Malignant Mesenterial Mesothelioma in Stroke Patients

Dewa Gde Agung Budiyasa, I Dewa Nyoman Wibawa

ABSTRACT

Mesothel is the cell lining of serosal surface of the pleura, peritoneum, pericardium, and testis. Malignant mesothelioma is a highly aggressive tumor from mesothel that has a tendency to grow rapidly and invade locally. Although the incidence of malignant mesenterial mesothelioma is not so high, the case fatality rate is very high. The aim of this case report is to report the rare and difficult case with several complications.

A Balinese man, 64 years old, came with chief complaint of weakness, abdominal enlargement, and nausea, with history of previous liver disease. On physical examination were found a decrease of consciousness, subfebrile, abdominal distension, ascites, negative Traube space, and paralysis of the left side of the body. Laboratory examination results showed leukocytosis, hypochromic-micrositic anemia, trombocytosis, hypoalbuminemia, increase of alkaline phosphatase, and mild hyponatremia. Abdominal USG showed intraperitoneal mass which some of them attach to abdominal wall, possibly from mesenterium and ascites, esophagastroduodenoscopy (EGD) revealed reflux esofagitis and anthral erosive gastritis, skull CT scan showed small infarction at left parietal medulla and right basal ganglia, cytology showed spreaded and grouped mesothel with reactive lymphocyte and amorph back ground. FNAB result showed malignant mesothelioma, and normal colonoscopy. Based on the above data, the diagnoses were malignant mesenterial mesothelioma, reflux esofagitis and anthral erosive gastritis, and non hemorrhagic stroke.

Malignant mesenterial mesothelioma should be considered in patient with the combination of unexplained ascites and abdominal pain. Although the result of treatment is very disappointing, the patient had to be treated optimally to increase quality of life.

Key words: malignant mesenterial mesothelioma, stroke.

INTRODUCTION

Mesothel is the cell lining of serosal surface of several organs in our body, such as pleura, peritoneum, pericardium, and testis. Malignant mesothelioma is an aggressive tumor of serosal surface. This tumor was once rare, but its incidence is increasing worldwide, probably as a result of widespread exposure to asbestos. Malignant mesothelioma is a highly aggressive tumor that has a tendency to grow rapidly and invade locally. The cause of this tumor is often associated with exposure to asbestos that happened more than 50-70% of all cases. There is substantial interest in this disease on the part of the medical community and the general public, because millions of people have been exposed to asbestos, and many articles about the danger of asbestos have been published. In the US, about 8 million people are exposed to asbestos in the workplace. Malignant mesothelioma has also been linked to therapeutic radiation using thorium dioxide and zeolite, a silicate in the soil. An etiological role for Simian Virus 40 in malignant mesothelioma has also been suggested, but the most tendencious cause is asbestos exposure.

Epidemiologically, malignant mesothelioma is more common in men, with male-to-female ratio of 3 : 1. It can also occur in children, and has no racial predilection. The incidence of this tumor is about 2000-3000 cases per year, with the highest number 40 cases/million people/year in Australia, the world wide incidence is 9 cases/million people/year. The incidence increases with age and is approximately 10 times higher in men aged 60-64 years than in those aged 30-34, and a peak risk 30-35 years after exposure. This makes this tumor be usually diagnosed in the fifth to seventh decades of life. Median survival is 11 months, about 15% of patients have an indolent course.

Clinical features of malignant mesothelioma depend on the predilection and spreading of the tumor. In pleural mesothelioma, the patients commonly present...
with breathlessness and often accompanied by chest-wall pain, chest discomfort, fatigue, fever, cold sweating, and decrease of body weight. The chest pain may be pleuritic, lateralized, dull or diffused pain. Dyspnea may be resulted from accumulation of pleural fluid, pleural thickening, thoracic restriction, and lung encasement.\textsuperscript{1,7,8,10} In peritoneal tumor, clinical features were from abdominal pain, distention due to ascites, to shortness of breath due to abdominal distention, and finally bowel obstruction. Patient can present asymptomatically, especially at early phase.\textsuperscript{10} In rare case, clinical manifestations present spinal cord compression, brachial plexopathy, Horner syndrome, or superior vena cava syndrome.\textsuperscript{14}

The treatments for patient with malignant mesothelioma were surgery, chemotherapy, radiotherapy, and multimodality therapy.\textsuperscript{7,8,10,14} Multimodality therapy consists of debulking tumor, radiotherapy for residual local disease, and systemic chemotherapy for the metastase.

**CASE ILLUSTRATION**

Mr. P, 64 years old, a Balinese, presented at Sanglah General Hospital with chief complaints of weakness since a day prior to admission, such that he could only move his extremities, and couldn’t communicate. The weakness began suddenly and still occurred when he arrived at the hospital, couldn’t feel relief by resting or drinking water with sugar. He had also suffered from abdominal enlargement since 6 months prior to admission, sometimes on and off, and since 1 month prior to admission getting bigger, make him unable do daily activities. He felt nausea without vomiting. Yellowish eyes, dizziness, fever, extremity’s edema, skin’s spot. Right upper abdominal pain was denied. Bowel habit was still normal, yellowish stool, once a day, without blood and blackish stool. Urination was still normal, with yellowish urine, 2-3 times/day, and dark urine was denied.

The patient had been hospitalized 3 months before with liver disease, and abdominal USG and EGD performing. He is a diabetic patient for 1 year and regularly checked up to a general practioner. History of hypertension was denied.

None of his family was suffering from the same disease, nor suffering from diabetes mellitus and hypertension.

The patient was an employee at a building material store and had already retired. History of smoking and alcoholism are denied.

On physical examination, clinicians found severe illness appearance, decrease of concousness (E4V1M4), axillary temperature was 37.2\textdegree C, blood pressure 130/80 mmHg, pulse rate 96 x/m, respiratory rate 20 x/m. There was no abnormality on ENT examination, heart examination, and lung examination. There was spider nevi at chest skin. Abdominal examination, distension was found, bowel sound was within normal limit, there was sign of ascites. Liver and spleen unevaluated, with traube space dullness. Extremity was warm without edema. Laboratory examination found leukosite 27.6 K/uL, Hb 10.5 g/dl, MCV 72.8 fl, MCH 23 pg, Plt 618 K/uL, HCT 33.3\%, total protein 7.5 g/dl, albumin 1.7 g/dl, total bilirubin 0.8 mg/dl, direct bilirubin 0.10 mg/dl, AST 20 IU/l, ALT 11 IU/l, ALP 174 IU/l, Cholesterol 176 mg/dl, BUN 18 mg/dl, SC 1.2 mg/dl, Blood sugar 104 mg/dl, Na 130 mmol/l, K 5.1 mmol/l.

Electrocardiography showed sinus rhythm 84 x/m. EGD result was esofagitis reflux and anthral erosive gastritis. Three months before, the patient had already undergo abdominal USG which observed chronic liver disease with ascites and portal hypertension. Based on previous data, he was diagnosed as hepatic cirrhosis with suspected malignant degeneration, hepatic encephalopathy grade I, suspected spontaneous bacterial peritonitis with sepsis, hypoalbuminemia, and non emergency hyponatremia. Treatments for the patient were free protein diet, IVFD asering: aminoleban: dextrose 10%= 1:1:1, 20 drops/m, cefotaxim 1 gram TID, paramomycin 500 mg QID, lactulosa syrup, lavement every 12 hours, albumin transfusion until albumin level >2.5 g/dl.

On the second day of admission, the patient suddenly had paralysis at the left side of the body and rigid tongue, he could not speak well, had headache, without fever. Patient was consulted to Neurology Department. According to skull CT scan the patient has cerebral infarction, non hemorrhagic stroke and treated

![Chest X-Ray](image-url)
with piracetam 3 gram QID. During the treatment, the patient’s condition did not improve. On the 13th hospitalization day, abdominal USG was performed with the result of chronic liver disease, cholesystitis, and ascites. The new laboratory result, ascites fluid analysis showed cell 324/mm³ (MN 70%, PMN 30%), bleeding time, clotting time, PPT, and APTT within normal limit, HBsAg non-reactive. The patient now was assessed with hepatic cirrhosis with malignant degeneration, hepatic encephalopathy grade II-III, acute cholesistitis, and non hemorrhagic stroke.

The level of consciousness of the patient became fully alert on 25th day of hospitalization. The latest laboratory results were SI 3 ug/dl, TIBC 11 ug/dl, reticulocyte 0.4%, blood smear: erytrocyte hypochromic-micrositic anisocytosis, increased leucocyte and thrombocyte count, urinalysis and feces routine within normal limit. CEA 1.04 ng/mL. Ascites cytology showed spreading and group of mesothel and amorph background.

On day 54th, laboratory results showed normal amylase, chest x-ray with cardiomegaly (LVH), abdominal CT scan showed chronic liver disease, acute cholecystitis, and ascites, and after repeating consultation to the radiologist, the conclusion was mass extra luminal, extra liver, extra spleen, extrapancreas, suspected mesenterial tumor. Colonoscopy was within normal limit, and repeated abdominal USG showed intraperitoneal mass, with part of them attached to abdominal wall, possibly from mesenterium and ascites.
FNAB showed morphology with malignant mesothelioma. The final diagnosis were malignant mesenterial mesothelioma, reflux esofagitis and anthral erosive gastritis, mild hypochromic micrositic anemia and Non hemorrhagic stroke. The patient was treated with acetosal 100 mg TID, piracetam 1200 mg QID, vitamin B complex tab 1 TID. Later, the patient was consulted to the oncology surgery, but on day 68th of hospitalization, the patient was dead. The cause of death was septic shock due to by hospital acquired pneumonia.

**DISCUSSION**

Based on anamnesis, we found weakness, nausea, vomiting, abdominal enlargement, decrease of conciousness, and history of liver disease, and the patient had been hospitalized due to liver disease. There are several possibilities of the disease that can make that condition, one of them is hepatic cirrhosis. On physical examination, GCS level E4V1M4, sub febris, spider nevi, and ascites, which condition usually happen in patient with hepatic cirrhosis. Decrease of conciousness was thought as hepatic encephalopathy. On hepatic cirrhosis condition, typical anemia was normo-normo, hypo-micro, or macrocytic. Leucocytosis
stage can be caused by spontaneous bacterial peritonitis. Hypoalbuminemia with globulin level more than albumin level shows hepatic cirrhosis condition. Transaminase serum, bilirubin, alkaliphosphatase, blood cholesterol, hemostatic function test are still within normal limit. Alkalyphosphatase in this patient was normal. Prothrombin time was prolonged and there was no abnormality in hemostatic function. Laboratory results that suitable for hepatic cirrhosis is only hypoalbuminemia. Since hypoalbuminemia has many causes, the hepatic cirrhosis was a weak diagnosis.

On the second day of admission, the patient complained of weakness on the left side of his body, and neurology department performed skull CT scan, and the result was infarction at the left parietal medulla and right ganglia base.

On the admission, general appearance of the patient getting better, with full conciousness, but verbal communication did not improve cause by stroke condition. Later the patient complained lower abdominal pain, worsening day by day. Patient underwent repeat abdominal USG and the result was CLD with acute cholecystitis and treated according to acute cholecystitis treatment. After 1 week, abdominal pain worsened, patient looked anemia, and then was performed blood culture, fungus culture, blood amylase, liver function test and all of the result was normal. The only one result refering to infected condition was leukocytosis and the possible site of infection was spontaneous bacterial peritonitis (SBP), acute cholecystitis and acute pancreatitis. SBP was not suitable for this condition because ascites culture was negative. Pancreatitits was also not suitable because blood amylase result was normal. So, we had to perform abdominal CT scan to confirm diagnosis. The abdominal CT scan result was tumor mesenterium, ascites fluid cytology result was mesothel at the medium, FNAB refering to cell morphologic was malignant mesothelioma, and colonoscopy within normal limit. So the diagnoses of the patient were malignant mesothelioma, reflex esophagitis, antral erosive gastritis, and non hemorrhagic stroke. Although abdominal USG and CT scan refered to CLD, but from 3 times abdominal USG always shows the different conclusion, and latest abdominal USG refer intraperitoneal mass, possibly from mesenterium. Abdominal CT scan refering to mass with suspicion of mesenterial tumor, EGD result also did not show portal hypertension sign that usually happens at hepatic cirrhosis.

Malignant mesothelioma is an aggressive tumor at serosal surface of the body, such as pleura (87%), peritoneum (5.1%), pericardium (0.4%), testis, tunica vaginalis, and the other place.1-3,10,12,14,15 Its diagnostic and treatment are a big challenge, and often make frustration to both doctor and patient.1,7 Mesenterium is a peritoneal layer that has function to “hange” organ in abdominal cavity.5 It localize blood vessel and nerves that have function to connect blood circulation and nerve from our body to the intraperitoneal organ. The structure and topography of peritoneum are the same to organs that part of peritoneum such as mesenterium, omentum, or umbilicus.11 Incidence of malignant mesothelioma at mesenterium is unknown, perhaps it’s included in the incidence in peritoneum.

The combination between ascites and unexplain abdominal pain refers to early suspicion of malignant mesothelioma at peritoneum even if cytology finding result is negative.10 Diagnosis of malignant mesothelioma supported by laboratorium result, cytology, histopatologic, radiologic finding.10,14 Malignant mesothelioma can spread to organs around it. However, metastatic is rarely the cause of death. Local invasion, which is common, causes enlargement of the lymphnodes and may result in obstruction of the superior vena cava, cardiac tamponade, subcutaneous extension, and spinal cord compression.10 But this patient died caused by Hospital Acquired Pneumonia.

There are 3 histologic features of malignant mesothelioma: sarcomatous, epithelial, and mixed,7,8,10,14 which are related to morbidity and mortality. In general, median survival patient is 11 months, 9.4 months for sarcomatous, 12.5 months for epithelial, and 11 months for mixed types.14 Tabel 1 shows the comparison of sign, symptom and laboratory finding between the patient and the usual.
Accurate and rapid diagnosis of malignant mesothelioma is important for therapeutic and medicolegal reasons.\textsuperscript{10,14} Diagnosis of the tumor by clinical sign, symptom, and laboratory finding, and confirmed with cytology and histopathology finding. Cytology evidence is found in 33-84\% of all cases. If there is not any ascites or pleural effusion, tumor biopsy has to be done.\textsuperscript{10} Electron microscope can distinguish malignant mesothelioma from adenocarcinoma, and tumor markers are calretinin and cytokeratin.\textsuperscript{1}

Radiologic examination is very important to diagnosed. X-ray finding can determine ascites or pleural fluid. CT scan can determine fluid, also is used to identify the sign of expansive such as plaque. MRI is useful in determining the extent of malignant mesothelioma, particularly when the tumor invade local structure, and is very helpful in radiotherapy planning for local spreading.\textsuperscript{10,14}

In general, the treatments of malignant mesothelioma are by surgery, chemotherapy, radiotherapy, and multimodality therapy.\textsuperscript{1,7,8,10,13,14} In malignant mesenterial mesothelioma, there is very less information on how to treat it. Surgery is usually for palliative therapy, and debulking surgery or radical resection is the best if combined with adjuvant therapy, radiotherapy and chemotherapy.\textsuperscript{10} Chemotherapy often performed in malignant mesothelioma is cisplatin (75mg/m\textsuperscript{2}/d) as single drug or combination with pemetrexed (500 mg/ m\textsuperscript{2}/d), every 21 days. Median survival with single cisplatin is 9.3 month, and combination with pemetrexed is 12.1 month. Folic acid and vitamin B12 are given to prevent pemetrexed’s adverse effect.\textsuperscript{14} The other literature says that chemotherapy with doxorubicin with median survival 7.3 months, and by metotrexat with median survival 11 month.\textsuperscript{8} Several combination usually performed are cisplatin and gemcitabine, cisplatin/doxorubicin/mitomicin C, bleomicin/intrapleural hyaluronidase, cisplatin/doxorubicin, carboplatin/gemcitabine, and cisplatin/vinblastin/mitomicin C. Combination of cisplatin/gemcitabine gives best result.\textsuperscript{14} Radiotherapy so far has still given the disappointing result.\textsuperscript{14} Radiation gives better result if combined with the other modality, and performed to palliative therapy and to prevent tumor seeding.\textsuperscript{7} Multimodality therapy was performed for the first time by Sugarbaker especially to malignant mesothelioma at pleura that are combination between debulking tumor, radiotherapy for residual local disease, and systemic chemotherapy for far spreading target.\textsuperscript{14}

The prognosis for patient with malignant mesothelioma is very bad. Without treatment, mesothelioma is fatal within 4-8 months. Median survival patient with malignant mesothelioma is 12 months. With multimodality therapy, some patients have survived 16-19 month. A few have survived as long as 5 years, with the rates of 14\% for all types and 46\% for the epithelial type. However, the numbers are small.\textsuperscript{14}

CONCLUSION

Although the incidence of malignant mesenterial mesothelioma is not so high and the case fatality rate very high, we always have to be concerned about the increase in cases. If we found the combination of unexplained ascites and abdominal pain, we have to consider about this case. To diagnose malignant mesothelioma, we have to perform laboratory, cytology, histopathology, and radiology examination. If there is mismatching between clinical sign and supporting examination, we have to perform the other more useful supporting examination as soon as possible. In this case, we have to perform abdominal CT scan after the first abdominal USG, because the USG result does not match with the clinical appearance. So far, there has been no relationship between the carcinoma and stroke condition.

REFERENCES


