**INTRODUCTION**

- Cancers of unknown primary (CUPs) = 2-5% of all new cancer diagnosis = 32,880 cases in the US in 2021
- Median overall survival of 8-12 months from diagnosis
- 85% of CUP cases are moderately to poorly differentiated adenocarcinomas
- NCCN recommends a systematic approach starting with a thorough H&P and routine labs, followed by diagnostic imaging, and core needle biopsy with immunohistochemistry

**DISCUSSION**

- This case illustrates a CUP that no longer resembled its tissue of origin
- Expedited workup is imperative in CUPs to avoid disease progression that can limit therapeutic options
- Molecular cancer classifier assays can identify the primary site 85-90% of CUPs
- If still indeterminate, clinicians must use serum markers, radiographic features, patterns of spread, and immunohistochemistry to develop a therapeutic plan despite imperfect information.

**REFERENCES**