Neurofibromatosis Type 1 With Ampullary Somatostatinoma, Small Bowel GISTs, and Extra-Adrenal Composite Pheochromocytoma-Ganglioneuroma

Patrick Hickey DO
Lehigh Valley Health Network, Patrick.Hickey@lvhn.org

Rohit Sharma MD
Lehigh Valley Health Network, Rohit.Sharma@lvhn.org

Shanth A. Goonewardene MD
Lehigh Valley Health Network, Shant_A.Goonewardene@lvh.com

Shashin Shah MD
Lehigh Valley Health Network, Shashin.Shah@lvhn.org

Hiral N. Shah MD
Lehigh Valley Health Network, hiral_n.shah@lvhn.org

Published In/Presented At

Hickey, P., Sharma, R., Goonewardene, S., Shah, S., Shah, H. (2015, October). *Neurofibromatosis Type 1 With Ampullary Somatostatinoma, Small Bowel GISTs, and Extra-Adrenal Composite Pheochromocytoma-Ganglioneuroma.* Poster presented at: American College of Gastroenterology 2015 Annual Scientific Meeting, Honolulu, HI.

Neurofibromatosis Type 1 With Ampullary Somatostatinoma, Small Bowel GISTs, and Extra-Adrenal Composite Pheochromocytoma-Ganglioneuroma

Patrick Hickey, DO, Rohit Sharma, MD, Shanth Goonewardene, MD, Shashin Shah, MD and Hiral Shah, MD
Lehigh Valley Health Network, Allentown, PA

Background

- Neurofibromatosis type 1 (NF1) is an autosomal dominant hereditary tumor syndrome
- Increased risk of GI tumors including neurofibromas, GISTs, and periampullary carcinoids is reported
- Periampullary somatostatinomas as well as true neurogenic tumors including extra-adrenal pheochromocytomas (paragangliomas) and ganglioneuromas have also been reported
- This case study reviews a patient with NF1 and multiple intra-abdominal neoplasms

Initial Case Description

- A 32 year old male presented with six months of jaundice, dark urine, and weight loss
- CT: dilated intrahepatic ducts, and elevated bilirubin and ALP
- ERCP with biopsy of the ampulla: invasive malignancy with neuroendocrine differentiation
- Pancreaticoduodenectomy showed low-grade somatostatinoma of the ampulla and an incidental duodenal GIST

Case Continuation

- CT scan at year two found an enlarging upper abdominal mass concerning for nodal metastasis
- Ex-lap removal found a paraganglioma in association with ganglioneuroma
- Given the pathology, the diagnosis of NF1 was confirmed with mutation analysis showing a truncating mutation in NF1
- His exam showed multiple café au lait spots on the trunk and upper extremities, multiple neurofibromas, and axillary freckling
- Years later he had a progressive right adrenal nodule and elevated plasma/urine metanephrines
- Resection of a paracaval functional paraganglioma and partial right adrenalectomy with postoperative XRT to the right adrenal bed was performed
- One year later, CT and OctreoScan showed a tumor corresponding with nodularity in the jejunal limb and pancreaticobiliary anastomosis
- Surgery confirmed proximal and distal jejunal GISTs
- Systemic octreotide treatment is under consideration

Discussion

- Alterations in the NF1 gene (tumor suppressor) encodes for the protein neurofibromin
- Unlike sporadic GISTs, NF1 associated GISTs do not usually harbor c-KIT or PDGFRA mutations
- Pheochromocytomas reportedly affect 0.1-6% of NF1 patients. 3/14 reported cases of composite pheochromocytoma-ganglioneuroma were associated with NF1
- The combination of pheochromocytoma and GIST has been described in 14 NF1 cases
- Periampullary tumors in NF1 patients are most commonly carcinoid, but most do not develop somatostatinoma syndrome
- To our knowledge this if the first case of a patient with NF1 diagnosed with ampullary somatostatinoma, small bowel GISTs, and extra-adrenal composite pheochromocytoma-ganglioneuroma occurring together

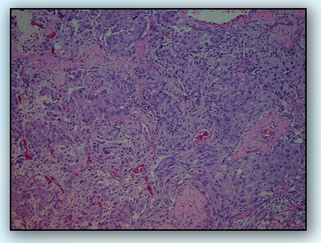

Figure 1: Paraganglioma Intermediate Power.

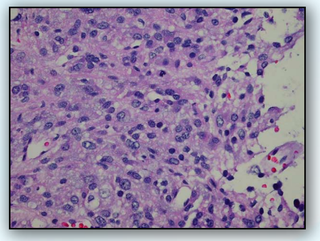

Figure 2: Paranglioma High Power.

References:

1. Agaimy, A., Vassos, N., & Croner, R. S. (2012). Gastrointestinal manifestations of neurofibromatosis type 1 (Recklinghausen's disease): clinicopathological spectrum with pathogenetic considerations. *International journal of clinical and experimental pathology,* 5(9), 852.
2. Brems, H., Beert, E., de Ravel, T., & Legius, E. (2009). Mechanisms in the pathogenesis of malignant tumours in neurofibromatosis type 1. *The lancet oncology,* 10(5), 508-515.
3. Relles, D., Baek, J., Witkiewicz, A., & Yeo, C. J. (2010). Periampullary and duodenal neoplasms in neurofibromatosis type 1: two cases and an updated 20-year review of the literature yielding 76 cases. *Journal of Gastrointestinal Surgery,* 14(6), 1052-1061.
4. Vlenterie, M., Flucke, U., Hofbauer, L. C., Timmers, H. J., Gastmeier, J., Aust, D. E., ... & Lenders, J. W. (2013). Pheochromocytoma and gastrointestinal stromal tumors in patients with neurofibromatosis type I. *The American journal of medicine,* 126(2), 174-180.