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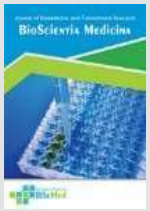

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Collecting Duct Carcinoma in the Kidneys: A Rare Case Report

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A B S T R A C T

Background: Collecting duct carcinoma (CDC) is one of the rare pathological subtypes of renal cell carcinoma, with high malignancy and poor prognosis. Pathological examination is the gold standard in confirming the diagnosis of CDC. CDC is described as a tumor that has a tubulopapillary architecture and forms a hobnail pattern along the glandular tube. **Case presentation:** A 56-year-old woman with the main complaint of a lump in the right abdomen for 1.5 months before entering the hospital. The lump in the stomach is getting bigger, complaints are accompanied by intermittent pain, nausea, vomiting, body feeling weak, and decreased appetite. The patient then underwent a CT-Scan examination of the abdomen and concluded that fluid/water was found next to the right kidney, and a hypodense lesion appeared in segment 6 of the right lobe of the liver. Histopathological examination of large tissue shows pieces of kidney tissue with a connective tissue capsule on the outside containing glomeruli and tubules lined by cuboidal epithelium as well as a proliferation of tumor cells that grow infiltratively in the connective tissue stroma which is partly desmoplastic and fatty tissue between the glomeruli and tubules. Tumor cells are arranged to form tubulopapillary and tubulocystic structures. These cells with pleomorphic nuclei, some hyperchromatic, some vesicular, coarse chromatin, clear nuclei, and atypical mitoses can be found and tumor cell embolism in the blood vessels and perineural invasion can be seen. There were spots and clusters of lymphocytes and plasma cells as well as areas of bleeding and necrosis. **Conclusion:** The patient was diagnosed with collecting duct carcinoma (CDC).

1. Introduction

Collecting duct carcinoma (CDC) or also known as bellini duct carcinoma is a malignant epithelial tumor originating from the primary cells of the renal collecting ducts bellini. This tumor is very rare, with an incidence of 1-2% of all types of renal cell carcinoma. Collecting duct carcinoma is one of the rare pathological subtypes of renal cell carcinoma, with high malignancy and poor prognosis. The incidence of premature death is high with 60 to 70% of patients dying within 3 years of diagnosis. The research was conducted by Fleming et al; about 2200 patients with malignant kidney tumors between 2007 and 2017 and CDC only accounted for about 0.5% of all malignant tumors, which is less than 1%.[1-3]

Duct carcinoma is distinguished from other renal cell carcinomas by its location and characteristic histologic appearance. Pathological examination is the gold standard in confirming the diagnosis of CDC. In the course of the disease, the tumor usually infiltrates the pelvis, cortex, and hilus of the kidney. Visually, the tumor is mainly found in the renal medulla, gray or yellow in color, accompanied by necrosis or bleeding. Meanwhile, microscopically, CDC is described as a tumor that has a tubulopapillary architecture and forms a hobnail pattern along the glandular tube. Poorly differentiated tumor cells usually show an adenoid or sarcomatoid cystic, nest-shaped

morphology, with or without interstitial connective tissue reaction.[4-7]

Most of these tumors are associated with poor outcomes due to their very aggressive clinical course, high prevalence of metastases, and limited response to immunotherapy or chemotherapy.[1] The majority of patients already have metastases at the time of diagnosis and half of patients die within the first year. Overall survival rates are reported to be approximately 60% for the first 6 months, 50% for 1 year, and 20% for 2 years after diagnosis. In patients with metastases, the median survival rate is 6 months.[8-10]

2. Case Presentation

A 56-year-old woman referred from Adnan Payakumbuh Hospital went to the urology surgery clinic at Dr. M. Djamil General Hospital Padang on June 6th, 2022, with the main complaint of a lump in the right stomach for 1.5 months before entering the hospital. The lump in the stomach is getting bigger, complaints are accompanied by intermittent pain, nausea, vomiting, body feeling weak, and decreased appetite. The patient also complained of black stools since 4 days before entering the hospital, urination was within normal limits. The patient did not have a family history of diabetes mellitus, hypertension, or malignancy. Physical examination showed a moderate general condition, cooperative compos mentis consciousness, blood pressure 120/80 mmHg, pulse frequency: 85x/minute, respiratory frequency: 20x/minute, temperature: 36.7°C. Examination of the eyes revealed anemic conjunctiva, pupil isochore 3 mm/3 mm in diameter. Examination of the thoracic region is visible normochest, the right fremitus is the same as the left, sonor, bronchovesicular breathing sounds, no rales, and no wheezing. A cardiac examination revealed regular first and second heart sounds. Abdominal examination, on inspection there was a palpable mass in the right abdomen the size of an adult's fist, solid consistency, positive upper right abdominal tenderness, and positive normal bowel sounds on auscultation. Left and right extremities were within normal limits.

Laboratory examination results on June 6th, 2022 showed hemoglobin 5.0 g/dL, leukocytes 11,900/mm^3, platelets 216,000/mm^3, hematocrit 15%, erythrocytes 1,870,000/uL. Basophil count 0%, eosinophil 3%, neutrophil 80%, lymphocyte 12%, monocyte 5%, globulin 3.9 g/dL, total bilirubin 1.0 mg/dL, direct bilirubin 0.4 mg/dL, indirect bilirubin 0.6 mg/dL, SGOT 37 U/L, SGPT 23 U/L, blood urea 86 mg/dL, blood creatinine 3.6 mg/dL, instant blood sugar 146 mg/dL, sodium 125 mmol/L, potassium 4.5 mmol/L, chloride 97 mmol/L. Conclusion: Anemia, leukocytosis with neutrophilia, APTT exceeds the reference value, Globulin increases, SGOT increases, urea and creatinine increase, sodium decreases. A provisional diagnosis of suspected right kidney tumor malignancy, severe anemia and acute bleeding, melena and peptic ulcer, acute chronic kidney disease, and hyponathermy. Then the patient was consulted by a urology specialist who recommended right nephrectomy and treatment together with a specialist in internal medicine.

On April 19th, 2022, the patient had previously undergone an ultrasound examination of the whole abdomen with the conclusion of hepatomegaly, left nephrolithiasis, and suspected intra-abdominal mass (Figure 1). Suggestion: CT scan of the abdomen with contrast. On June 6th, 2022, a chest radiology examination was carried out and it was concluded that there were no radiological abnormalities visible on the chest radiography (Figure 2). The patient then underwent a CT-Scan examination of the abdomen and concluded that fluid/water was found next to the right kidney, and a hypodense lesion appeared in segment 6 of the right lobe of the liver (Figure 3).

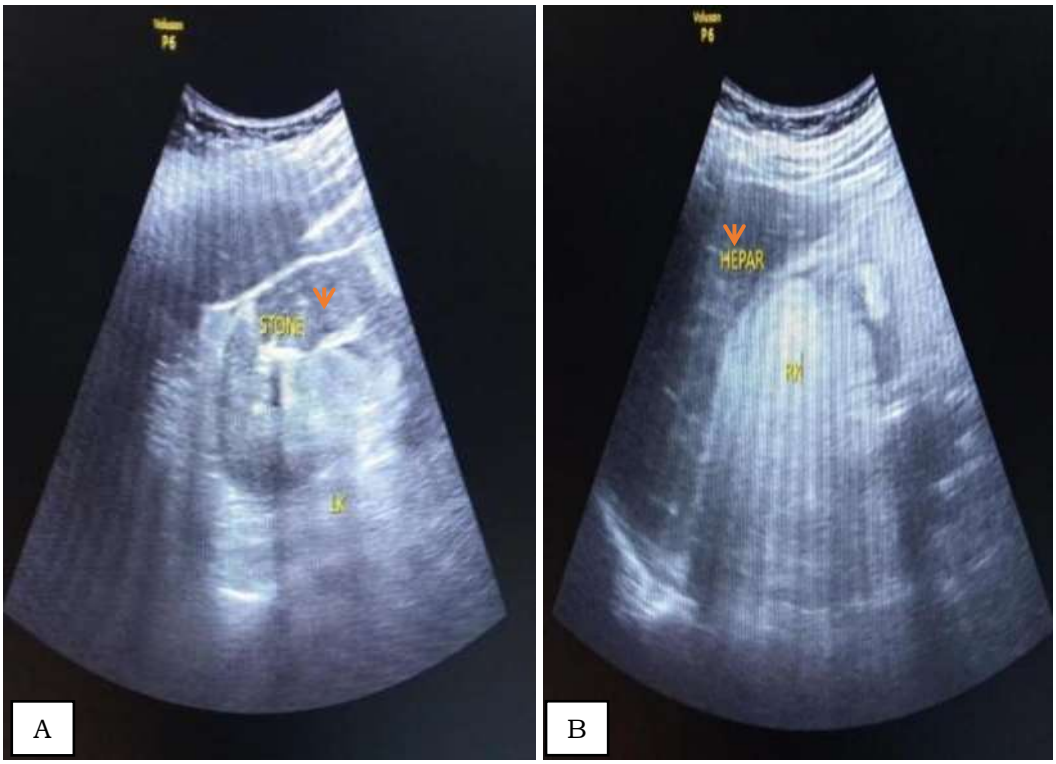

Figure 1. Ultrasound of the whole abdomen: (A) Left kidney: left nephrolithiasis (B) Right kidney: Hepatomegaly and hyperechoic shadow indecisive boundary in the right middle abdomen ec suspected intraabdominal mass.

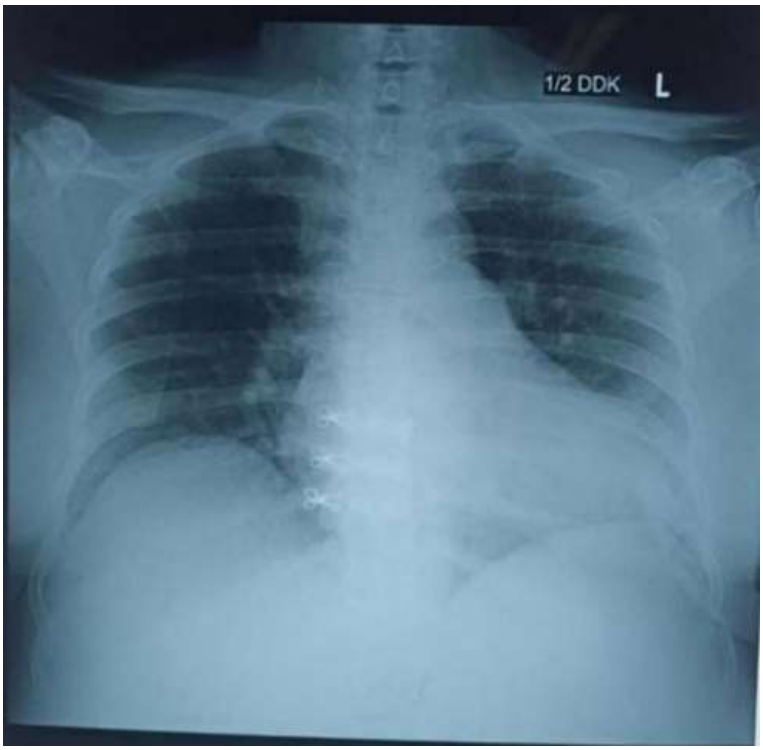

Figure 2. Thoracic radiography: no radiological abnormalities appear on thoracic radiography.

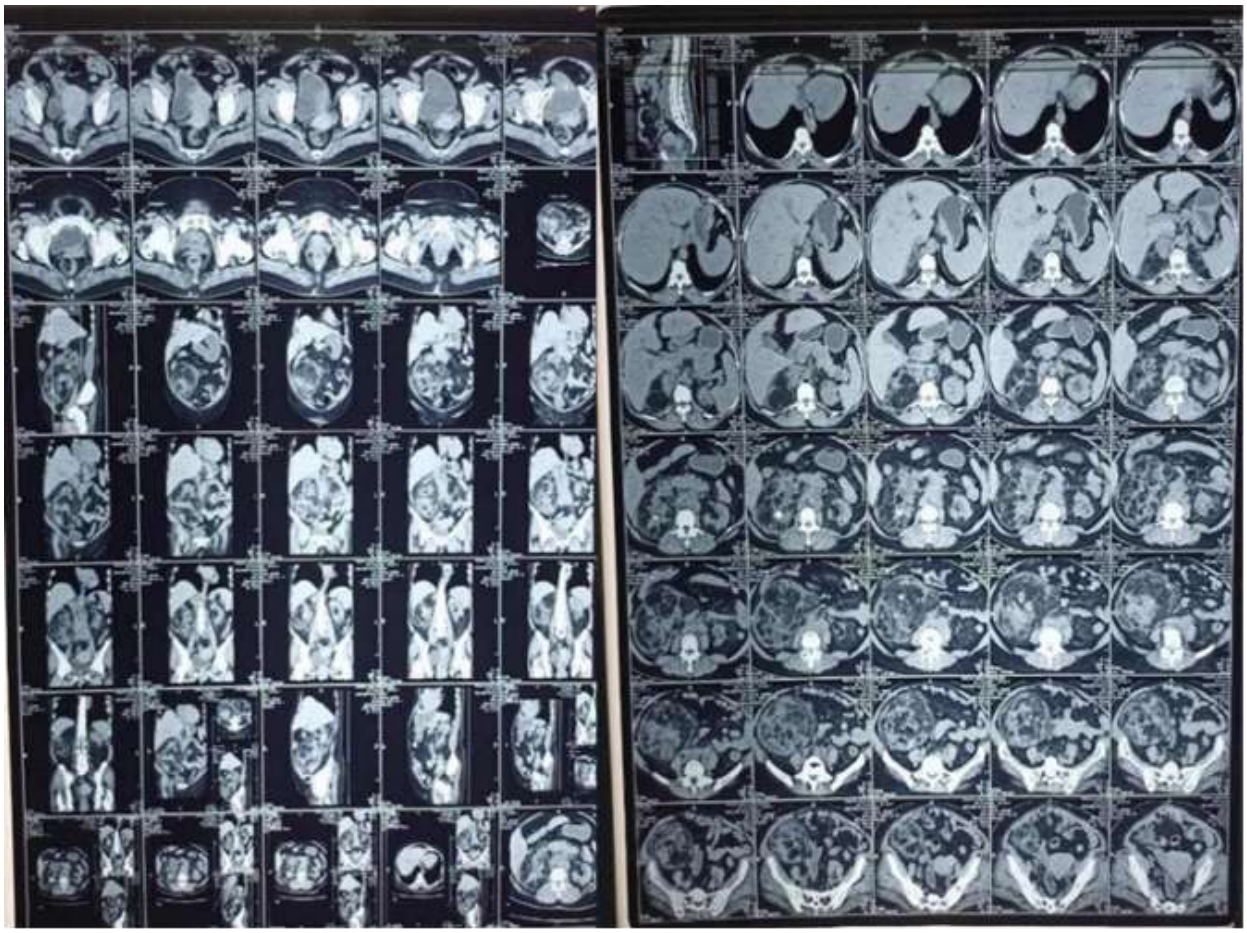

Figure 3. CT Scan of the abdomen: (A) Fluid/water next to right kidney (B) Hypodense lesion in segment 6 of the right lobe of the liver.

On June 17th, 2022 at 8.30 the patient underwent open radical nephrectomy surgery with a postoperative diagnosis of right kidney tumor. After the operation, the patient was treated in the ICU in moderate condition, conscious under the influence of medication, hemodynamically stable, breathing assisted by a ventilator, and received a 3-unit PRC transfusion. Patients receive RL infusion fluids, injection ceftriaxone 2x1 gr, omeprazole 2x40 mg, ketorolac 3x30 mg, tranexamic acid 3x1g, vitamin C 3x10 mg, paracetamol 1g when necessary. The surgical tissue was received in the anatomical pathology laboratory on June 17th, 2022. Macroscopic examination showed a large piece of tissue and a small piece of tissue, (I) a large piece of tissue, brownish white, fatty, firm, and chewy measuring 26x16.5x10 cm, in cross-section a solid white mass with a diameter of 21.5 cm, there is a necrotic part filling the cavity and the ureter is visible and several stones with a diameter of 0.5 to 1 cm (II) a smaller piece of tissue appears to be a brownish white mass and there is a yellowish, rubbery solid piece measuring 11.5x5x3 cm in cross-section a solid white mass appears 4 cm in diameter, 2 pieces were found which were suspected to be KGB with a diameter of 0.6-0.7 cm, brownish white in cross-section. The macroscopic picture can be seen in (Figure 4).

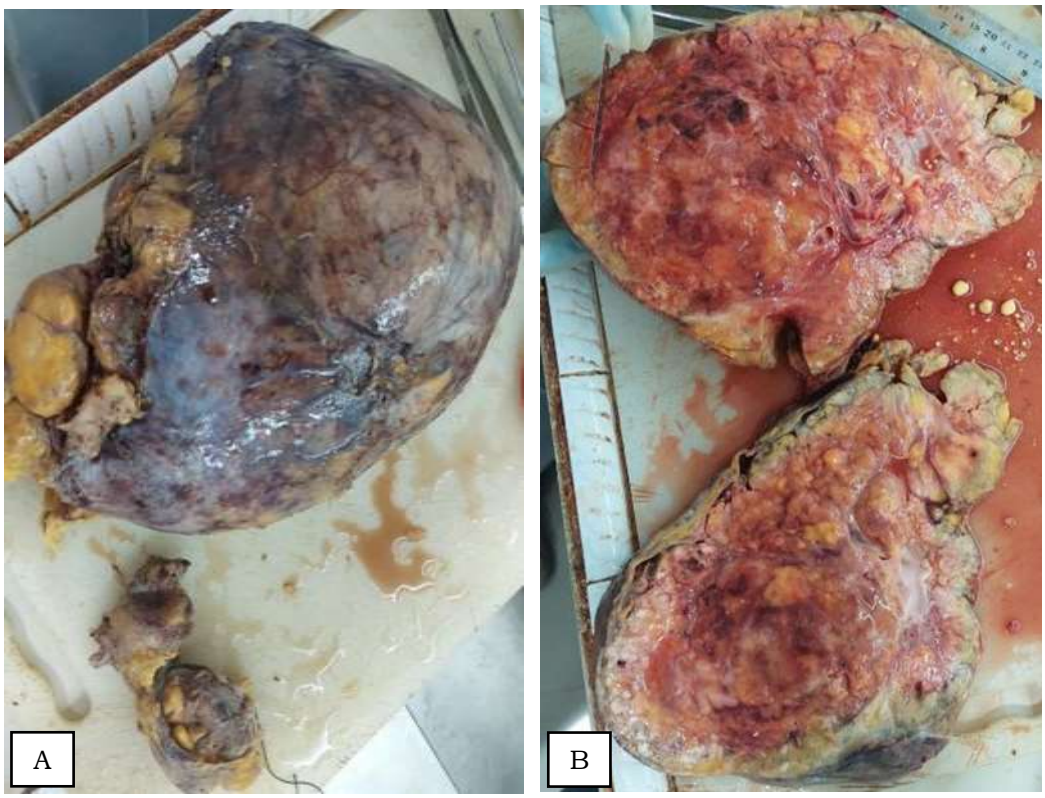

Figure 4. Macroscopic picture: (A) A large piece of tissue and a smaller piece of tissue, (B) The cross-section appears as a dense white mass and there is a necrotic part filling the cavity.

Histopathological examination (I) of large tissue shows a piece of kidney tissue with a connective tissue capsule on the outside containing glomeruli and tubules lined by cuboidal epithelium as well as a proliferation of tumor cells that grow infiltratively in the connective tissue stroma which is partially desmoplastic and fatty tissue between the glomerulus and tubule. Tumor cells are arranged to form tubulopapillary and tubulocystic structures. These cells with pleomorphic nuclei, some hyperchromatic, some vesicular, coarse chromatin, clear nuclei, and atypical mitoses can be found and tumor cell embolism in the blood vessels and perineural invasion can be seen. There were spots and clusters of lymphocytes and plasma cells as well as areas of bleeding and necrosis. Histopathological examination (II) of small tissue shows that pieces of tissue consist of connective tissue stroma containing proliferation of tumor cells that grow infiltratively in the connective tissue stroma, some of which are desmoplastic and fatty tissue that forms tubulopapillary and tubulocystic structures. These cells with pleomorphic nuclei, some hyperchromatic, some vesicular, coarse chromatin, real nuclei, and atypical mitoses can be found. There were clusters of lymphocytes and plasma cells as well as areas of bleeding and hyperemic capillaries. Based on these findings, conclusions were drawn collecting duct carcinoma, minimal staging pT3a Nx Mx, there is lymphovascular invasion, and there is perineural invasion (Figure 5). On June 24th, 2022, the patient was discharged in stable condition with complaints of pain in the surgical wound and was advised to go to the clinic for control. On July 7th, 2022 the patient was declared dead at Adnan Payakumbuh Hospital, the family was less cooperative in asking further questions so it was difficult to confirm the cause and chronology of the patient's death.

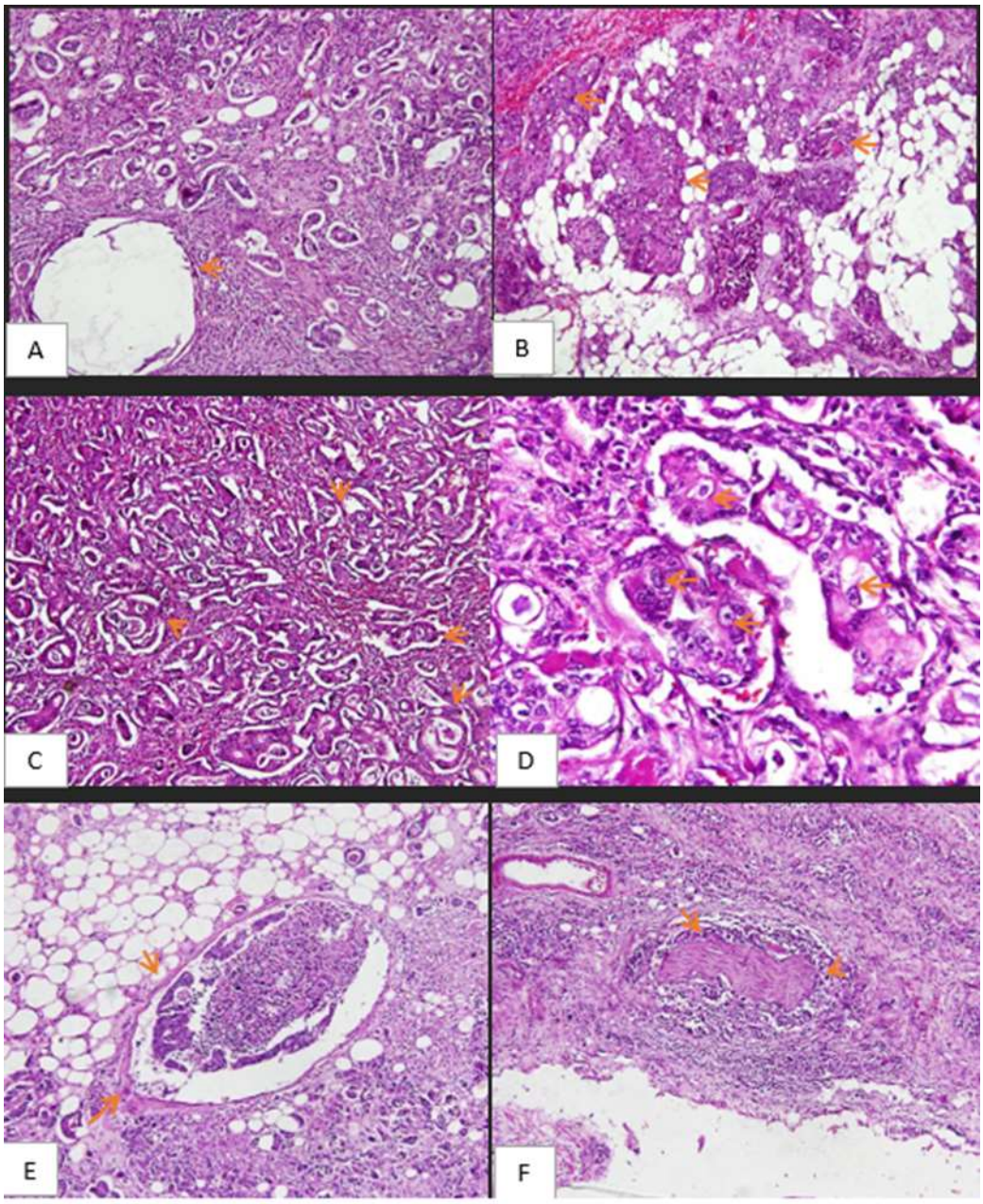

Figure 5. Histopathological examination results. (A), (B), and (C) Proliferation of tumor cells that grow infiltratively in stroma connective tissue and fatty tissue with tubulopapillary and tubulocistic structures (magnification 100x, HE). (D) Cells with a pleomorphic nucleus, partly hyperchromatic, partly vesicular, crude chromatin, daughter of real nuclei (magnification 400x, HE). (E) and (F) Tumor cell embolism within blood vessels and perineural invasion (100x, HE. magnification).

3. Discussion

A case has been reported collecting duct carcinoma in a 56-year-old female patient. Collecting duct carcinoma is a relatively rare and aggressive malignant tumor. This tumor originates from the epithelial layer collecting ducts bellini in the renal medulla. In this case, a 56-year-old female patient was reported, where the patient was elderly. The age of patients with CDC was in a wide range, ranging from 14 to 89 years with an average age of 59 years. In addition, the incidence of this tumor is higher in adult men aged between 41 and 71 years, with a male-to-female ratio of 2:1. Many risk factors are thought to be associated with CDC events, including demographics, smoking, phenacetin

use, obesity, lack of physical activity, exposure to industrial or environmental agents, hypertension, hyperglycemia, and hypertriglyceridemia. Research has reported that obesity can increase the risk of developing CDC up to 20-35% higher when compared to individuals with a normal body mass index. In this patient, no data was obtained regarding risk factors associated with the occurrence of CDC. The clinical symptoms in this patient were swelling in the right abdomen since 1.5 months ago. The patient also complained of nausea, vomiting, decreased appetite, and black stools for the past 9 days. Clinical manifestations of CDC vary according to tumor size, location, and invasiveness. Collecting duct carcinoma often causes nonspecific clinical manifestations, including a palpable mass in the abdomen, hematuria, low back pain, and symptoms of distant metastases. Another study reported that 50% of patients with CDC came with the main complaint of hematuria, 33.3% of low back pain, 16.7% were asymptomatic, and 16.7% of patients came with complaints of fever. Supporting examinations in the form of laboratory blood tests showed a decrease in hemoglobin (5g/dl), hematocrit (15%), and erythrocytes (1,870,000). Apart from that, there was also an increase in leukocytes (11,900), direct bilirubin (0.4 mg/dl), SGOT (37 U/L), urea (86 mg/dl), and creatinine (3.6 mg/dl). Anemia in patients can be caused by the course of the disease due to the malignancy they are experiencing. Cancer-related anemia has biological and hematological features similar to anemia due to chronic inflammatory disease. Proinflammatory cytokines, especially IL-6 released by tumors and immune cells trigger changes in erythroid progenitor proliferation, erythropoietin production, circulating erythrocyte lifespan, iron balance, and energy metabolism ultimately leading to anemia.[11-14]

Anemia in patients can also be caused by upper gastrointestinal bleeding which is characterized by complaints of melena in patients. Although rare, kidney malignancies can also metastasize to the pancreas and gastrointestinal tract, namely the duodenum. Metastases to the duodenum may be a potential source of bleeding in patients with a history of gastrointestinal bleeding and renal *cell carcinoma*. This is supported by another study, namely a 59-year-old man with renal *cell carcinoma* who came with the main complaints of melena and recurrent dizziness. Therefore, the recommendation in this case is an examination of esophagogastroduodenoscopy (EGD) which can show the appearance of a large fragile mass in the duodenum. Apart from that, in this case, hepatomegaly and an increase in liver enzymes were also found, which could indicate tumor metastasis to the liver. This is based on other studies which report that around 20% of patients with RCC experience tumor metastasis to the liver, but without liver metastasis, malignancy in the kidney can also cause hepatomegaly and abnormal liver function test results due to hepatotoxic hormones secreted by the tumor. However, after tumor resection, these liver abnormalities can return to normal. Apart from metastases to the liver, other studies also reported that 32.4% of patients with CDC experienced metastases to the lymph nodes, 13.5% metastases to the bones, 8.1% to the lungs, 2.7% to the brain, and 5.4% to the adrenal glands. Liver metastases in this case were also supported by findings on CT-Scan which showed a hypodense lesion in segment 6 of the right liver lobe. Approximately 20% of patients demonstrate metastases at initial diagnosis, and 20–40% of all patients who have undergone curative nephrectomy develop metastases. The most frequent location of metastases is the lymph nodes (55%), while distant hematogenous spread (33%) most often occurs in the liver. Imaging modality in the form of CT-Scan can also help in confirming the diagnosis of CDC and is the most common method used. On CT-Scan, CDC tumors are solitary, solid, and poorly defined. The tumor has a cystic component, and calcifications, and may be accompanied by lymph node metastases. The tumor is centered in the medulla producing compression of the renal pelvis. The degree of enhancement lesions is lower when compared with normal renal cortex and medulla. This indicates an atypical tumor with low blood supply.[15-17]

Macroscopic examination showed a large piece of tissue and a smaller piece of tissue, brownish white, fatty, firm chewy measuring 26x16.5x10 cm and 11.5x5x3 cm. The cross-section showed a white, solid mass and there were necrotic parts filling the cavity. These findings are in accordance with the macroscopic picture presented by the literature, namely a white to brown tumor with hemorrhage and necrosis. The tumor sizes that have been reported range from 2.5 to 15 cm in diameter. Lymph node metastases are also common, and lymphatic spread around the ureters may be found. More than 70% of patients with CDC present at stage pT3 or higher. Collecting duct carcinoma is often located in the inner medulla, however, because most cases have large tumors, this medullary location may not be confirmed. Tumor borders are unclear and irregular with extension into the cortex and often beyond the kidney. On histopathological examination of this case, there was a proliferation of tumor cells that grew infiltratively in the connective tissue stroma, some of which were desmoplastic and fatty tissue that formed tubulopapillary and tubulocystic structures. These findings are in accordance with the literature which states that CDC is a tumor consisting of a mixture of dilated tubules and papillary structures lined by a single layer of cuboidal cells, often forming a cobblestone appearance. Microscopically, the presence of tubular or tubulopapillary infiltrative patterns, intense stromal desmoplasia, and chronic inflammatory cell infiltration in and around the tumor can help in establishing a definitive diagnosis of CDC. Several other tumors can show a picture similar to the CDC, therefore additional examinations are needed to support the diagnosis, one of which is an immunohistochemical examination. Most CDCs express PAX8, high molecular weight cytokeratin, CK7, and strong positive for epithelial membrane antigen (EMA), focally reactive with vimentin, but did not express CK20, CD117, CD10, GATA-3, and p63 on immunohistochemical staining. Paired box gene 8(PAX8) is a transcription factor of lineage specificity thyroid, Mullerian ducts, and nephric. Non-neoplastic renal tubules, including inclcollecting ducts, have been shown to express PAX8 and not p63 which is generally used for urothelial differentiation. Based on the examination, a diagnosis is obtained collecting duct carcinoma, minimal staging pT3aNxMx, LVI (+), PNI (+). Radical nephrectomy and regional lymphadenectomy are usually performed as management of CDC. This tumor exhibits aggressive characteristics and a tendency for distant metastasis with a median survival of 12 months. Currently, the GC regimen (gemcitabine cisplatin) is considered the first-line systemic treatment of metastatic CDC because no other chemotherapeutic agents have shown beneficial effects.[18,19]

Most of these tumors are associated with outcome which is poor due to their very aggressive clinical course, high prevalence of metastases, and limited response to immunotherapy and chemotherapy. The patient in this case came with the main complaint of swelling in the right abdomen since 1.5 months ago. Referring to the results of research conducted by Tang C in 2021, patients with smaller tumor sizes (<7 cm) had survival rates higher when compared with larger tumors (24 months and 13 months, respectively). Based on the examination, a diagnosis is obtained collecting duct carcinoma, minimal staging pT3aNxMx, LVI (+), PNI (+). Survival rates were also related to T stage, and the median survival times of T1, T2, T3, and T4 were 81 months, 56 months, 13 months, and 7 months, respectively. In addition, tumor metastasis to the liver and duodenum based on the history, physical examination, and supporting examinations is also a prognostic factor in patients. The liver is one of the most common metastatic sites causing a dramatic decrease in the 5-year survival rate to 20%. The poor prognosis of the disease after demonstrating metastatic spread is due to the ineffectiveness of conventional therapies such as systemic chemotherapy, radiation, or hormone therapy. The difference in survival time in patients with and without distant metastases is statistically very significant, namely 7 months and 53 months.[20,21]

4. Conclusion

A CDC case was reported in a 56-year-old woman whose diagnosis was confirmed by histopathological examination with the main complaint of swelling in the right abdomen since 1.5 months ago. In the microscopic picture, there is a proliferation of tumor cells that grow infiltratively in the connective tissue stroma, some of which are desmoplastic and in the fatty tissue between the glomerulus and tubule. Tumor cells are arranged to form tubulopapillary and tubulocystic structures. These cells with pleomorphic nuclei, some hyperchromatic, some vesicular, coarse chromatin, clear nuclei, and atypical mitoses can be found and tumor cell embolism in the blood vessels and perineural invasion can be seen. There were spots and clusters of lymphocytes and plasma cells as well as areas of bleeding and necrosis.

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