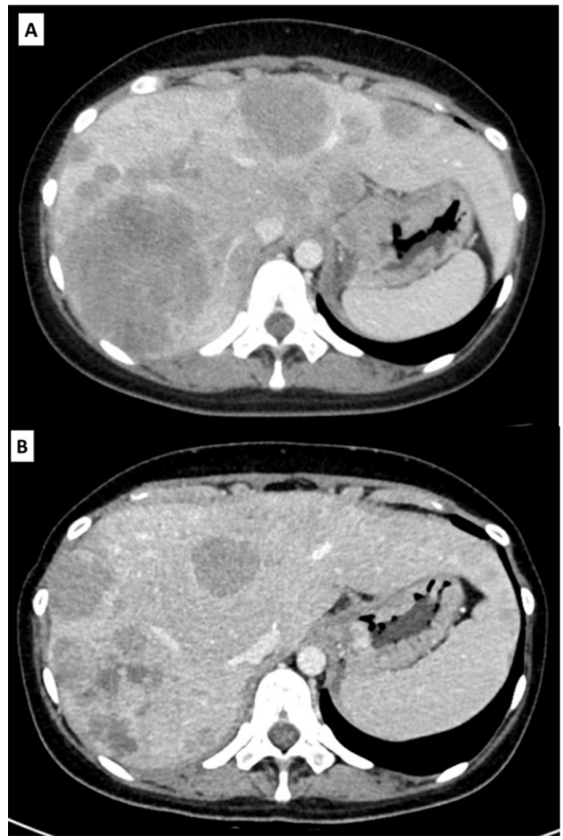

Figure 2. A) Multiple liver metastasis with the largest lesion in right lobe liver. B) Decreased size of liver metastasis after chemotherapy.

presentation and had a dominant yolk sac tumor component. Due to limitation, isochromosome 12p analysis was not performed in our case. Nevertheless, if possible, the integration of this technique would have contributed to the diagnostic certainty of the case.

The management of EGGCTs typically involves chemotherapy with agents such as cisplatin, bleomycin, and etoposide (BEP regimen), which has shown high efficacy in germ cell tumor treatment. Early diagnosis and timely initiation of chemotherapy are key factors in improving the prognosis of patients with these rare tumors.

One key aspect of managing EGGCTs, particularly in the case of liver metastases, is the timely initiation of chemotherapy. Delays in treatment can lead to progression of the disease, worsening of liver function, and a decline in overall prognosis. Our patient's rapid response to the first cycle of chemotherapy, with marked improvements in liver function and tumor markers, aligns with the favorable outcomes seen in other studies of women with extragonadal germ cell tumors. Moreover, despite the aggressive nature of the disease, the fact that this patient is now stable and in remission after completing chemotherapy further underscores the potential for cure with appropriate treatment.

This case highlights the importance of considering extragonadal germ cell tumors in the differential diagnosis of esophageal masses, especially in young patients presenting with unexplained symptoms. The favorable outcome in this patient after chemotherapy further emphasizes the potential for curability even in the presence of distant metastases.

Conclusion

Esophageal extragonadal germ cell tumors are extremely rare, and this case represents an unusual occurrence of a mixed germ cell tumor at a primary site in the esophagus. Timely diagnosis and prompt chemotherapy with the BEP regimen resulted in a positive clinical outcome. This case underscores the importance of early intervention and accurate diagnosis in improving the prognosis for patients with rare and aggressive tumors like EGGCTs.

What is already known on this topic?

EGGCT is extremely rare in young women especially in the gastrointestinal tract. It is usually responses well to the standard chemotherapy with favourable outcomes.

What this study adds?

Physicians should cconsider extragonadal germ cell tumors in the differential diagnosis of esophageal masses, especially in young patients presenting with unexplained symptoms. Early intervention and accurate diagnosis help improve the prognosis for patients with rare and aggressive tumors like EGGCTs.

Ethics statement

Written informed consents were obtained from all patients. This study was approved by the Institutional Review Board of the Khon Kaen University Ethics Committee for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines (HE591330).

Acknowledgements

The present study supported by Research of Khon Kaen University (RP68-5-001).

Conflicts of interest

The authors declare no conflict of interest.

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