

# Diagnostic anchoring in metastatic adenocarcinoma – Was the turning point too late?

Dear Editor,  
we read with great interest the case report by Pešek et al. published in the August 2026 issue of *Klinická onkologie* entitled “FGFR2 fusion as the key to targeted therapy – a case report with a diagnostic turning point.” The authors appropriately emphasized the importance of repeated biopsy and molecular profiling when clinical behavior is inconsistent with the initial diagnosis. We would like to highlight an additional important lesson from the first case – the possibility of diagnostic anchoring at initial presentation [1].

The patient presented with metastatic adenocarcinoma with multiple pulmonary nodules and dominant hepatic lesions. Most importantly, the authors noted that the pulmonary lesions appeared radiologically more suggestive of metastases, while large liver lesions dominated abdominal imaging. Nevertheless, a primary lung adenocarcinoma was diagnosed based on extensive immunohistochemistry and thyroid transcription factor-1 (TTF-1) positivity.

This underscores an important caveat in TTF-1 interpretation. Although TTF-1 supports pulmonary adenocarcinoma, its expression is not exclusive to lung primaries. Diagnostic performance varies according to tumor type and antibody clone, and TTF-1 positivity has been reported in extrapulmonary adenocarcinomas [2–4]. Consequently,

a positive lineage marker should complement, rather than override, the overall clinical and radiologic presentation.

In this case, the distribution of disease at presentation should arguably have prompted consideration of an extrapulmonary primary, given the liver-dominant disease and metastatic appearance of the pulmonary lesions. A broader differential diagnosis and appropriately directed immunohistochemical panel might therefore have been considered before establishing primary lung cancer as the leading diagnosis. The subsequent liver re-biopsy demonstrated adenocarcinoma of pancreatobiliary origin leading to complete revision of the diagnosis.

We therefore suggest that this episode reflects not only a “diagnostic turning point,” but also diagnostic anchoring – when an initial impression continues to influence subsequent interpretation despite discordant evidence. In metastatic adenocarcinoma of unknown primary origin, the presumed site is most robust when continuously tested against the entire disease pattern rather than inferred from a single immunohistochemical marker. When radiologic distribution, clinical behavior, and pathology are discordant, early multidisciplinary reassessment and repeat biopsy can help realign treatment with actual tumor biology.

We commend Pešek et al. for demonstrating the value of re-biopsy and



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molecular profiling. Their case also reminds us that revisiting the presumed primary site early may be just as vital as identifying an actionable molecular alteration. Recognizing when to pause and reassess may be the most valuable diagnostic turning point.

## References

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