A Case of an Aggressive Neuroendocrine Tumor with a Primary Bone Marrow-related Presentation.

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\textbf{Introduction}

- About 90,000 people in the US will have a cancer of unknown primary (CUP) by the end of 2020.\textsuperscript{[1][2]}
- CUPS are metastatic cancer with no identifiable site of origin despite thorough workup.\textsuperscript{[1][3]}
- Neuroendocrine tumors (NETs) of unknown primary are rare, making up less than 5% of all CUPs.\textsuperscript{[4]}

\textbf{Case Description}

- 73 year-old-female with a history of depression and hypertension.
- Present with a 30lb weight loss over 2 months and bright red blood per rectum for a day.
- Physical exam: petechiae and flat dry purpura across her upper and lower extremities; no jaundice, lymphadenopathy, or hepatosplenomegaly.
- Colonoscopy and barium enema revealed internal hemorrhoids as the bleeding source.
- Laboratory workup for thrombocytopenia showed no distinct etiology, but further workup with a right iliac bone marrow biopsy revealed a well-differentiated NET.
- The tumor cells only expressed keratin 7, chromogranin, and synaptophysin, and variably expressed neuroendocrine marker INSM1.
- CT scan of chest, abdomen, and pelvis revealed a left thyroid nodule measuring 2.4 cm that was found to be suspicious for a NET on an octreotide scan. However, a biopsy of the left thyroid nodule revealed follicular neoplasm.

\textbf{Case Progression}

- Started Lanreotide for management of well-differentiated NET.
- Patient remained thrombocytopenic and severely anemic requiring multiple blood transfusions despite undergoing hemorrhoidectomy.
- Repeat CT scan and MRI of the head done for increased confusion and disorganized speech two months later showed metastatic disease involving the brain and skull.
- The patient could not tolerate further workup or cytotoxic chemotherapy and wished to proceed with comfort measures only. She went home with hospice care and died one week after discharge.

\textbf{Discussion}

- NETs can arise from neuroendocrine cells located in any part of the body, most commonly in the gastrointestinal tract, lungs, or pancreas, and on extremely rare occasions from the bone.
- Conventionally, well-differentiated NETs are indolent and accompanied by carcinoid symptoms.
- Localization of the primary tumor is vital in the management of NETs and can be done via imaging and subsequent biopsy and immunohistochemistry.\textsuperscript{[5]}
- In this case, right iliac bone biopsy revealed a well-differentiated NET that is positive for Keratin 7 suggesting a primary site in the small bowel, stomach, or pancreas. However, despite extensive workup, primary localization of tumor was unsuccessful.
- The combination of the absence of a site of origin, the predominance of hematologic pathology (pancytopenia), and the highly invasive nature of this patient’s malignancy are suggestive of a primary well-differentiated NET of the bone marrow.

\textbf{References}