



Multiple Liver-directed Therapy including Theraspheres for Recurrent Metastatic Jejunal Carcinoid Tumor

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Introduction:

Majority of patients with neuroendocrine tumors (NET) harbor hepatic metastases at presentation, posing therapeutic challenge. Multiple liver-directed treatment modalities have been employed with variable success. Herein is presented successful outcome in a patient whose recurrent metastatic liver metastases from NET was managed using multidisciplinary approach.

Aim:

We present long-term 18-years course of a patient with liver metastases from midgut carcinoid. She had successful outcome using repeated surgery, radiofrequency ablation, octreotide, and therasphere therapy in succession. Minimally invasive therapy of therasphere using transarterial yttrium 90 can be used safely for recurrent hepatic metastatic neuroendocrine tumor.

Case Presentation:

A 61-year old female with hepatic metastases from non-functioning jejunal carcinoid had resection of 25 cm of small bowel containing 5 cm of carcinoid tumor, resection of 5 cm mesenteric metastatic lymph node, resection of hepatic segments 3 and 4 containing 232 G tumor measuring 7.5 cm. This was followed 10 years later by resection and radioablation of recurrent hepatic metastases. Two years later MRI and octreoscan revealed multiple liver metastases, with abnormal circulating CGA (100 ng/ml; Ref. <93) and received on going monthly octreotide injections. Four years later liver metastases progresses with additional lesions. Liver biopsy revealed metastatic neuroendocrine grade 2 tumor (Ki-67 index 4.5%). In view of her diabetes PRRT was not given; instead she received therasphere therapy. 90 yttrium, tumor dose 164 Gy was injected into left hepatic artery. Patient tolerated it well with no side effects. A year later MRI showed resolution of tumor with atrophic left lobe, and hypertrophic right lobe.

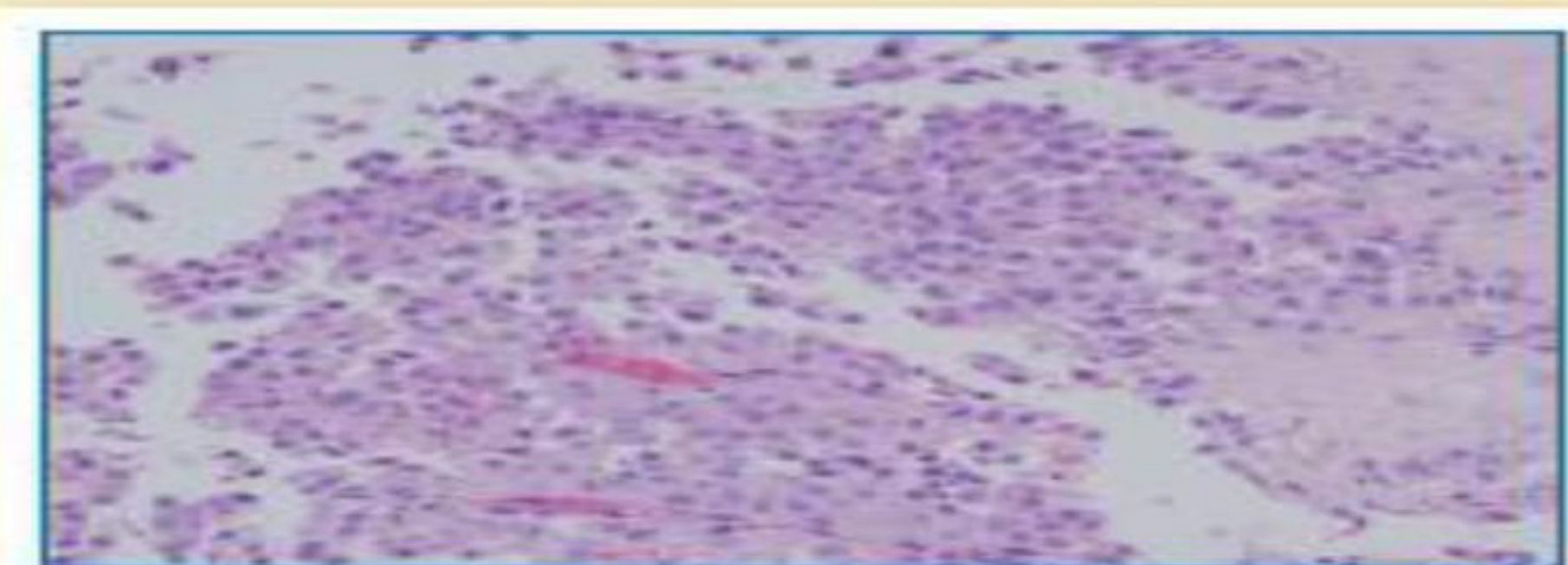
Discussion:

TheraSphere® is an emerging, well-tolerated Y-90 glass microsphere therapy for transarterial radioembolization (TARE) in liver-dominant metastatic NETs.

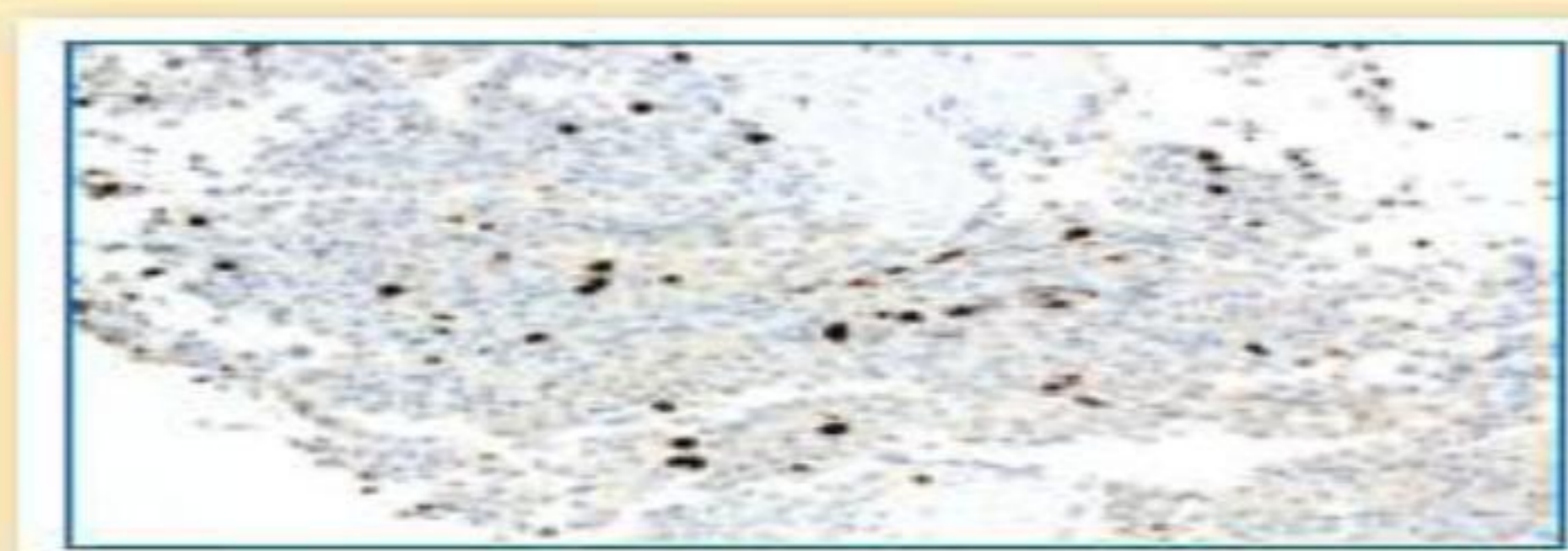
It consists of millions of small glass microspheres (20 to 30 micrometers in diameter) containing radioactive yttrium-90. TheraSphere®, a localized, minimally embolic therapy, capitalizes on the hypervascularity nature of tumors delivering yttrium-90 microspheres, a source of beta energy, via the hepatic artery to the tumor bed. The distribution of arterial blood flow is 3 to 7 times greater within the tumor than the surrounding noncancerous tissue. Consequently, there is preferential delivery of microspheres to the tumor capillary bed allowing for higher doses of radiation to be delivered to the tumor relative to the surrounding nontumor parenchyma. The ability to concentrate radioactive microspheres within the tumor leads to an «inside-out» radiation, which in turn exerts a local tumoricidal effect. This form of radioembolization therapy keeps future treatment options open should liver metastases progress. However, patient selection is important and following criteria are considered contraindication for therasphere therapy; infiltrative tumor type, AST or ALT > 5 times ULN, bilirubin > 2 mg/dL, tumor volume > 50% combined with an albumin < 3 g/dL, or significant hepatopulmonary shunt that may lead to high radiation dose to the lungs. (30 Gy cumulative or 20 Gy per session)

Conclusion:

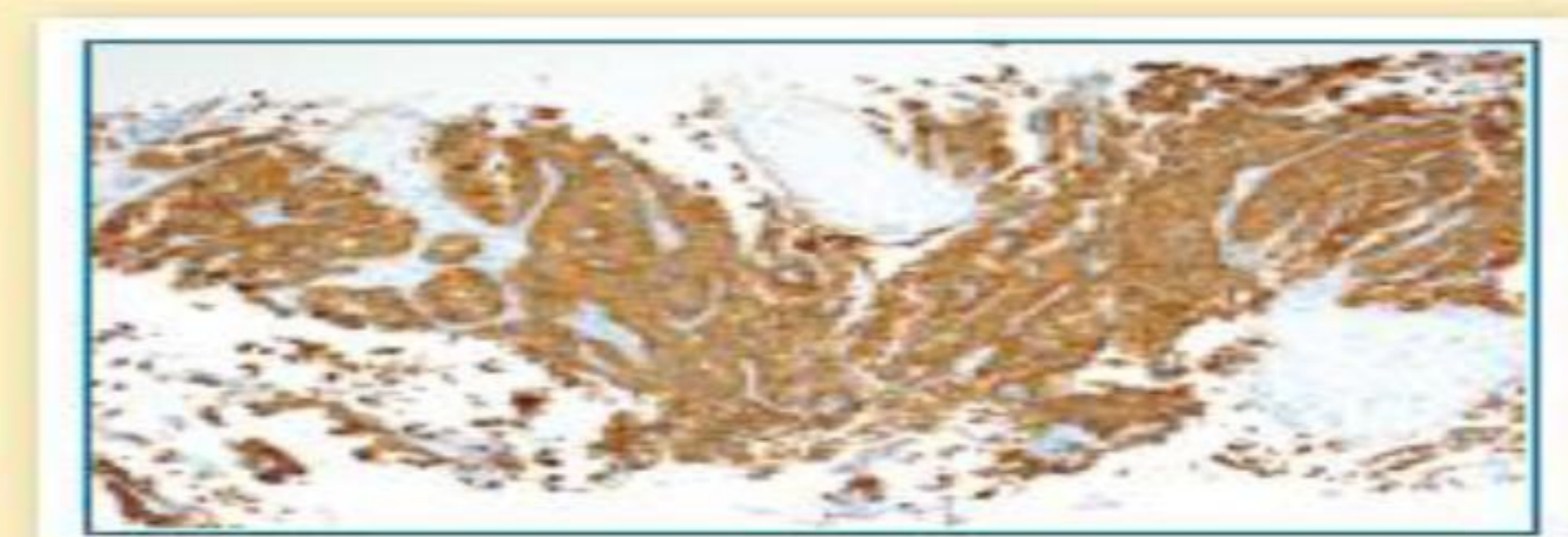
Majority of patients with neuroendocrine tumors present with liver metastases. Despite therapeutic challenge hepatic metastases can be meaningfully managed by a combination of surgical, radioablation, medical and radioembolization therapy using Yttrium 90.



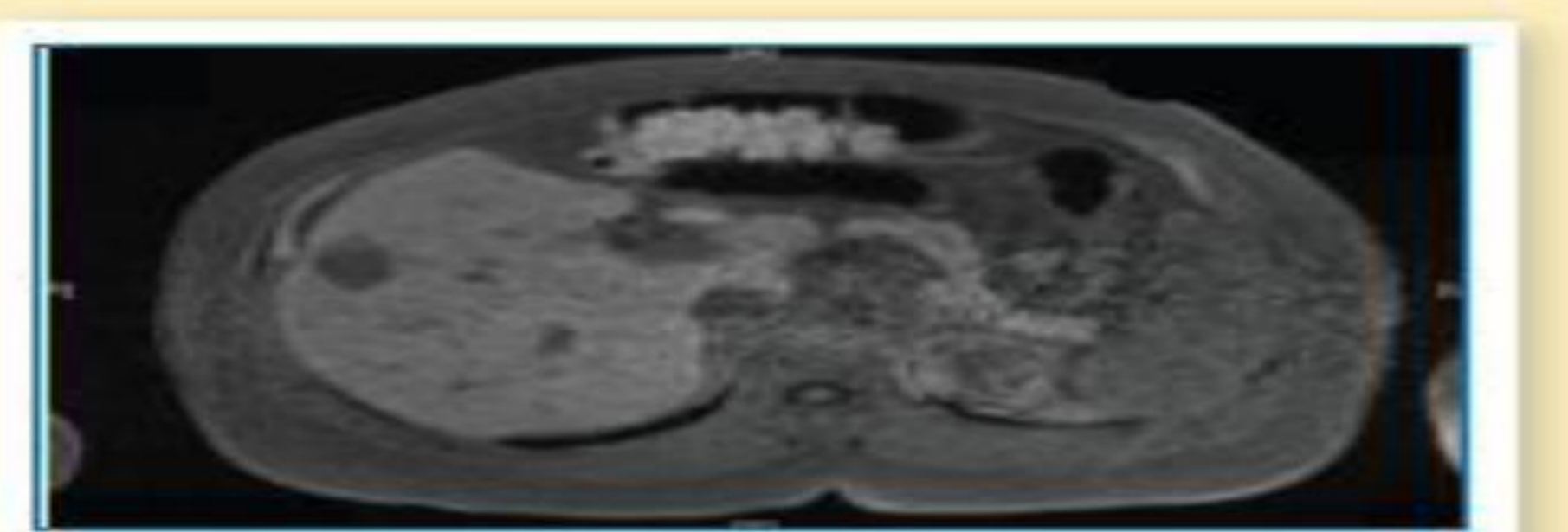
H&E
Intermediate magnification of the liver lesion seen in the biopsy. Nests of monotonous cells with low nuclear grade and virtually no mitoses in this limited sample.



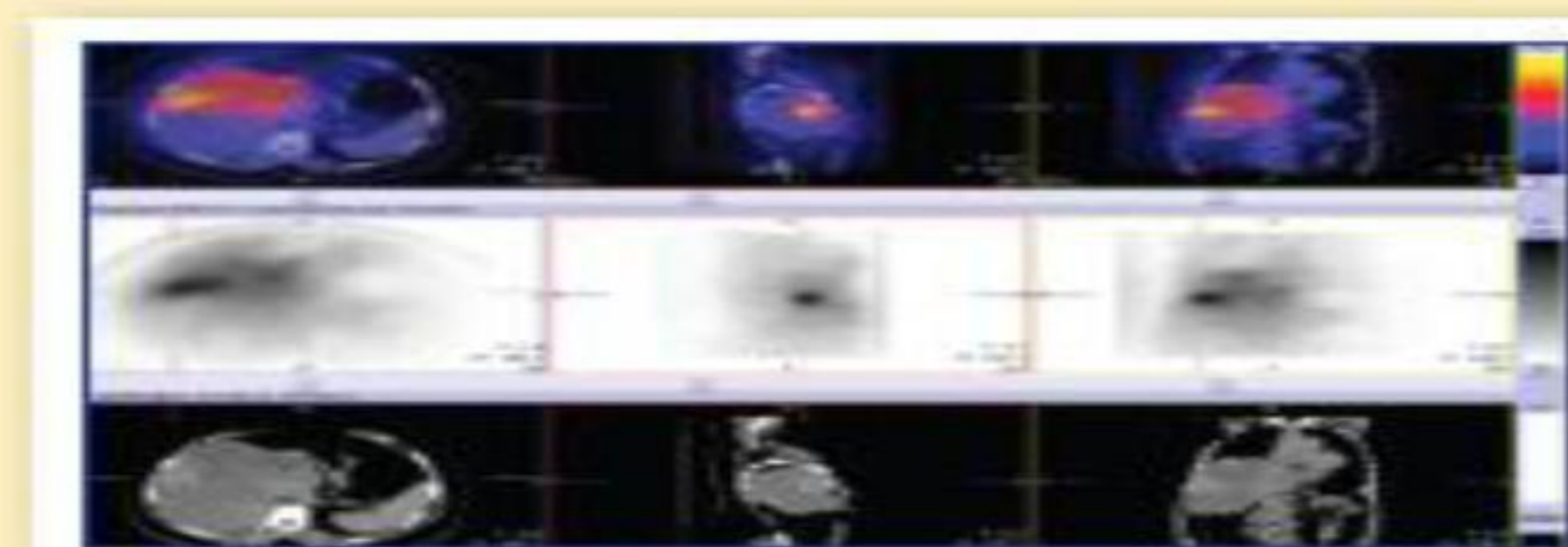
SYNAPTOPHYSIN
Tumor cells are strongly and diffusely positive for synaptophysin confirming the H&E impression of a neuroendocrine tumor.



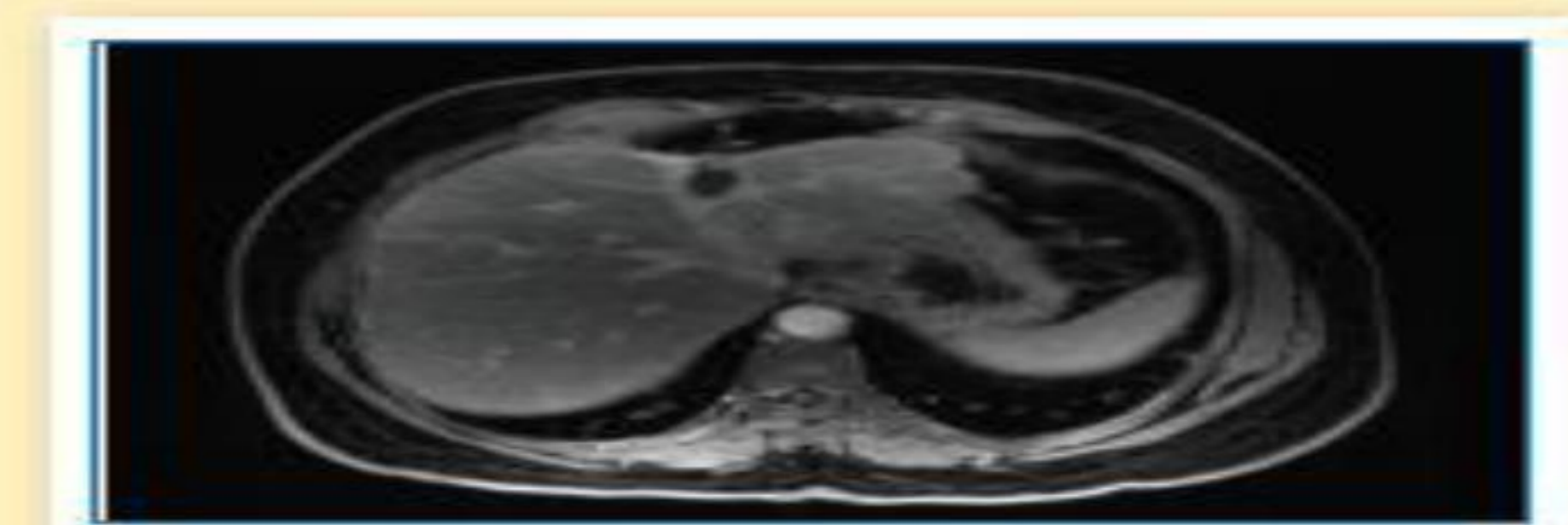
Ki-67
The Ki-67 index is around 4.5% after exclusion of the positive endothelial cells and intravascular leukocytes. This case illustrates the complementary value of using Ki-67 with H&E in limited samples.



MRI
There are several liver metastases of jejunal carcinoid showing low T1, high T2, diffusion restricting arterially enhancing lesions with washout. There are at least four new liver metastases. The largest in segment #4A measuring 13 x 21 mm.



A microcatheter was inserted in the left hepatic artery and a dose of 20 GBq of yttrium 90 TheraSphere was injected giving tumor dose of 164 Gy.



Post-Theraspheres treatment, MRE shows atrophy of the left hepatic lobe particularly hepatic segment #4 and hepatic segment #3 and part of segment #2 with mild intrahepatic biliary dilatation at this region due to fibrosis post treatment of the metastatic lesion at this region. There is no significant enhancement noted at the multiple hepatic lesions with very thin subtle peripheral enhancement. The appearance is in keeping with significant response to therapy.

