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CASE REPORT

Positive DOG-1 GIST Malignant in Colon with Metastasis in Paraovary Tissues and Ascites Fluids

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Abstract

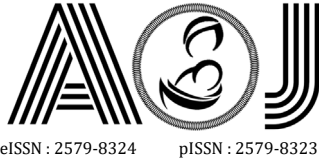
Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm of gastrointestinal tract that originate from Interstitial Cell of Cajal (ICC). The correct diagnosis of GISTs is important for therapeutic reasons of imatinib. Recently, DOG-1 has been introduced as an important diagnostic marker with high sensitivity and specificity. We report a case of 40 years old woman with pain and swollen stomach in left lower quadrant since four months before she came to the hospital. Ultrasound examination showed hypoechoic lesion in the posterior of uterus and ascites. Paraovarian mass attached to the transverse colon and ascites was found on surgery. Histopathology diagnosis was a mesenchymal stromal tumour suggestive malignant GIST. Cytological examination of ascites fluid show malignancy metastases. Immunohistochemistry showed negative for c-kit and positive for DOG-1, the conclusion is a GIST. Immunohistochemistry examinations are important to make definitive diagnosis for GIST. C-kit-negative GISTs are still rare, but definitive diagnosis must be made because related to target therapy. DOG-1 has been proven in 89% of c-kit-negative GIST and claimed more sensitive and specific.

Keywords: GIST, c-kit, DOG-1, ICC, paraovary

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most mesenchymal neoplasm found in the digestive tract originating from the Interstitial Cell of Cajal (ICC).^{1,2} The estimated incidence is about 2 cases per 100,000 people per year. The most common age at diagnosis is 50-60 years. There is no gender predilection in these tumors in general and is very rare in children. Before the 1990s the data relating to the GIST incident was not very accurate because GIST was not well known at the time. Now GIST is well known and epidemiological data on GIST are already abundant. An epidemiological survey in the United States recorded a reported GIST of 0.32 per 100,000 population and a prevalence of 1.62 per 100,000 population per year over a 15-year period.^{3,4}

GIST can be found primarily along the gastrointestinal tract with various symptoms that vary depending on the origin of the tumor such as abdominal pain, gastrointestinal bleeding



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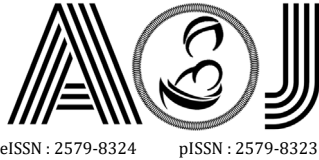
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to acute abdomen such as in cases of perforation and obstruction.⁵ GIST is most often present in the stomach (around 60%), jejunum and ileum is the second largest place (about 30%), followed by the duodenum (about 5%), colorectum (about 4%) and the esophagus or appendix (1%). GIST can appear as a well-demarcated tumor, most often from the propria muscular layer of the gastrointestinal tract. Tumor size varies. These tumors have fleshy pink or tan-white cut surfaces with foci of bleeding, central cystic degeneration or necrosis.⁶ A small (less than 5%) cases of GIST can occur primarily outside the gastrointestinal tract (without evidence presence of GIST along the gastrointestinal tract) such as mesentery, omentum, peritoneum, retroperitoneum, uterus, ovaries and bladder known as Extra gastrointestinal tumor (EGIST).⁵ The histological appearance of GIST varies greatly and sometimes this variation depends on the location of the tumor. Most GISTs appear as spindle patterns (60-70%), while epithelioid cytology is seen in 20-30% of cases and pleomorphic patterns are rare (<5%). GIST often grows between smooth muscle fibers, often causing micronodular and plexiform patterns.⁴

Hematogenous metastases can generally occur in the liver and less commonly in the bones and lungs. Very rare GIST metastases have been reported to peripheral soft tissues such as the arm, axilla and abdominal wall.⁴ In such cases diagnosis is often difficult, especially in cases where the history of GIST is previously unknown or interrupted.⁴

Abdominal ultrasound examination is an initial imaging test that can be done in the investigation of patients with abdominal pain or mass associated with this GIST, but often tumors are found to be so large that sometimes it is difficult to identify the organ from which this tumor originated. Preoperative radiological examination such as CT (Computerized Tomography) scan or MRI (Magnetic resonance imaging) can be very helpful especially in determining the configuration, expansion and relationship of tumors with adjacent organs. CT scans usually can also provide an assessment of metastases from these tumors.^{4,7}

Gastrointestinal stromal tumor originates from Interstitial Cell of Cajal (ICC), a pacemaker cell that controls the peristalsis of the gastrointestinal tract.⁸ These cells are cells in the gastrointestinal tract that show CD117 immunophenotype. Most GISTs have proto-oncogenic c-KIT (CD117) mutations that encode the CD117 protein, transmembrane tyrosine kinase receptors.^{3,9} KIT protein is detected by immunohistochemical staining of approximately 80%. However, a small portion of GIST shows immunonegativity for CD117. The platelet-derived growth factor receptor- α (PDGFRA) gene is detected around 10% in GIST.^{3,9} The correct diagnosis for negative GIST CD117 is very important because more than two-thirds of cases are still sensitive to imatinib which is an effective target therapy for GIST.³ Immunohistochemical staining is considered important for diagnosis, but if the tumor is negative for KIT, CD34, S-100, and smooth muscle actin (SMA), definitive diagnosis is often challenging. It has been reported that DOG1 allows the diagnosis of KIT-negative nuclei, so



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this molecule can be an alternative to GIST with negative CD117. DOG1 has been shown to be positive in 89% of GIST without CD117 or PDGFRA mutations. In addition, DOG1 is claimed to be more sensitive and specific than CD117 in many studies, although in some studies there are still conflicting results.³

GIST has a broad spectrum of pathological patterns and biological traits ranging from typical benign and accidental diagnoses to extremely malignant forms. The relative frequency of benign and malignant GISTs varies. Although the prediction of benign and malignant a tumor can be defined by histological criteria, in certain cases sometimes the prediction of potential biological properties of this tumor can be difficult especially for cases of advanced tumors. Classically there are three criteria used to determine Malignant GIST, and also as a known parameter to find out the potential outcome of this GIST which includes the location of tumor origin (small intestine tumors and rectal tumors more aggressive than gastric tumors), tumor size (> 5 cm) and mitotic figures (> 5/50 hpf). Cytological examination alone can determine whether the tumor is benign or malignant, but has not been able to distinguish GIST from other gastrointestinal tumors. DOG 1 mutation analysis has been reported as one of the prognostic factors in both early and advance stage cases.¹⁰⁻¹³ Most GISTs are mesenchymal tumors that express KIT. There is also a small group of GIST that shows mutation activation in PDGFRA.¹⁴ The discovery of KIT expression as a diagnostic sign of GIST not only causes a change in criteria in the classification of GIST, but can also explain the histogenesis of this tumor. The equation between KIT immunoreactivity and ultrastructural appearance between GIST and intestinal pacemaker, the interstitial cell of cajal (ICC), shows that GIST originates from or differentiates from ICC derivatives.¹⁴

We report a case entitled Metastasis Malignant GIST DOG1 positive in ascitic fluid and paraovary fluid. Difficulties and challenges in the diagnosis and management of these patients will be discussed later in the case report.

CASE REPORT

A female patient, aged 40 years, sent a delivery oncology clinic M. Djamil Padang Hospital with a clinical diagnosis of ovarian tumors and sectio scars once. Based on the history of the disease obtained information that the patient initially felt uncomfortable in the lower left abdomen, often bloating, pain and stomach began to enlarge, nausea was absent, vomiting was absent, weight loss was present, bowel movements and normal urination. Past medical history, no history of hypertension, diabetes, heart, lung, kidney and liver disease. Family history of disease There is no history of infectious disease, malignancy and heredity.

Physical examination found that the general condition looked moderate pain, cooperative compositional awareness, systemic examination found within normal limits. On abdominal examination found no tenderness, no loose pain. Examination of the vaginal

toucher and rectal toucher results in palpable mass of suspected mass outside the uterus between the intestine and uterus.

Supporting examinations that have been carried out are abdominal ultrasound examination and abdominal CT scan. Abdominal ultrasound examination (Figure 1), the results obtained: Uterus antefleksi measuring $\pm 5 \times 3 \times 3.5$ cm, Fluid (+). Inhomogenic hypoechoic lesions posteriorly of the uterus, lesion size $6.6 \times 3.4 \times 3.5$ cm, suspicious ovarian carcinoma. After that, an abdominal CT scan is performed with the appearance of a mass inhomogenous density with an indefinite border on the posterior pelvic wall suspect myoma uteri.



Figure 1. Abdominal ultrasound, inhomogenous hypoechoic lesions on the posterior side of the uterus.

Hysterectomies are performed in patients and optimal debulking is indicated by ovarian tumors and a mass appears attached to the transverse colon. Tissue resulting from surgery and ascitic fluid is examined at the Anatomic Pathology (PA) laboratory.

Macroscopically (Figure 2) paraovary tumor labeling tissue, appearing in pieces of dense brownish white tissue with a size $13 \times 8 \times 2.5$ cm in brownish white cross section, dense springy there is a hollow part of 0.5-1.5 cm in diameter. On the mass label in the transversum colon, in the form of a piece of dense white fat brownish intestinal tissue with a size of $4 \times 3 \times 2$ cm, visible cross-section of the mass on the outer wall of the intestine, 3 cm in diameter. While the ascitic fluid received ± 8 cc volume is reddish yellow, runny.

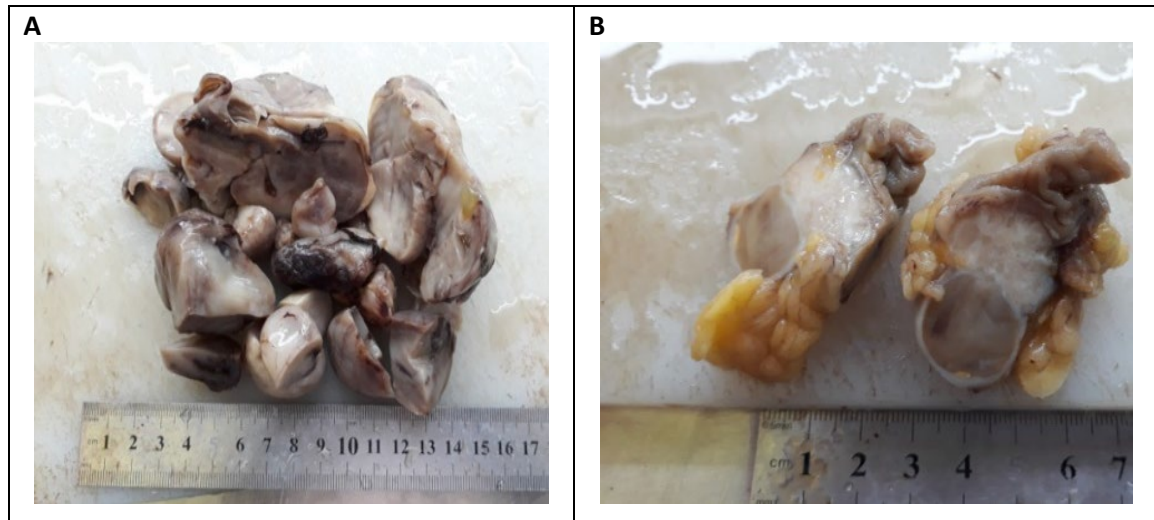


Figure 2. Macroscopic. A. Label the paraovary tumor. B. The mass label in the transverse colum.

Microscopic features of paraovary label tumors appear to be pieces of tissue composed of proliferation of cells with rounded-oval nuclei partly hyperchromatic, partly vesicular, coarse chromatin, real nucleus children, atypical mitosis can be found. These cells are arranged diffusely, including the appearance of hyperemic blood vessels. The diagnosis of anatomic pathology is mesenchymal stromal tumor suggestive malignant GIST. In white masses in uterine and ovarian label tissue, microscopic pieces of tubal tissue are seen, in other parts nodules contain proliferation of cells as in paraovary tumors. Microscopic masses in the transverse colon appear pieces of colon tissue with mucosal surfaces coated by goblet-celled columnar epithelium growing to form regular kripti. The lamina propia is called lymphocytes and plasma cells. Underneath the submucosal layer, tumor nodules consist of the proliferation of spindle cells with a round-oval nucleus, coarse chromatin, a partially real nucleus. These cells are composed of solid separated by connective tissue septa including capillaries. The diagnosis of anatomic pathology is mesenchymal stromal tumor suggestive of malignant GIST (Figure 3). Recommendations for CD117 (c-kit) and DOG1 examinations. Microscopic of ascitic fluid that is grouping of cells with increased N / C ratio, round-oval nucleus, hyperchromatic. The impression of anatomic pathology is metastasis of a malignancy (Figure 4). After that the CD117 (c-kit) and DOG1 tests were performed with negative results for CD117 and positive for DOG1, the conclusion being GIST. (Figure 5)

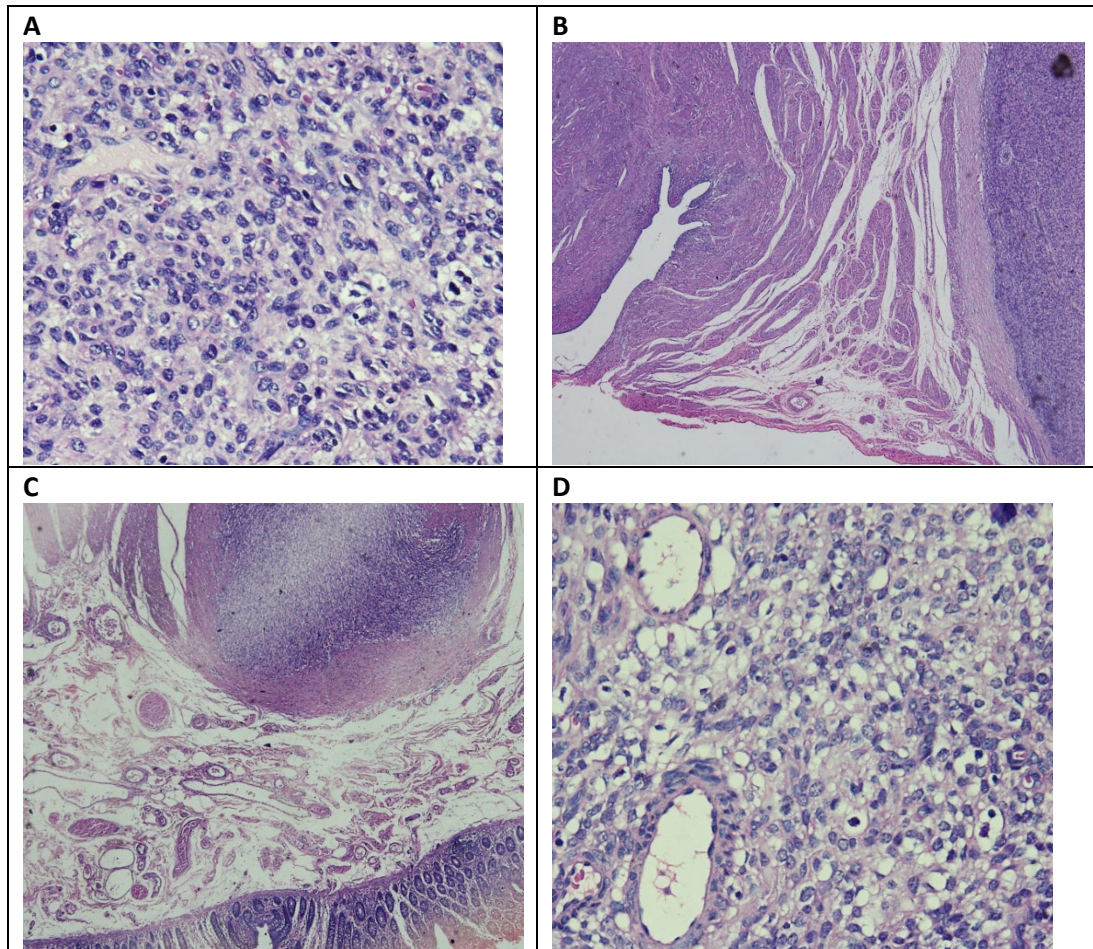


Figure 3. Microscopic. A. Paraovary tumors (HE 40x10). B. Visible pieces of tubal tissue, and tumor nodules such as in paraovarian tumors (HE 4x10) C. Mass in the transverse colon, visible pieces of colon tissue, beneath the submucosal layer appear tumor nodules in a solid arrangement separated by septa connective tissue (HE 4x10). D. (HE 40x10).

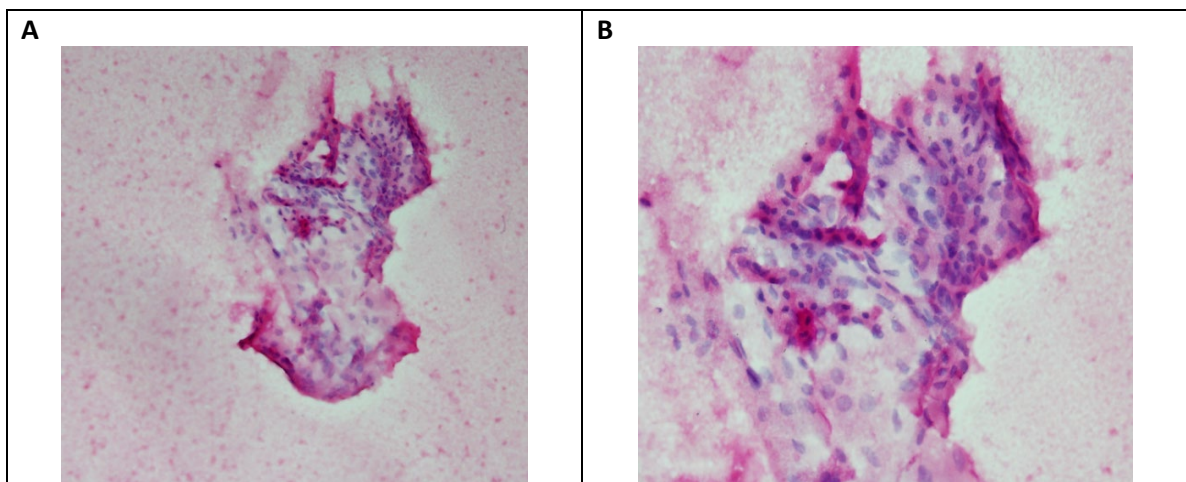


Figure 4. Ascites fluid cytology. A. Cell clusters appear with an increased N / C ratio, round-oval nucleus, hyperchromatic (20x10) .B. (40x10).

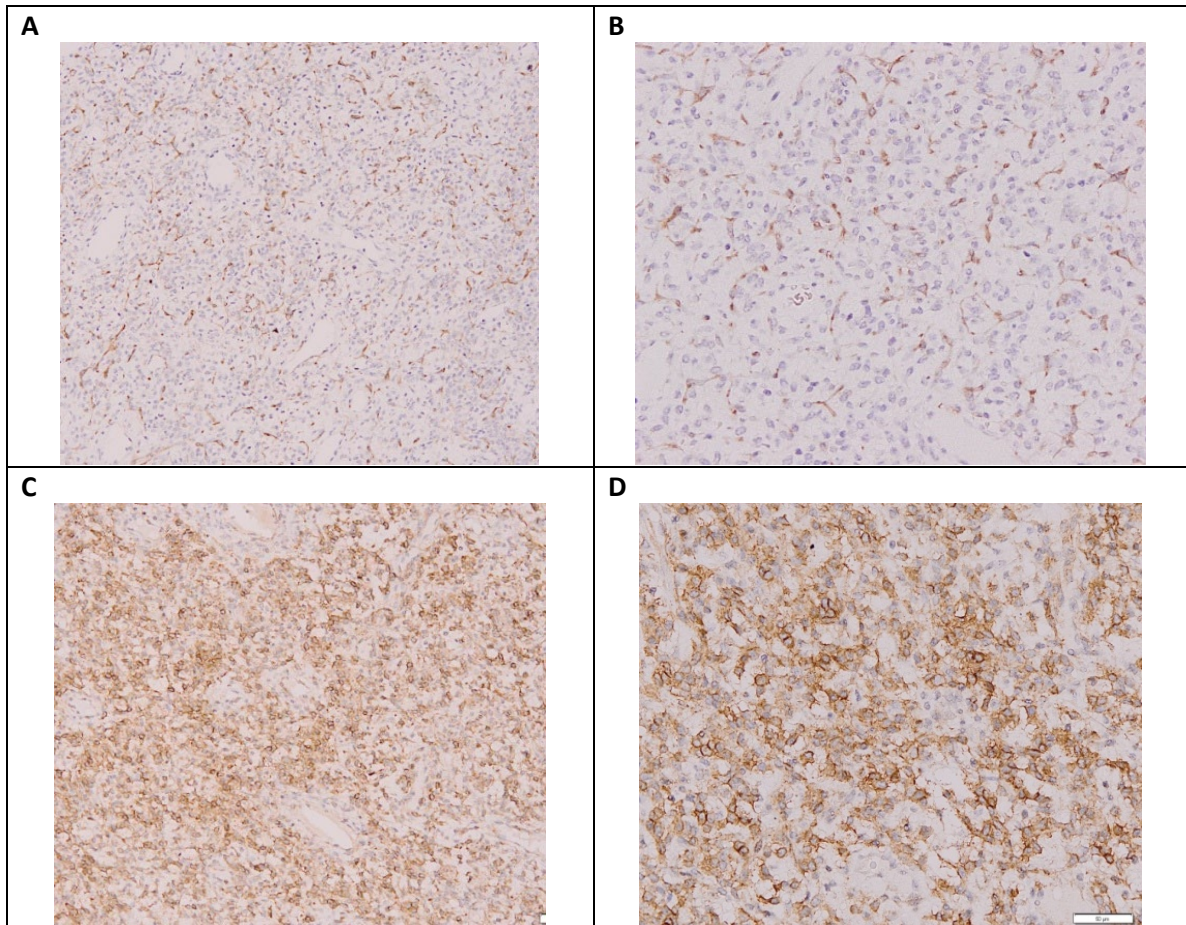


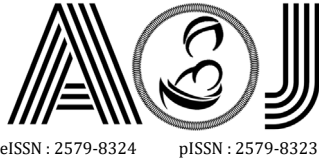
Figure 5. A. Negative C-kit immunohistochemical staining in cytoplasm (100x). B. (200x) .C. Immunohistochemical staining of positive Dog1 on cell membranes and cytoplasm (100x) .D. (200x).

DISCUSSION

A case of a Malignant GIST Metastases was reported in ascitic fluid and paraovary fluid in a 40-year-old female patient. This case occurred at a younger age. Based on the literature the most common age at diagnosis is 50-60 years. There is no gender predilection in these tumors in general and is very rare in children.^{3,4}

Patients present with complaints of discomfort in the lower left abdomen, often bloating, pain and stomach begin to enlarge since about 4 months before coming to the hospital. This is in accordance with the findings of the patient's surgery in which a mass was found in the paraovary and around the transverse colon and ascites fluid was found. GIST can be found primarily along the gastrointestinal tract with a variety of symptoms that vary depending on the origin of the tumor such as abdominal pain, gastrointestinal bleeding to acute abdomen such as in cases of perforation and obstruction.⁶

Abdominal ultrasound was performed before the patient was operated with the result: an anteflected uterus measuring +/- 5 X 3 X 3.5 cm. Fluid (+). Inhomogenic hypoechoic lesions



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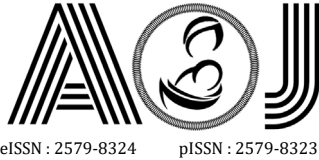
posteriorly of the uterus, lesion size 6.6 X 3.4 X 3.5 cm, Suspected ovarian carcinoma impression. There is a difference between the estimated origin of the tumor on ultrasound and the surgical findings. Abdominal ultrasound examination is an initial imaging test that can be done in the investigation of patients with abdominal pain or mass associated with this GIST, but often tumors are found to be so large that it is sometimes difficult to identify the organ from which this tumor originates.^{4,7}

This patient had also undergone a previous CT scan with the results showing a picture of a mass with inhomogenous density with no firm boundary in the posterior pelvic wall suspect myoma uteri. In this case the CT scan is also less precise in determining the actual location of the tumor. Preoperative radiological examinations such as CT (Computerized Tomography) scans can determine the configuration, expansion and relationship of tumors with adjacent organs. CT scans are usually also able to provide an assessment of the metastases from these tumors.^{4,7} This can happen because the size of the tumor is large enough and the density is inhomogenous causing the boundaries between organs become unclear so determining the actual origin of the tumor location becomes incorrect.

Intraoperative in this patient was found mass in the transverse colon so that obgyn joint and digestive surgery were performed. After histopathological examination, histopathological diagnosis of mesenchymal stromal tumor suggestive of malignant GIST was obtained, both for tumors in the ovaries and those found in the transverse colon. To confirm this histopathological diagnosis, CD11 (c-kit) and DOG1 tests were performed with negative results for CD117 and positive for DOG1, the conclusion being GIST. This is interesting because cases of GIST with negative c-Kit are still very rare but on the other hand a definite diagnosis of GIST must be made because it is related to the target therapy of the GIST.

DOG-1 has been shown to be positive in 89% of GIST without CD117 or PDGFRA mutations.³ In addition, DOG-1 is claimed to be more sensitive and specific than CD117 in many studies, with some conflicting results in the literature.¹⁵ About one-third to half of CD117 GIST-negative reported positive for DOG-1. Although the diagnostic utility of DOG-1 for accurate diagnosis of GIST is being studied extensively, its prognostic role is still little evaluated in the literature. Some recent studies suggest that DOG1 expression influences prognosis with some conflicting results.¹⁵

Cytological examination was also carried out on the ascitic fluid of this patient with an anatomic pathology diagnosis of a metastatic malignancy. Ascites is an accumulation of pathological fluid in the abdominal cavity. The most common cancers associated with ascites are ovarian adenocarcinomas, mammaes, colon, stomach and pancreas. There are many potential causes of ascites in cancer patients, including peritoneal carcinomatosis, lymphatic system obstruction by malignancy, portal venous thrombosis, increased portal venous pressure, congestive heart failure, constrictive pericarditis, nephrotic syndrome and peritoneal



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infection.¹⁸ The possibility of ascitic fluid in these patients is a peritoneal carcinomatosis. However cytological examination cannot distinguish GIST from other intra-abdominal tumors. Ascites cytology examination usually can be indicated for prognosis and therapy.¹⁸

A small portion (less than 5%) of GIST cases can occur primarily outside the gastrointestinal tract (without evidence of GIST along the gastrointestinal tract) such as, mesentery, omentum, peritoneum, retroperitoneum, uterus, ovaries and bladder known as Extra gastrointestinal tumors (eg, gastrointestinal tumors) EGIST).⁵ But however the GIST that grows in the mesentery, omentum and peritoneum is more often a metastasis.⁴

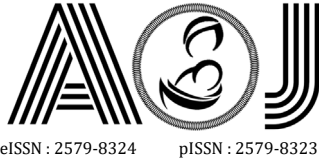
In this patient macroscopic tumors in the paraovary form pieces of solid brownish white tissue with a size of 13 x 8 x 2.5 cm while tumors in the transverse colon form a piece of brownish white intestinal tissue with a solid, springy size of 4x3x2 cm. In this case there is little anomaly where the size of the tumor metastases exceeds the size of the primary tumor. This can happen because even a very small GIST can recur or metastasize after years of surgery.¹⁷ And based on the literature it is stated that the majority of malignant GIST originates from the colon and the incidence of GIST originating from the colon of all GIST is quite rare (1%).⁴

The prognosis and possibility of recurrence of this patient is quite poor where the tumor size is large enough and at the time of diagnosis a metastasis to the peritoneal cavity (ascites) and paraovary has been established. Potential curative surgery for primary GIST that has not metastasized, but the possibility of recurrence depends on the characteristics of the tumor. Tumors that are initially inoperable can be treated early with imatinib to increase resectability (called neoadjuvant therapy). Therapy with imatinib can also be considered after removal of the primary GIST with a higher risk of recurrence. Patients with GIST metastases should be given drug therapy even after the tumor has been removed. Patients who are resistant to imatinib can be given sunitinib as a second-line drug. Regorafenib has been approved by the FDA as a third-tier drug in patients who do not respond to imatinib or sunitinib.¹⁶

CONCLUSION

A 40-year-old female patient with a malignant GIST in the transverse colon has metastasized in the ovaries and peritoneal (ascites) has been reported. Gastrointestinal stromal tumor (GIST) is the most mesenchymal neoplasm found in the digestive tract originating from the Interstitial Cell of Cajal (ICC). Anatomic pathology examination of GIST has their respective roles. Cytological examination cannot distinguish GIST from other gastrointestinal tumors, but can be used to see the potential for malignancy which is useful in screening (initial examination), follow-up, prognosis and therapy.

Histopathological examination itself has an important enough role to determine the type of tumor and malignancy. Immunohistochemical examination is very important to



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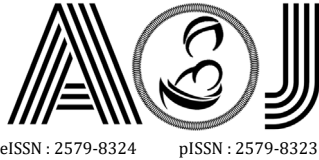
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confirm the definitive diagnosis of GIST because it is related to target therapy. Many immunohistochemical tests that can be done are related to GIST, but if the tumor is negative for KIT, the exact diagnosis is often challenging. It has been reported that DOG-1 allows the diagnosis of KIT-negative nuclei, so that this molecule can be an alternative to GIST with CD117 negative. In the future it may be necessary to conduct a broader study whether DOG1 can be one of the prognostic factors in GIST in both early and advance stage cases.

REFERENCES

1. Zhou Y. Coexistence of gastrointestinal stromal tumor, esophageal and gastric cardia carcinomas. *World Journal of Gastroenterology* [Internet]. 2013 [cited 2019 Jul 17];19(12):2005. Available from: <http://www.wjgnet.com/1007-9327/full/v19/i12/2005.htm>
2. Niazi AK, Kaley K, Saif MW. Gastrointestinal stromal tumor of colon: a case report and review of literature. *Anticancer research*. 2014;34(5):2547–2550.
3. Kang G-H, Srivastava A, Kim YE, Park H-J, Park CK, Sohn TS, et al. DOG1 and PKC- θ are useful in the diagnosis of KIT-negative gastrointestinal stromal tumors. *Modern Pathology* [Internet]. 2011 Jun [cited 2019 Jul 17];24(6):866–75. Available from: <http://www.nature.com/articles/modpathol201111>
4. Miettinen M, Lasota J. Gastrointestinal stromal tumors (GISTs): definition, occurrence, pathology, differential diagnosis and molecular genetics. *Pol J Pathol*. 2003;54(1):3–24.
5. Gaballa KM, Metwally IH, Refky B, AbdElKhalek M, Saleh S, Abdelaziz AM, et al. Ovarian gastrointestinal stromal tumor: does this diagnosis exist?. *European journal of gynaecological oncology*. 2017;38(1):147–149.
6. Foo WC, Liegl-Atzwanger B, Lazar AJ. Pathology of Gastrointestinal Stromal Tumors. *Clinical Medicine Insights: Pathology* [Internet]. 2012 Jan [cited 2019 Jul 25];5:CPATH.S9689. Available from: <http://journals.sagepub.com/doi/10.4137/CPATH.S9689>
7. King DM. The radiology of gastrointestinal stromal tumours (GIST). *Cancer Imaging* [Internet]. 2005 [cited 2019 Jul 25];5(1):150–6. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1665232/>
8. Idema DLM, Daryanani D, Sterk LMT, Klaase JM. Collision Tumor of the Stomach: A Case of an Adenocarcinoma and a Gastrointestinal Stromal Tumor. *Case Reports in Gastroenterology* [Internet]. 2008 [cited 2019 Jul 17];2(3):456–60. Available from: <https://www.karger.com/Article/FullText/129707>



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Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

9. Odze RD, Goldblum JR. Odze and Goldblum surgical pathology of the GI tract, liver, biliary tract, and pancreas [Internet]. 2015 [cited 2019 Jul 20]. Available from: <https://www.clinicalkey.com/dura/browse/bookChapter/3-s2.0-C20110697145>
10. Van Roggen JFG. The histopathological differential diagnosis of gastrointestinal stromal tumours. *Journal of Clinical Pathology* [Internet]. 2001 Feb 1 [cited 2019 Jul 25];54(2):96–102. Available from: <http://jcp.bmj.com/cgi/doi/10.1136/jcp.54.2.96>
11. Sözütek D, Yanık S, Akkoca AN, Sözütek A, Özdemir ZT, Avşar ÇU, et al. Diagnostic and prognostic roles of DOG1 and Ki-67, in GIST patients with localized or advanced/metastatic disease. *International journal of clinical and experimental medicine*. 2014;7(7):1914.
12. Vij M, Agrawal V, Kumar A, Pandey R. Cytomorphology of gastrointestinal stromal tumors and extra-gastrointestinal stromal tumors: A comprehensive morphologic study. *J Cytol* [Internet]. 2013;30(1):8–12. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3643373/>
13. Dudani S, Kalhan S, Sharma S, Gupta A. Gastrointestinal stromal tumours (GIST)- Pathology and clinical applications of recent molecular advances–A perspective review. *Çağdaş Tıp Dergisi*. 2014;4(2 EK):100–90.
14. Antonescu CR. Gastrointestinal stromal tumor (GIST) pathogenesis, familial GIST, and animal models. *Seminars in Diagnostic Pathology* [Internet]. 2006 May 1;23(2):63–9. Available from: <http://www.sciencedirect.com/science/article/pii/S0740257006001390>
15. Sahin S, Ekinci O, Seckin S, Dursun A. The diagnostic and prognostic utility of dog1 expression on gastrointestinal stromal tumors. *Turkish Journal of Pathology* [Internet]. 2016 [cited 2019 Jun 19]; Available from: <http://www.turkjpath.org/doi.php?doi=10.5146/tjpath.2016.01376>
16. GIST Treatment Guidelines | GIST Support International [Internet]. [cited 2019 Aug 13]. Available from: <https://www.gistsupport.org/treatments/gist-treatment-guidelines/>
17. Prognosis | GIST Support International [Internet]. [cited 2019 Aug 15]. Available from: <https://www.gistsupport.org/about-gist/prognosis/>
18. Saif MW, Siddiqui IA, Sohail MA. Management of ascites due to gastrointestinal malignancy. *Annals of Saudi medicine*. 2009;29(5):369–377.