CASE HISTORY

A 69 year old female had a history of a metastatic melanoma to the left groin without identification of a primary site 4 years prior to presentation. The groin lesion was resected and one out of 14 nodes was positive for melanoma, and the patient was ultimately staged as having pTx N1b M0 stage IIIC melanoma. At that time, she was treated with ipilimumab. Three years prior to presentation she developed a left inguinal lymph node recurrence, which was resected. This year, the patient underwent a surveillance CT scan which revealed a generous ampulla and elevated serum liver chemistries and was referred to endoscopy. At endoscopy, the ampulla was generous without obvious mucosal neoplasia. (Figure 1) Endoscopic ultrasound revealed a hypoechoic, 15x19mm mass lesion in the ampulla below the mucosa. (Figure 2) The lesion compressed the CBD, but the duct was still patent. The lesion was sampled via EUS-guided core biopsy using a 22 gauge core needle. Pathologic analysis revealed metastatic melanoma. (Figure 3). The patient was referred back to oncology and initiated treatment with pembrolizumab.

Discussion

Malignant melanoma develops from melanocytes mainly present in the skin, eyes, meninges and gastrointestinal (GI) mucosa, which can arise anywhere from the mouth to the anus. Melanoma is rare, comprising only 1-3% of all tumors. While the primary site of melanoma is the skin, it is known that melanoma can metastasize to the GI tract. The propensity of a primary malignant tumor to metastasize depends on the Clark staging, with >70% of Clark level III and Clark level IV lesions involving the GI tract. Metastatic melanoma has been seen in the esophagus, stomach, small intestines, and colon. 1-4% percent of patients with malignant melanoma show clinically apparent gastrointestinal tract involvement during the course of their disease and are diagnosed ante mortem, while up to 60% of all patients with melanoma are found to have metastases at autopsy. Due to these findings, some have recommended that all patients with known melanoma should be screened to rule out any gastrointestinal spread.
The clinical presentation for patients with metastatic melanoma can be asymptomatic or can include the following: abdominal pain, upper or lower GI tract bleeding, anemia, weight loss, intestinal obstruction, perforation, or intussusception. The anorectal region is the most common site for primary gastrointestinal melanomas, due to the presence of melanocytes. On the other hand, metastases of the GI tract are seen more frequently in the small intestines (35% to 97%). Reports on the prevalence of metastatic melanoma in the gastrointestinal tract show 0.1-0.5% cases in the esophagus, 5%-50% cases in the stomach and duodenum, and 5%-32% cases in the colon. When examining these rates separately, reports found 12%-19% occurrence of malignant melanoma in the duodenum and 24%-26% in the stomach. The average time from initial diagnoses to the finding of intestinal metastases ranges from 21.6 months to 54 months. While primary GI and biliary melanomas are rare, it can be difficult to distinguish between a primary mucosal, metastatic GI, and biliary melanoma from an unknown or regressed primary site. If a primary lesion has already been diagnosed, the clinician can usually determine that the melanoma in the GI tract is in fact metastatic. This particular patient did have a prior history of melanoma that had metastasized to other areas. Metastases of the GI tract often occur late in the history of the disease and have an overall poor prognosis. Once melanoma has metastasized to the GI tract and other visceral sites, the median survival is four to nine months for these patients.

While it is uncommon to find metastatic melanoma in the biliary tree it has been previously documented. Unfortunately, the incidence of isolated metastases to the ampulla is far less known with only a few reports to analyze. The literature separates the cases of primary biliary tract melanomas and ampullary melanomas. One publication suggests that many of the ampullary melanomas may have metastasized from cutaneous or vaginal primary melanoma. Metastatic melanoma to the common bile duct can present itself as a lesion located above the ampulla. One study reported the metastatic melanoma of the common bile duct extending to the ampulla and involving the gall bladder. This particular case found the patient’s lesion in the ampulla compressing her CBD. At postmortem examinations, 6% of patients with a known malignant melanoma have unexpected bile duct involvement while 15% with metastatic melanoma have gallbladder...
Melanoma Metastatic to the Ampulla of Vater Diagnosed via EUS-Guided Core Biopsy

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involvement. Melanoma metastatic to the ampulla is rare and can cause biliary obstruction. Patients diagnosed with metastatic melanoma of the ampulla presented symptoms of nausea, vomiting, cholestasis, and melena.

The appearance of metastases during an endoscopy may take the form of ulcers, nodules, or polyps, which may be pigmented or amelanotic. Diagnostic yield of biopsy from the margins of these ulcerations or lesions is >90%. The 15x19mm mass lesion found in the patient’s ampulla below the mucosa was analyzed and a EUS-guided fine needle biopsy was taken. The 22 gauge needle used to collect the biopsy is specifically used in diagnosing pancreatic and non-pancreatic lesions where the tip of a fine needle aspiration (FNA) is not optimal.

Recent months have seen the development of biopsy needles designed for core tissue acquisition that provide sufficient tissue for histologic evaluation. One multicenter study on EUS-FNB reported on the histological specimens being adequate in 89.47% of the patients and having a diagnostic yield of 92.9% of patients. Core EUS-FNB needles can provide higher histologic yield despite requiring fewer needle passes compared to the standard EUS-FNA needles. The endoscopist, for this particular case, saw it beneficial to use a EUS-FNB, with a 22-gauge needle, to sample the lesion on the patient’s ampulla.

EUS-FNB needles can come in a variety of gauge sizes, including 19, 22, and 25 gauge. While the larger diameter needles may provide more tissue, there can be instances where 19 gauge needles are associated with an increase in blood and cellular debris contamination, adverse events, or technical failures. A prospective study comparing of a 25-gauge and 22-gauge FNB needles found the diagnostic accuracy of the two were 98% and 95%, respectively. While the 25-gauge needle produced adequate core biopsies for histological examination in 87.5% lesions in comparison to 82.1% of lesions that were sampled with a 22-gauge needle. A study on EUS guided fine needle biopsy (FNB) sampling compared a forked-tipped biopsy needle to a FNA needle found that the FNB needle provided a higher yield of core tissue with fewer passes. This particular study found histology cores in 95% of the fine needle biopsy samples in comparison to only 59% of

Figure 3a. and 3b. Touch preparations with Diff-Qwik stain, 200X magnification
These touch preparations are highly cellular and reveal dispersed, large, single epithelioid to slightly spindled cells with prominent nuclear atypia including occasional mirror-image nuclei, multinucleation, prominent nucleoli, and nuclear pseudoinclusions. These morphological features are diagnostic of melanoma.

Figure 3c. Core biopsy, H&E stain, 400X magnification
The core biopsy shows sheets of highly atypical cells with irregularly shaped, vesicular nuclei and prominent nucleoli. Interspersed melanophages containing brown melanin pigment are also identified.

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the fine needle aspirate samples. The median number of passes for FNB needles during this study was two while four passes remained the median for FNA needles. Another result of this particular study was that the authors found a diagnosis of a specific lesion type was obtained with no more than two passes in 80% of the FNB group but only in 14% of the FNA group.

Another study analyzed two specific core needles; one with a reverse-bevel design and another with a 6-cutting edge and opposing bevel design. In this study, 99% of the specimens obtained with the opposing bevel needle were adequate for histopathologic interpretation in comparison to only 87% of the samples obtained from the needle with the reverse bevel. This study also found the opposing tipped needle providing higher sensitivity (90.1% vs 71.1%) and overall accuracy (92% vs 74%) than the reverse bevel needles. The FNB needle used during our patient’s EUS provided adequate core biopsies for pathologists to complete a histopathologic interpretation. The sufficient amount of core collected aided the pathologists in diagnosing the lesion as metastatic melanoma in the ampulla.

While endoscopy can help identify any ulceration or lesion, metastatic melanoma may be completely amelanotic with a variable cytological appearance. In order to confirm the diagnosis of malignant melanoma immunohistochemical stains are needed; the S100 sensitivity varies between 33-100%, HMB-45 antibodies has sensitivity between 80-97%, but the specificity is high (100%). Proper tissue acquisition is important in diagnosing these lesions because an adequate sample must be obtained for the immunohistochemical stains. The EUS-guided core biopsies collected in this case were more than for diagnosing the patient’s lesion as metastatic melanoma and provided tissue for both cytologic and histologic analysis.


