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RESEARCH ARTICLE

ACUTE PANCREATITIS AFTER TRANSARTERIAL CHEMOEMBOLIZATION BEFORE LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: A CASE REPORT.

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Key words:-

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Abstract

Introduction: Acute pancreatitis is one of the rare complications of transcatheter arterial chemoembolization with an incidence ranging from 2% (clinical pancreatitis) to 40% (biological pancreatitis). It may result from the development of ischemia caused by regurgitation of embolic materials into the vessels supplying the pancreas. This complication has a significant morbidity and mortality potential when it is associated with other complications.

Case report: We report a case of acute pancreatitis in a 58 year-old North African male, developed within 24h after a first selective chemoembolization proposed as locoregional bridge therapy for the treatment of hepatocellular carcinoma before liver transplantation. In this case, the first possible etiology of acute pancreatitis was transcatheter arterial chemoembolization, because there were no other causes of acute pancreatitis, the chronology was compatible and the vascular opacification has showed a regurgitation of embolic materials during the procedure. Through this case and review of literature, we focused on the mechanisms and diagnosis difficulties of acute pancreatitis following chemoembolization.

Conclusion: Acute pancreatitis is a rare complication of transcatheter arterial chemoembolization, and may clinically mimic a postembolization syndrome at the early stage. The knowledge of this complication must lead to a systematic monitoring of serum pancreatic enzymes in cases of abdominal pain after chemoembolization.

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Introduction:-

Transcatheter arterial chemoembolization (TACE) has been recognized as an effective palliative therapy for hepatocellular carcinoma (HCC), not only for antitumoral effect but also for survival benefit [1]. Currently, most transplant centers use TACE as locoregional bridge therapy for HCC before liver transplantation (LT) in the absence of underlying decompensated cirrhosis [2]. However, ischemic damage to various extrahepatic organs may complicate TACE due to unintentional embolization of the vessels supplying these organs. Acute pancreatitis (AP) is one of the ischemic complications of TACE. It has an incidence ranging from 2% (clinical pancreatitis) to 40% (biological pancreatitis), but fatal outcome is generally low (1-2%) [3]. The risk factors associated with acute pancreatitis after TACE were unselected angiography, number of procedures, and the volume of embolic material.

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We report a case of acute pancreatitis developed within 24 hours after a first selective TACE proposed as waiting treatment of HCC before LT, and intend to discuss its mechanism.

Case report:-

A 58 year-old North African male, with no significant medical history, was hospitalized for the treatment of HCC complicating hepatitis B cirrhosis. At admission, the patient had no clinical symptoms, and physical examination was normal except mild conjunctival jaundice and splenomegaly. Biological tests found: Platelet count: 61000/ μ l, Prothrombin level: 60%, AST: 36UI/l(N:35), ALT: 38UI/l, Alkaline phosphatase: 104 U/l (N<91), GGT: 53 (N<50) U/L, total Bilirubin: 21 mg/L, Albumin: 32g/l, AFP: 4,36ng/ml and PCR DNA HBV : 5.83 Log. Abdominal computed tomography (CT) showed a focal hypodense nodule in the right hepatic lobe(segment VII) measuring 4,7cm with hyperenhancement at axial arterial phase (Figure 1) and washout of contrast agent at delayed phase; associated to liver dysmorphism, splenomegaly, portosystemic shunt and gastroesophageal varices. There is no portal thrombosis or gallbladder stones. Upper endoscopy revealed oesophageal varices grade III with red spots, gastroesophageal varices (GOV II) and hypertensive gastropathy. Overall, our patient had Cirrhosis (Child B7Meld 13) with a single HCC measuring less than 5cm, classified as BCLC early stage (stage A) with signs of portal hypertension and elevated bilirubin levels. Multidisciplinary meeting retained liver transplantation for the management of this patient and proposed locoregional therapy by TACE as a waiting treatment. TACE was performed with selective catheterization of the right hepatic artery and injection until cessation of blood flow of lipiodol and anticancer drug emulsion (containing 5ml Lipiodol, 50mg cisplatin, and 20mg doxorubicin). Arterial embolization was performed using a gelatin sponge. The regurgitation of embolic materials was found during the procedure and arteriography after TACE was showed disappearance of blood flow in the right hepatic artery and fixation of lipiodol localized in the HCC (Figure 2A and B). The patient complained of abdominal pain immediately after the procedure with nausea and vomiting. His vital signs were stable with moderate epigastric tenderness. Serum lipase levels were markedly increased to 1655UI/l (21N) with moderate cytolysis and cholestasis AST: 100UI/l(2,8N), ALT: 85UI/l(2N), Alkaline phosphatase: 80UI/l (N<91), GGT: 70UI/l(1.5N), total bilirubin: 37 mg/l. while other serum biochemical levels were within normal ranges. Computed tomography (CT) performed 48 hours later demonstrated a swelling of the pancreatic head with infiltration of peripancreatic fat and antroduodenal wall thickening. The Balthazar score of acute pancreatitis was grade C (Figure 3). The diagnosis of acute pancreatitis secondary to TACE was retained after having eliminated the usual causes of pancreatitis (biliary stones, alcohol consumption, drug-induced pancreatitis, metabolic disorders particularly those related to hyperlipidemia and hypercalcemia and tumors), This PA is related to regurgitation of the embolic materials into gastroduodenal artery supplying pancreatic head. The patient was treated for 4 days with general management of acute pancreatitis: pain control, hydration, fasting and total parenteral nutrition. The patient's symptoms improved, Titer of pancreatic enzymes gradually decreased and oral diet was permitted. Abdominal CT control showed decreased pancreatic lesions and the patient was discharged from the hospital.

Discussion:-

HCC is the third most lethal malignancy, with approximately 80% of cases of HCC developing in patients with a cirrhotic liver [4]. Liver transplantation is a radical management, treating both cancer and cirrhosis. However, the scarcity of liver donors and increasing number of candidates for LT are progressively causing an increase in the waiting period. Currently, Most transplant centers widely use locoregional therapies before LT as neo-adjuvant treatment with two intents. The first one is to prevent the dropout from the waiting list in patients meeting accepted criteria of transplantability. The second one is to treat patients initially outside criteria for LT in order to fulfill Milan criteria [5], University of California San Francisco criteria [6], or other criteria, which allows entry to the waiting list for LT after an adequate period of follow-up. This neoadjuvant treatment include TACE, radiofrequency ablation, percutaneous ethanol injection and liver resection, which should be selected according to the Barcelona Clinic Liver Cancer (BCLC) scoring system.

In the present case, the patient had cirrhosis Child-Pugh B7 Meld13 with a HCC classified as BCLC early stage with signs of portal hypertension. The indication of TACE was retained in multidisciplinary meeting as locoregional bridge therapy before liver transplantation.

Multiple trials showed that TACE increases objective tumor responses, slows tumor progression and improves survival benefits [7, 8]. However, TACE can lead to several possible complications, It was reported that the incidence of major complications was 2.7% per TACE procedure [9]. The main complication of TACE is the "postembolization syndrome" including abdominal pains (26 to 55%), vomiting (17 to 50%), fever (33 to 55%) and liver cytolysis, it occurs in up to 90% of patients after the procedure. The etiology of this syndrome is not fully

understood but it is probably resulting from a combination of tissue ischemia and an inflammatory response to chemoembolization [10, 11]. The other common complications include intrahepatic biloma, cholecystitis, liver abscess, biliary tract injury, renal failure, splenic infarction, gastrointestinal mucosal lesions, multiple intrahepatic aneurysms, and rare but more severe complications include acute hepatic failure, necrotizing pancreatitis, pulmonary embolism or infarction, tumor rupture, hepatorenal syndrome, and variceal bleeding [12].

Acute pancreatitis is a rare complication of the TACE for HCC but it has a significant morbidity and mortality potential. It usually develops within 24 h of the procedure. As reported in the literature, the incidence of acute pancreatitis after TACE varies between 2% (clinical pancreatitis) to 40% (biological pancreatitis) and a few cases of necrotizing pancreatitis complicated by abscess formation after TACE have been reported [13, 14]. It may result from the development of ischemia caused by regurgitation of embolic and chemotherapeutic agents into the pancreatic arteries. Another study suggested that superselective TACE may reduce the risk of pancreatic tissue damage by embolic materials [15]. Hepatic artery injury due to repetitive TACE can cause the development of parasitic tumor feeding vessels from the non-hepatic artery, which can increase the extrahepatic ischemic injury. Also, it has been reported that the injecting of more than 2 ml embolic material compared to less than 2 ml caused a significant increase in the incidence of acute pancreatitis. From the anatomic variation aspect, the chance of developing ischemic injury can be affected when many vessels arise from a common trunk with early bifurcation. Moreover, in advanced atherosclerosis patients, the iatrogenic dissection of the gastroduodenal artery during the procedure can cause acute pancreatitis through the ischemic mechanism because the anastomosis of the superior pancreaticoduodenal artery and the superior mesenteric artery can be ineffective. Therefore, to prevent ischemic complications of TACE, the catheter tip should be placed in the distal branches of the hepatic artery, and injection of embolic materials should be done carefully to avoid the regurgitation [16]. In our case, TACE is the first possible etiology of AP because there were no other causes of AP, the chronology was compatible and the vascular opacification had showed a regurgitation of embolic material during the procedure explaining the pancreas ischemic injury.

It is difficult to differentiate between early onset pancreatitis and post TACE syndrome based on symptoms like abdominal pain and nausea. Therefore, dosage of serum pancreatic enzymes should be performed systematically in patients complaining of abdominal pain after TACE. In this case report, lipase levels were checked early on 7th hour after TACE because his abdominal pain was not controlled by analgesics. Cases of AP induced by TACE are usually benign, occurring within 24 hours, with favorable spontaneous evolution, but some forms with pancreatic necrosis exist. Its treatment is conservative, as in acute pancreatitis from other causes.



Figure 1:-Abdominal computed tomography showed a nodule in the segment VII enhanced at axial arterial phase (arrow).

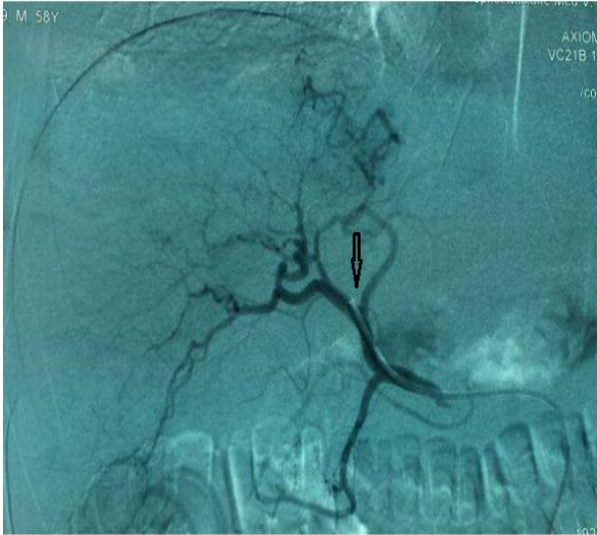


Figure 2A



Figure 2B

Figure 2A and 2B:-Arteriography after selective TACE showed the catheter tip placed at the right hepatic artery (arrow) and lipiodol accumulated in the tumor in segment VII.



Figure 3:- Abdominal computed tomography demonstrated a swelling of the pancreatic head with infiltration of peripancreatic fat and antroduodenal wall thickening.

Conclusion:-

Acute pancreatitis is a rare complication of transcatheter arterial chemoembolization for hepatocellular carcinoma, and may mimic postembolization syndrome at the early stage. The pathophysiological mechanisms of acute pancreatitis after selective TACE remain unclear. Although it seems to have a multifactorial etiology but ischemic mechanisms might be the most important causes of pancreatic inflammatory reactions after this procedure. The knowledge of this complication must lead to a systematic monitoring of serum pancreatic enzymes in cases of abdominal pain after TACE for the early detection and treatment of acute post procedural pancreatitis.

Competing interests:-

The authors declare that they have no competing interests.

Authors' contributions:-

H.Basr, F.Rouibaa and B.Aitbihi evaluated the patient and were major contributors in writing the manuscript. R.Saouab and M. Mahi analyzed CT data and realized TACE. RF and MM reviewed the manuscript. All authors read and approved the final manuscript.

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