Case Report

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Increasing Cases of Retroperitoneal Fibrosis After Covid-19: Case Report, Did She Die Retroperitoneal Fibrosis or Cancer?

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Abstract

This case report details the unfortunate journey of a 59-year-old breast cancer survivor who developed secondary Retroperitoneal Fibrosis (RPF) in 2022. Despite diligent treatment efforts, her condition took a devastating turn when, in June 2023, she was diagnosed not only with persistent RPF but also with advanced liver, omental, and duodenal cancer. Tragically, her condition deteriorated rapidly, leading to her passing on day 41 following her presentation. This case underscores the challenges of diagnosing and treating RPF. It highlights the importance of considering cancer development in advanced RPF cases that do not respond to treatment, often leaving limited options for effective intervention.

Keywords: Retroperitoneal fibrosis, liver cancer, metastasis, steroid, azathioprine.

Introduction

Retroperitoneal-fibrosis (RPF) is a rare fibroinflammatory disease that usually occurs in the retroperitoneal space surrounding the ureters and vascular structures such as the abdominal aorta, inferior vena cava, iliac artery, and ureters, often causing ureteral obstruction and renal failure. The annual incidence of RPF is 0.1/100.000, and the prevalence is 1.4/100.000 (1). Men are affected by the disease more than women. The male-to-female ratio is between 2/1 and 3/1. The mean age at diagnosis is 50-60 years. RPF is etiologically divided into idiopathic and secondary causes. Idiopathic RPF accounts for approximately 2/3 of all patients. Secondary RPF can be caused by drugs, malignancy, surgery, infection, and radiation. Malignancies are essential among secondary causes, accounting for 8-10% of all RPF cases. Malignancy-related RPF can be caused by desmoplastic tissue resulting from the impact of metastatic cells in the retroperitoneum or by the presence of a primary mass such as Hodking, Non-Hodking Lymphoma, and sarcomas. Although metastases from all malignancies can occur in the retroperitoneum, the most common ones are from the breast, stomach, colon, prostate, lung, and kidney. Surgical and medical treatment is used. The majority of the etiology needs to be clarified; symptoms and signs are non-specific, they are confused with many other conditions in differential diagnosis, and there is no generalizable treatment regimen (2).

Case Report

A 59-year-old female smoker was diagnosed with a 28*18 mm solid lesion or mass in the upper outer quadrant of the left breast on ultrasonography and magnetic resonance imaging performed in 2015. She was diagnosed with invasive carcinoma in TRU-CUT biopsy results evaluated at a university hospital. She underwent left breast-conserving surgery + chemotherapy + radiotherapy + anastrozole treatment for five years, and regular follow-up visits were performed.The female case, who was vaccinated with three doses of sinovac, had covid-19 twice in January and December 2021.

In September 2022, the patient was admitted to our center with complaints of leg swelling and inability to urinate and underwent a non-contrast MRI due to mildly elevated urea and creatinine values.. He was diagnosed with bilateral renal RPF and hydronephrosis. Laboratory tests revealed Fasting Blood Glucose (FBSG): 90 mg/dL, Urea: 41 mg/dL, Sodium: 143 mmol/L, Potassium: 4.8 mmol/L, Gamma Glutamyltransferase (GGT): 46 U/L, Calcium: 9.3 mg/dL, ALT (SGPT): 16 U/L, AST (SGOT): 14 U/L, Creatinine

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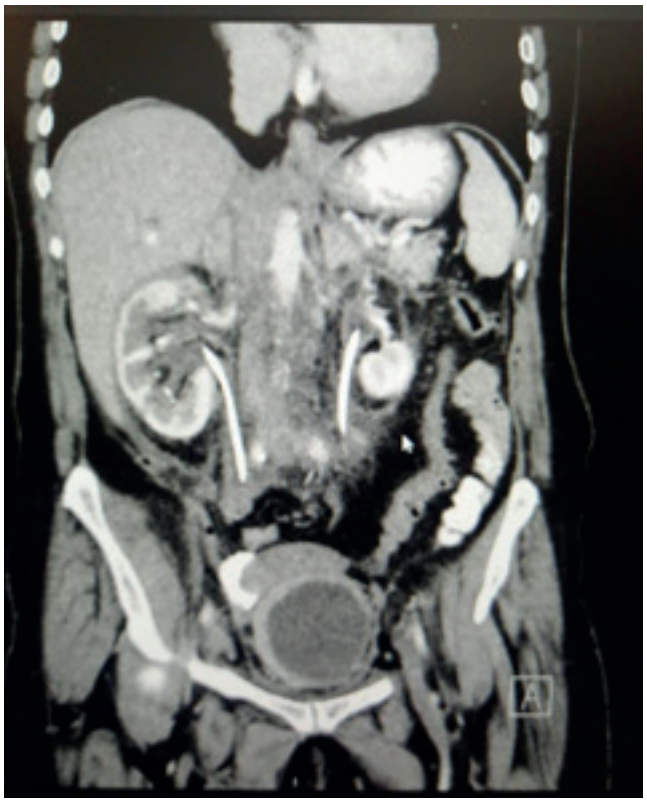

Figure 1. At the level of both retroperitoneal areas, diffuse thickening and heterogeneity extending along the paraaortic, paracaval, and aortocaval areas surrounding both kidneys.

(Serum): 1.96 mg/dL, CRP (quantitative): 13.3 mg/L. A bilateral double-J catheter (3 months use) was placed in both kidneys three days after the diagnosis. The biopsy obtained from RPF was also negative for urothelial carcinoma. The patient was referred to the Rheumatology Outpatient Clinic for RPF treatment at the same center, and therapy with Prednol 48mg was started. She received lymphedema treatment from the Physical Therapy Department at the same center for swelling and leg edema.

Afterward, he was followed up regularly for two months and continued to use Prednol. However, the patient continued complaining of edema and leg pain despite having bilateral double-J catheters. Upper abdominal computed tomography revealed diffuse heterogeneous density changes in the retroperitoneal area extending from the paraaortic neighborhood inferiorly towards the iliac artery neighborhood. Laboratory tests at the same center revealed creatinine values of 1.78 mg/dL, CRP 23.6 mg/L, GGT 77.00. In November 2022, the patient's bilateral double-J catheter was removed and replaced with a bilateral double-J (6 CH tumor stent) catheter for one year. Imuran 50 mg 1*1 was started in addition to Prednol for RPF. She received lymphedema treatment from the physical therapy department for both legs. The patient continued regular rheumatology, nephrology, gastroenterology, and urology visits.

In June 2023, the patient was admitted to our center complaining of vomiting, abdominal pain, abdominal distension, constipation, and flank pain. Contrast-enhanced MRI and ultrasound revealed a 24x18 mm hypoechoic solid mass lesion (metastasis) at the left lobe lateral segment level in the liver. At the level of both retroperitoneal areas, diffuse thickening and heterogeneity were observed extending along the paraaortic, paracaval, and aortocaval areas surrounding both kidneys (Figure 1). The findings were due to retroperitoneal diffuse fibrosis. Hospitalization was recommended, and the patient was followed up. Contrast-enhanced MR examination of the abdomen revealed a subcapsular mass in the left lobe of the liver, and a US-guided percutaneous biopsy was performed. Pathology revealed a diagnosis of poorly differentiated carcinoma in the liver on true-cut biopsy. Laboratory tests revealed AST 109.8, ALT 181.1, GGT 487, and hemoglobin 9.6. Surgery revealed a two cm metastatic mass in segment 4 of the left lobe of the liver. It was excised with the help of ligasure. Bleeding was controlled with a liver suture, and a surgicelle was placed. There was diffuse fibrosis in the abdomen due to retroperitoneal fibrosis (also evident in the duodenum). The boundaries of the tumoral mass could not be palpated clearly because it was diffuse, and fibrosis surrounded all vital vessels. Duodenal obstruction was present due to retroperitoneal fibrosis.Biopsies were taken from the liver, omentum, and duodenum during surgery. Gastroenterostomy and metastasectomy were performed. During surgery, metastasectomy was performed on a 2 cm. diameter mass in liver segment 4. There were multiple millimetric metastatic masses in the mesosoma and omentum of the small intestine. Biopsies were also taken from these. The duodenum tumor was considered unresectable due to the extent of metastasis. Gastroenterostomy was performed due to the absence of duodenal passage. The patient was placed on NG. She was fed with TPN. Medical treatment was applied (Table 1). On post-op day 2, NG was removed, and water was given. However, when vomiting recurred, NG was inserted and fed with TPN. The patient's general condition was good on post-op day 5. When no fluid came from the clamped NG, it was removed, oral nutrition was started and he was discharged on post-op day 10. However, two days later, she presented to our center again with vomiting, pain, and constipation.Pathology results revealed adenocarcinoma of the liver, duodenum, and omentum. On post-op day 13, GGT 279, CRP 313, Bilirubin 12, Na 126, and hemoglobin 8.3 were evaluated in laboratory tests. Hyponatremia and hyperbilirubinemia were detected. Medical treatment was initiated (Table 1). Antibiotherapy, fluid replacement therapy, and TPN continued. Percutaneous Transhepatic Cholangiography, Percutaneous Biliary Drainage, and Percutaneous Choledochal Dilation were performed post-op day 16. Durogesic treatment was started. Due to low hemoglobin, two units of ES were given. A biliary stent and drain for ascites were placed by interventional radiology on post-op day 20. The patient continued to vomit 5-6

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Table 1: Drugs administered to the patient for 41 days

Medicine Name	Amount
PANTONIX IV MG 1 FLK	21 Pieces
ANTI-NAUSEA IM/IV 10MG/2ML INJECT. COZ. ICRN. AMP	37 Pieces
PARACEROL 10MG/ML 100 ML FLK	34 Pieces
DORIFEN 400 MG 4 ML	12 pieces
KEMOSET 8 MG 4 ML AMPOULE	15 pieces
HYPERTONIC SODIUM CHLORIDE 3%150 ML OSEL	144 Pieces
POLYNUTHREE EN-550 1000 ML	18 Pieces
ISOTONIC SODIUM CHLORIDE 0.9%500 ML NEOFLEX	9 pieces
SAFRAX Capsules 250 mg pack of 100 capsules	48 Pieces
ISOTONIC SODIUM CHLORIDE 0.9%500 ML	15 pieces
METICURE LIYO 20 MG AMP	7 pieces
CİPRASEL I.V 400- 200 ML	12 pieces
MANNITOL 20%100 ML OSEL	4 pieces
MIDAJECT 15 MG/3 ML IM/IV/RECTAL SOLUTION CONTAINING 5 AMPOULES	2 pieces
FENTAVER IM/IV Ampoule0,5 mg/10 ml 1x10 ml ampoule	2 pieces
MOLIT 1 ML 6 AMPOULES	2 pieces
PRILOC 2% INJECTABLE VIAL	4 pieces
KONAKION MM.10 MG.5 AMPOULES	2 pieces
DUROGESIC 25 MCG/HOUR TRANSDERMAL PATCH	2 pieces
ALDACTONE-A 25 MG TABLET	35 Pieces
NUTRICLIN N7-1000E 1500 ML	3 pieces
GENTHAVER 160 MG.1 AMPOULE	1 Piece
ISOTONIC SODIUM CHLORIDE 0.9%100 ML TURK-TIPSAN	1 Piece
IRRIGATION ISOTONIC SODIUM CHLORIDE 0.9%1000 ML TURKTIPSAN	1 Piece

times a day. Medical treatment continued. The patient was mobilized and could walk 500 m. per day until post-op day 30. It gradually decreased in the last week, and on the 37th day, he was mobilized at the bedside, cared for, walked four to five steps towards the bed, and lost consciousness when he moved to the bed. Post-op 38 days, he was in the 1st-level intensive care unit. There was no septic shock or sepsis status, or need for ventilation. On day 39, the patient was transferred to our intensive care unit due to respiratory failure. In the 2nd level intensive care unit, septic shock occurred. However, there was no sepsis and no need for ventilation. On day 41, the patient died due to terminal malignancy and concomitant RPF.

Discussion

RPF is a rare disease characterized by inflammation and fibrosis in the retroperitoneal region, starting at the level of the renal vessels and involving the ureters, periaortic, and parailiac. Although the histological event in the tissue is benign, it is a malignant disease when the clinical course is considered. The main difficulty in diagnosing the disease is that patients do not consult a physician before renal function deteriorates and specific symptoms occur, or a non-specific symptom such as abdominal pain is the most common. Peripheral edema associated with deep vein thrombosis may occur due to vena cava compression. Gastrointestinal complications include constipation and abdominal angina due to vascular compression (3). In this case, RPF started with abdominal pain and bilateral leg edema. Evaluation of renal and urinary tract involvement is essential in patients affected by RPF. At diagnosis, 8-30% of patients lose renal function due to persistent hydroureteronephrosis, which is usually asymptomatic and leads to a delay in diagnosis (4). A 59-year-old woman was admitted to a university hospital with renal dysfunction, but the diagnosis was delayed by three months. The patient was admitted to our center and diagnosed with RPF and hydronephrosis in bilateral kidneys after an MRI.

The role of smoking in the progression of RPF is also essential (5). Goldoni et al. (6) reported that exposure to cigarette smoke is a significant risk factor for RPF. Raglianti et al. (7) argued that smoking increases the progression of RPF disease. In this case, a 59-year-old female patient was found to be an active smoker for 40 years.

In the literature, most patients were given corticosteroids for the medical treatment of RPF. In addition, methotrexate, azathioprine, mycophenolate mofetil, and tamoxifen were use(8). In this case, a steroid was used in the initial diagnosis. As the patient's complaints did not change, azathioprine (3 months in total) was used in addition to steroids (6 months in whole) after the second double j catheter was inserted. Medical treatment was discontinued due to deterioration in the general condition and persistence of complaints.

In studies, high rates of developing cancer within one year have been recorded in RPF patients. Cancer cases are mostly in the stomach, lung, colon, and renal pelvis(9). Studies have shown that cancers that develop after RPF cases progress and spread more rapidly. Malignant RPF has a poor prognosis with a median survival of up to 3-6 months(10). In the study by Chen et al. (4) 56 of the 80 patients followed unfortunately died due to the progression of primary malignancy (4). Lee et al. (2) found that patients diagnosed with RPF were associated with subsequent cancer. In our case, a metastatic lesion in the liver was detected

approximately nine months after the diagnosis of RPF, and primary duodenal malignancy was seen within 15 days. RPF and cancer spread very rapidly.

Conclusion

Early diagnosis is essential in RPF. The physician should be determined to use advanced diagnostic tests before renal dysfunction occurs and specific symptoms develop. The possibility of cancer development in RPF patients should be emphasized. Since malignancy is frequently associated with RPF, malignancy should be meticulously investigated with contrast-enhanced studies if necessary, especially if the symptoms progress rapidly. However, cancers detected after the diagnosis of RPF are typically advanced. Unfortunately, the options for effective treatment are limited.

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