Title: The Floating Imposter: A Patient Safety Collaboration between Anatomic and Molecular Pathology

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Introduction: Floaters are tissue fragments that can contaminate histology slides at various stages of specimen processing including tissue collection, grossing, and sectioning. Floaters can occur in 0.01% to up to 2.9% of slides and can lead to diagnostic errors if not identified as tissue originating from another patient. Floaters can be extremely difficult to identify especially when a small fragment of malignant tissue is present in an otherwise benign specimen of similar histologic type and can result in a false positive diagnosis. In such scenarios, an objective assessment of tissue identity can dramatically impact the final diagnosis and management of the patient. Modern identity testing utilizes length polymorphisms in short, non-coding, repetitive sequences in the human genome (i.e. Short Tandem Repeats (STRs) or Microsatellites). Comparing the lengths of multiple STR loci can reliably distinguish tissue originating from different individuals. Here we present a case where careful histology review and STR testing identified a floater that otherwise would have led to a false diagnosis of cancer for a patient.

Case Presentation: A 64-year-old female presented with a several month history of diarrhea and weight loss. She underwent upper and lower GI endoscopies at an outside institution which showed LA grade A esophagitis, an ascending colon polyp, and unremarkable duodenum. Biopsies from the duodenum, right colon, and left colon were obtained. The lower GI biopsies showed normal colonic tissue with no specific pathologic changes; however, the biopsy from the duodenum was noted to contain “highly atypical cells, suspicious for carcinoma.” These atypical cells were positive for AE1-3 and had a Ki-67 proliferative index of >80%. Three weeks later, the patient underwent a small bowel enteroscopy where an area of erosion/nodularity was seen in the duodenal bulb that was extensively biopsied. These new biopsies showed acute and chronic duodenitis without evidence of malignancy. Upon review of the slides at HUP, the surgical pathologist considered the possibility of contamination. To determine whether these “highly atypical cells” belonged to the patient, STR testing was performed. DNA was isolated from the small intestinal erosion from the second biopsy, the benign component of duodenum from the first biopsy and the atypical component from the first biopsy (Figure 1; Samples 1-3, respectively). A panel of 15 STR markers plus one gender marker was used to generate an identity profile for each sample using a multiplex PCR assay (PowerPlex 16, Promega). The genotypes of Samples 1 and 2 were identical at all 15 STR loci and the sex chromosome marker. However, Sample 3 (i.e. the potential floater) had a different genotype at every locus confirming that these cells did not originate from the same individual as the benign tissue samples (figure 2). Based on these results, the outside pathology lab identified a potential patient from which floater tissue originated (figure 3). The suspected sample was sent for STR testing and confirmed that the floater was from a vaginal biopsy specimen with serous carcinoma that was grossed on the same day as Samples 2 and 3.

Discussion: This case illustrates that floaters can cause diagnostic errors and pose a safety risk to patients if not identified. Designing a workflow that minimizes floater occurrence is important. However, when they occur, thorough review of histology sections coupled with STR testing are powerful tools to identify and confirm suspected contamination. This safety collaboration between Anatomic Pathology and Molecular Pathology highlights how intra-departmental efforts can help ensure patient safety.
Figure 1: H&E sections of samples evaluated by STR testing. Sample 2 and Sample 3 are from different areas of the same slide.

Figure 2: Partial results of STR testing showing identical genetic profiles of the small intestinal erosion in sample one, and the sample of normal small intestine from the first biopsy. The genetic profile of the tissue concerning for carcinoma is different.
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<th>Potential patient from which floater originate</th>
<th>Floater in our case</th>
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*Figure 3: H&E section of potential source of floater alongside the floater seen in this case.*