Hyperammonemia is an underdiagnosed prognostic complication in neuroendocrine neoplasm patients with liver metastases

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Background

Neuroendocrine neoplasms (NENs) are rare usually slow-growing tumors, often presenting with extensive liver metastases. Hyperammonemia due to insufficient hepatic clearance has been described in NEN cases, however no systematic evaluation of risk factors and outcomes of NEN-associated hyperammonemia exists so far.

Method

Case report and retrospective review of NEN patients developing hyperammonemia from the years 2000-2020 at the Erasmus Medical Center in Rotterdam, the Netherlands.

Results

44 NEN patients with documented hyperammonemia were identified. All patients had liver metastases with 30% (n=13) showing signs of portal hypertension. Patients who developed encephalopathy had higher median ammonia levels, but there was no association between the severity of hyperammonemia and liver tumor burden or presence of liver insufficiency. Eighty-four percent (n=37) of patients died during follow-up. Hyperbilirubinemia, hypoalbuminemia, elevated INR, presence of liver insufficiency, encephalopathy and ascites

were associated with worse outcome. Their role as independent risk factors for mortality was confirmed using the Child-Pugh score as a summary factor ($p<0.001$).

Patients with hyperammonemia had a shorter median overall survival (95% CI) of 56 months (38-73) compared to 131 months (81-180, $p=0.014$) of a control stage IV NEN cohort without hyperammonemia.

Conclusion

Hyperammonemia comprises a relevant and potentially underdiagnosed complication of NEN liver metastases and is associated with worse outcome. Assessment of signs of encephalopathy, risk factors and the Child-Pugh score could be helpful in selecting patients for whom ammonia levels should be measured.