

Case Report

Peritoneal carcinomatosis of unknown primary site: a case report of metastatic mucinous adenocarcinoma

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ABSTRACT

Metastatic mucinous adenocarcinoma, a distinct subtype associated with extensive mucin production presents diagnostic and therapeutic challenges. This case involves a 21-year-old male with high-grade mucinous adenocarcinoma manifesting as cancer of unknown primary site, characterized by widespread peritoneal carcinomatosis and rapid progression despite systemic chemotherapy. The tumor's aggressive behavior and thromboembolic complications underscore the need for tailored, multidisciplinary management strategies.

Keywords: Mucinous adenocarcinoma, Cancer of unknown primary, Peritoneal carcinomatosis, Thromboembolism, Tumor markers

INTRODUCTION

Mucinous adenocarcinoma (MAC), also called colloid carcinoma, is a distinct subtype of adenocarcinoma characterized by over 50% extracellular mucin, mainly produced by goblet cells in the GI tract, which aid in lubrication and immune defense.¹⁻⁶ Tumors with 10-50% mucin are classified as mucinous with cells suspended in mucus, often arising de novo or with precursor lesions like adenomas, especially in colorectal cancer, where 10-20% are mucinous and tend to have more aggressive features such as lymphovascular invasion and proximal colon localization.^{1,2,7-9} The incidence is higher among females and younger patients, with advanced disease stages and peritoneal spread.⁸ Diagnosing primary tumors can be challenging; often, metastases are identified first, and cases with extensive peritoneal involvement may be classified as cancer of unknown primary (CUP), which is highly aggressive and often diagnosed post-mortem. Diagnostic procedures include imaging (CT, PET-CT), laparoscopy, and immunohistochemistry (IHC) to identify tumor origin, though primary sites remain

unknown in 20-45% of cases after extensive testing.^{10,11} Peritoneal dissemination can follow patterns like random proximal distribution, complete redistribution, or widespread distribution, which influence surgical planning.^{12,13} Treatment strategies include cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemoperfusion (HIPEC), a standard for low-grade appendiceal mucinous tumors, involving heat-enhanced chemotherapy delivery with low mortality but significant morbidity.^{12,14} Candidate selection for CRS/HIPEC depends on disease extent, with many patients only receiving systemic chemotherapy, such as CAPOX or XELIRI, which improve response and survival but are less effective in high-grade or lymph node-positive tumors.^{12,15} Despite advances, prognosis remains poor in high-grade cases, especially with extraperitoneal spread or extensive disease.¹⁴

CASE REPORT

A 21-year-old male presented with complains of abdominal enlargement, general weakness and weight

loss. He was hospitalized due to intermittent abdominal pain during the month with an emphasize on the right hypochondrium. The patient underwent laparocentesis where 2900 ml volume of ascites was drained and sent for cytological examination.

The general condition of the patient was satisfactory. The skin was pale. The peripheral lymph nodes were not enlarged; they were palpated due to the asthenic physique of the patient. The abdomen, it was soft, painless, enlarged in size due to ascites upon palpation and no signs of peritoneal symptoms were detected. The liver was not determined due to ascites. The symptom of pounding was negative. Auscultation of the lungs revealed vesicular breath sounds throughout all areas of the lung. The heart tones were clear and rhythmic. The blood pressure and heart rate were normal, 120/80 mmHg and 72 beats/min respectively. The stool was unremarkable. And diuresis was within normal limits.

Investigations

The patient underwent imaging studies for a more detailed evaluation. A CT scan of the abdomen and pelvis revealed ascites along with numerous peritoneal implants. The CT of the chest demonstrated a solid nodule measuring 5mm with a glass frosted component, and ribbon-shaped thickening of the pleura in segments S8-10.6 on the left and S6-10 on the right. There was no enlargement of the mediastinal or intra-pulmonary lymph nodes. Supradiaphragmatic nodular lesions were observed on both sides, with the right-sided lymph node measuring up to 11×6 mm and the left side up to 23×12 mm, while pericardial nodules reached up to 27×9 mm. MRI identified the presence of free fluid in the pleural cavities, with a layer of up to 7mm on the right and 13mm on the left. Additionally, an uncountable number of tissue formations were scattered throughout the abdomen, involving the peritoneum, large omentum, mesentery, and the surfaces of the liver and spleen.

Immunoassays were performed to further characterize the disease, with results presented in Table 1. During diagnostic laparoscopy, approximately 4 to 5 liters of ascitic fluid were aspirated and sent for cytological analysis. The parietal and visceral peritoneum in visible areas exhibited overgrowth of whitish tumor masses, rendering the abdominal organs indistinguishable, as shown in Figure 1. An additional trocar was inserted in the right mesogastric region to facilitate biopsy of the peritoneum and tumor masses from various locations. Histopathological examination revealed groups of large, rounded cells loaded with mucin, featuring paracentral nuclei among ‘lakes of mucin’. In some cells, the nucleus was displaced to the periphery, creating ring-shaped structures. These findings suggested high-grade mucinous neoplasia of the peritoneum with ring-shaped cells.

To determine the most effective treatment regimen, considering tumor prevalence, clinical presentation, and

histology, molecular genetic testing was recommended to identify mutations in KRAS, NRAS, BRAF genes, as well as Her2 expression and microsatellite instability (MSI). However, no mutations were detected in the specific genes tested.

Table 1: Results of immunoassays.

Tumor Markers	Results	Normal range
Alpha fetoprotein	Normal	<10 ng/ml
Lactate dehydrogenase	239	140-280 U/l
Prostate specific antigen	0.779	<4.0 ng/ml
CEA	36	<5 ng/ml
CA-125	89.8	<35 U/ml
CA 19-9	2434	<37 U/ml
HCG	Negative	<5 mIU/ml

The interpretation of these results suggests that a negative HCG rules out germ cell tumors and trophoblastic disease, while normal AFP levels indicate no evidence of hepatocellular carcinoma or germ cell tumors. Normal LDH results help narrow the differential diagnosis, as elevations are commonly seen in lymphomas and testicular cancers. A PSA within the normal range suggests a low likelihood of prostate cancer. Elevated CEA levels may point toward colorectal cancer but can also be associated with other malignancies such as breast, lung, pancreatic and gastric cancers. Increased CA-125 levels are indicative of hepatocellular carcinoma, pancreatic malignancies, and rarely, malignant mesothelioma. Lastly, significant elevation of CA 19-9 is typically associated with pancreatic cancer but may also suggest other gastrointestinal cancers.

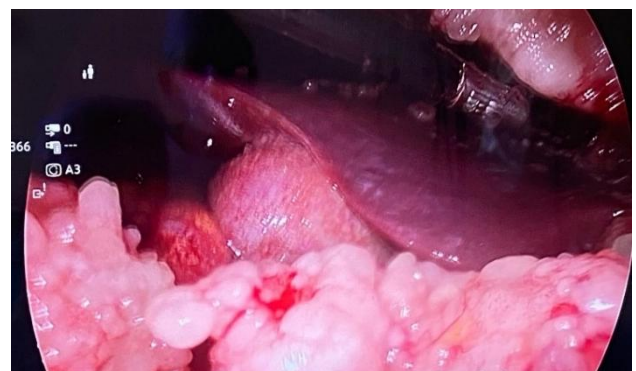


Figure 1: Image obtained during the diagnostic laparoscopy, revealing the presence of whitish tumor masses on the surface of the intra-abdominal organs and the peritoneum.

Management

Oncology and surgery department consultations were performed for the patient, and a multidisciplinary approach was discussed. The patient was provided the

diagnosis of Metastasis of mucinous adenocarcinoma to peritoneum with unknown primary site TxNxM1, IV stage after thorough counseling of his imaging and histopathological reports.

The patient was advised to undergo chemotherapy using the CAPOX regimen following the consultation decision. After three courses of chemotherapy, patient underwent a follow-up CT scan for assessment. The retroperitoneal, pelvic, and mesenteric tissues are compressed and thinned due to a significant accumulation of fluid, with a component along the peritoneal surfaces resembling tissue density (20-25 HU). This is observed along the diaphragm domes, jejunal and ileal loops, and the colon, with the largest thickness in the greater omentum reaching 34 mm (up from 25 mm), primarily with contrast accumulation noted in the venous phase. The right lobe of the liver measures up to 109 mm along the mid-clavicular line, with deformed contours indicating areas of parenchymal indentation due to a subcapsular component up to 19 mm thick. The spleen measures 40 x 107 mm and retains its usual shape, but its posterior-outer contour is also deformed by a cystic-solid component measuring up to 10 mm thick (previously 7 mm). The CT scan depicted the progression of disease during chemotherapy.

Table 2: Results of Coagulogram.

Parameters	Results	Normal range
APTT (s)	29.8	22-35
Prothrombin time (s)	18	9.4-12.5
Prothrombin activity complex (%)	47	83-150
MHO SYSMEX (INR)	1.61	0.85-1.3
Fibrinogen (g/l)	14.75	2.7-4.7
D-Dimer (ng/ml)	7.08	

There are no changes in the APTT and D-dimer levels. The following parameters reveal abnormalities.

In accordance with the progression of the disease and the recommendations from consultations, the patient was administered three courses of chemotherapy along with targeted therapy, employing the XELIRI regimen. A follow-up CT scan with contrast conducted after three courses of XELIRI chemotherapy revealed the development of a significant complication, specifically pulmonary artery thromboembolism (PE) involving large, medium, and small branches on the right side, as well as medium and small branches on the left side. Additionally, thrombosis was observed in the deep veins (DVT) of the right limb, including the popliteal and sural veins. The results of the relevant coagulogram is presented in Table 2. Anemia related to the underlying neoplastic process was also identified. Based on the findings of the follow-up CT scan, disease progression was observed alongside the identified complications. Consequently, consulting specialists recommended the ongoing XELIRI chemotherapy regimen and the addition of rivaroxaban to both treat the current thromboembolic events and prevent

future recurrences. Considering the pulmonary embolism and deep vein thrombosis, it was also advised to perform a follow-up ultrasound of the blood vessels to evaluate the resolution of the deep vein thrombosis contributing to the pulmonary embolism.

Extended prothrombin time (PT) and low prothrombin activity can indicate coagulopathy due to liver disease, vitamin K deficiency or anticoagulant use. An elevated INR suggests a higher bleeding risk, often seen in anticoagulated patients or liver failure. Elevated fibrinogen levels may reflect inflammation, tissue injury or hypercoagulable states emphasizing the complex relationship between coagulation and inflammation in various conditions.

DISCUSSION

This case highlights the clinical challenges of high-grade mucinous adenocarcinoma presenting as cancer of unknown primary (CUP) with extensive peritoneal carcinomatosis. The patient's initial symptoms, including ascites and widespread abdominal involvement, reflect the aggressive nature of mucinous tumors, which tend to extensively spread within the peritoneal cavity.^{8,10,11} Diagnostic workup involved comprehensive history, physical exam, imaging (contrast-enhanced CT, MRI), and laparoscopic biopsy, which confirmed mucinous adenocarcinoma with signet ring cells, but the primary tumor remained unidentified, a common feature in CUP cases.^{1,11} Serum markers such as CEA and CA 19-9 suggested a gastrointestinal origin, but were non-specific.¹¹ Molecular testing for mutations (KRAS, BRAF, MSI) was inconclusive. The disease progressed rapidly despite systemic chemotherapy with CAPOX and later XELIRI, demonstrating resistance typical of high-grade mucinous tumors.^{2,8,10} The patient also developed thromboembolic complications, including pulmonary embolism and deep vein thrombosis, linked to hypercoagulability common in advanced cancer (paraneoplastic hypercoagulable state). Imaging revealed widespread dissemination of tumor involving peritoneal surfaces, consistent with the Widespread Cancer Distribution pattern, characteristic of mucus-producing malignancies.¹³ While cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemoperfusion (HIPEC) is effective for select low-grade cases, extensive disease and complications like embolism precluded surgical intervention in this patient. Overall, the case underscores the limited response of high-grade mucinous adenocarcinoma to conventional therapies, highlighting the need for innovative or alternative treatment approaches specifically designed for this subtype.

CONCLUSION

This case report of high-grade mucinous adenocarcinoma presenting as cancer of unknown primary with extensive peritoneal carcinomatosis exemplifies the significant diagnostic and therapeutic challenges posed by this

aggressive malignancy. The patient's widespread peritoneal involvement, lack of identifiable primary site despite extensive workup, and rapid disease progression on standard systemic chemotherapy (CAPOX and XELIRI) highlight the limitations of current approaches. The development of severe thromboembolic complications further underscores the complex clinical course and increased risks associated with advanced disease and systemic treatment in this context. The observed widespread cancer distribution pattern is consistent with the aggressive, mucus-producing nature of the tumor. This case strongly suggests that high-grade mucinous adenocarcinomas, particularly in the setting of CUP and extensive peritoneal spread, may represent a distinct clinical and biological entity with reduced chemosensitivity and a heightened prothrombotic tendency, necessitating further research to elucidate underlying mechanisms and develop more effective, potentially subtype-specific, treatment strategies. The case also reinforces the need for careful patient selection for aggressive interventions like CRS/HIPEC and highlights the importance of proactive management of thrombotic risk in this patient population.

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