Splenic artery ligation for severe oxaliplatin induced portal hypertension: A way to improve postoperative course and allow adjuvant chemotherapy for colorectal liver metastases:

Letter to editor: Comment about “Nodular regenerative hyperplasia (NRH) complicating oxaliplatin chemotherapy in patients undergoing resection of colorectal liver metastases”

Keywords: Splenic artery ligation; Nodular regenerative hyperplasia; Chemotherapy induced liver injuries; Portal hypertension; Colorectal liver metastases; Major hepatectomy

To the Editor:

We have read with interest the article entitled “Nodular regenerative hyperplasia (NRH) complicating oxaliplatin chemotherapy in patients undergoing resection of colorectal liver metastases” by Morris-Stiff et al.1 which was published “online first” in European Journal of surgical oncology in December 2013.

In this study, the authors have explored the impact of NRH on post-operative outcome, in patients undergoing resection of colorectal liver metastases.

Among the spectrum of chemotherapy-induced liver toxicity and more precisely among microvascular lesions induced by chemotherapy, NRH is defined as the presence of regenerative nodules with expanded liver cell plates not limited by fibrosis but by small atrophic hepatocytes.2 Increased portal blood flow in the non obstructed sinusoids leads to a regenerative response whereas the poorly supplied acini become hypotrophic. Consequently non cirrhotic portal hypertension with low platelet count, splenomegaly and oesophageal varices not limited by fibrosis but by small atrophic hepatocytes.2

In this study by Morris-Stiff et al.1 neither postoperative morbidity nor mortality were modified by NRH and liver resection seems to be perform without caution. Because of the obviously limited number of major hepatectomy, the results of this study could only be considered as convincing for limited resections, according to the authors.

The impact of this chemotoxicity on postoperative course is still debated. An increased hepatic morbidity has been reported in patients with NRH, more precisely related to the low platelets rate (<preoperative platelet count of 150 × 10^3/μL). Other predictive factors have also been reported such as bilirubin and GGT levels.3 In addition, a high APRI score with low platelet count is also associated with severe sinusoidal lesions and altered post-hepatectomy outcome. An increased hepatic morbidity has been reported in patients with NRH, more precisely related to the low platelets rate (<preoperative platelet count of 150 × 10^3/μL). Other predictive factors have also been reported such as bilirubin and GGT levels.3

In addition, a high APRI score with low platelet count is also associated with severe sinusoidal lesions and altered post-hepatectomy outcome.1 It should be highlighted that thrombocytopenia and correlated splenomegaly have emerged as main findings associated with severe SOS lesions. There are 3 mechanisms of oxaliplatin induced thrombocytopenia: direct bone marrow toxicity, immune response which represents a minor cause, and splenic sequestration of platelets resulting from portal hypertension.8 Thrombocytopenia associated with a 50% splenic volume increase is usually irreversible as compared to direct toxicity. Overall, oxaliplatin induced portal hypertension leads to two main drawbacks; an altered regenerative process following major hepatic resection and a refractory thrombocytopenia which contra indicates adjuvant chemotherapy.

As in living donor liver transplantation, portal hyperperfusion syndrome has been widely studied leading to the development of portal flow modulation strategies. Splenectomy, splenic artery ligation or embolization are efficient in reducing the incidence of liver failure and graft loss in small graft recipients.9 Splenic artery obstruction is associated with a 50% decrease in portal flow in the first postoperative days. Moreover, splenic artery ligation may help to overcome severe thrombocytopenia and splenic artery embolization enables chemotherapy administration in this setting.10

Contrary to Morris-Stiff et al. we applied this portal flow modulation strategy using splenic ligation in four patients who underwent a major hepatectomy on severely with portal hypertension is considered as a contraindication to surgery by some surgeons due to the risk of portal hyperperfusion.

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vascular-injured livers with histologically proven diffuse NRH. These patients had received more than 9 cycles of oxaliplatin regimen. They developed thrombocytopenia and related splenomegaly, and portosystemic shunts before resection. None experienced liver insufficiency or portal hypertension complications. At last follow-up, signs of portal hypertension regressed but low platelet counts persisted in all but one patient. However, all patients received a postoperative adjuvant chemotherapy owing a significant platelet count improvement. Histological examination showed mild steatosis in one and centrolobular hemorrhagic necrosis without NRH after a switch to irinotecan.

We suggest that portal flow modulation using peroperative splenic artery ligation might be proposed in patients having severe vascular injuries associated with portal hypertension and requiring a major hepatectomy for colorectal liver metastases. This maneuver may help to minimize postoperative hepatic morbidity and allow to achieve a postoperative adjuvant chemotherapy.

Conflict of interest

None.

References


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