Perthera
The Therapeutic Intelligence Company

Perthera Case of the Month

"It's Elementary"

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Take Away Point

"When you have eliminated the impossible, whatever remains, however improbable, must be the truth?" — Sherlock Holmes

Comprehensive multi-omic profiling and its expert analysis in The Perthera Report can be helpful in solving mysteries when there is a question of the relationship between tumors or tumor sites.

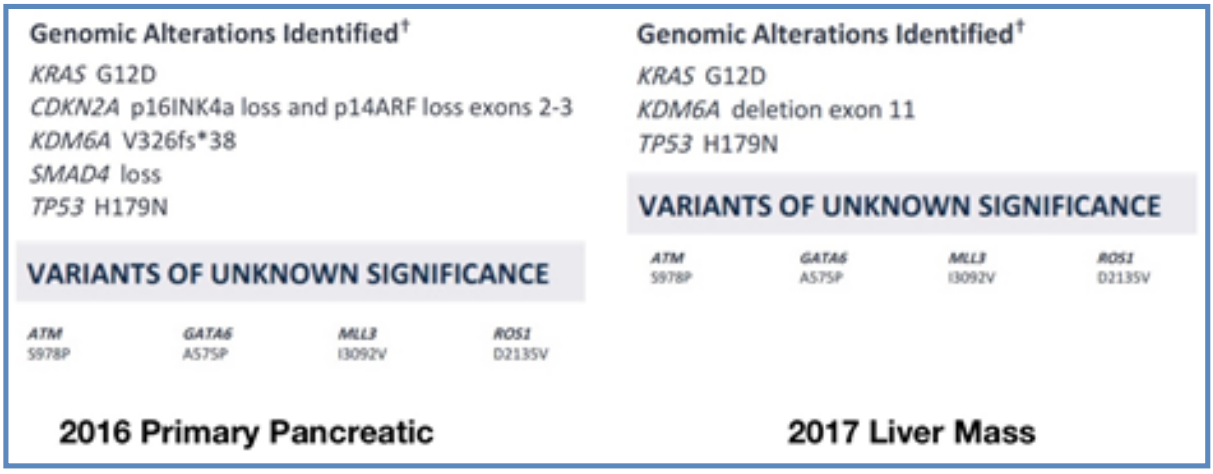
Case Discussion #1

A Case of Mistaken Identity?

A 67-year-old female had a poorly differentiated T3N1 pancreatic adenocarcinoma resected in 8/2016 and declined adjuvant therapy. In 9/2017, she was found to have a new liver mass which was biopsied and thought to be metastatic squamous cell carcinoma. The primary from 2016 was initially sent for profiling as shown in FIGURE 1 below. There was concern that the liver lesion represented a metastatic squamous cell carcinoma of unknown primary. Perthera requested the liver biopsy tissue to allow for a comparative analysis. The findings shown in FIGURE 1 confirm that the squamous liver mass is, in fact, a metastasis from the prior primary pancreatic adenocarcinoma. The identical variants of unknown significance (VUS) provide an additional "fingerprint" adds additional evidence they are one in the same tumor.

The Evidence

FIGURE 1: Pancreatic Primary versus Liver Mass



The Solution

A retrospective examination of the primary tumor revealed areas of squamous differentiation that had been overlooked initially suggesting the primary tumor was an adenosquamous pancreatic carcinoma and only the squamous component metastasized to the liver. In fact, the presence of KDM6A mutations has been shown to be typical of a subset of pancreatic cancer with squamous differentiation. Case solved!

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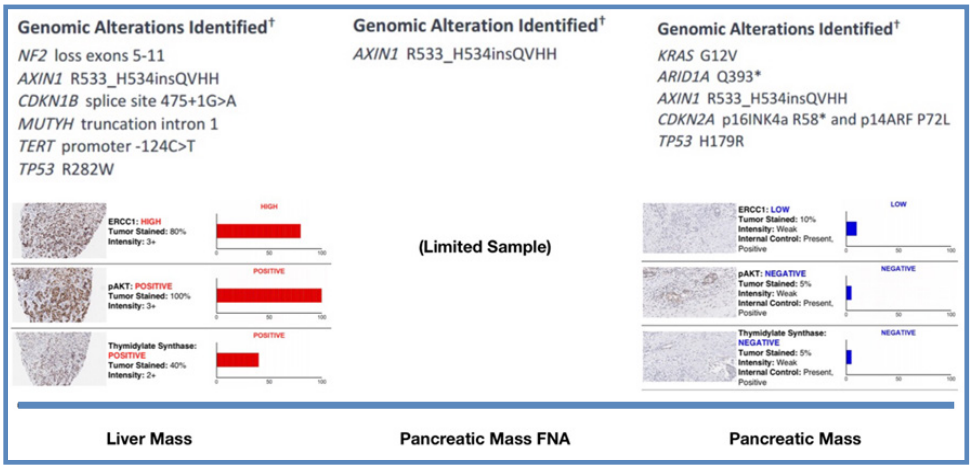
Case #2

Single or Multiple Perpetrators?

A 67-year-old female was found to have a synchronous mixed hepatocellular carcinoma/cholangiocarcinoma in the liver metastatic to the lung and a stage I pancreatic adenocarcinoma in 2016. The liver lesion was ablated, the lung nodule resected, and the pancreatic mass resected followed by adjuvant gemcitabine and capecitabine. Profiling of the pancreatic tumor from a suboptimal specimen showed only an AXIN1 insertional event (R533_H534insQVHH) that has been shown to be closely associated with hepatocellular carcinoma. Interestingly, HCC/cholangiocarcinoma showed the same exact AXIN1 insertion in addition to other genomic changes all consistent with hepatocellular carcinoma (NF2 and CDKN1B). This finding of a shared mutation between the pancreatic lesion and the liver lesion could only be explained by the two tumors being from one source or by the AXIN1 insertion being a germline mutation. In order to better understand this unusual situation, a second larger sample of the pancreatic mass was obtained and re-sent for comprehensive multi-omic testing that revealed that the only shared finding was the AXIN1 insertion with typical genomic changes of pancreatic cancer (KRAS, p53, and CDKN2A) and distinct proteomic profiles as shown in FIGURE 2.

The Evidence

FIGURE 2: Proteomic Profiles



The Solution

Thus it is clear that they are, in fact, separate primaries with a shared AXIN1 insertion suggesting that this could be a germline finding. AXIN1 abnormalities have been implicated in rare cases of familial renal cell carcinoma but is not a cause of a known cancer predisposition syndrome. Specific germline testing for this genomic change would be needed to confirm this suggestion. Case Solved!

The Power of Comprehensive Multi-omics

These cases clearly demonstrate the ability of complete multi-omic profiling and expert analysis through The Perthera Report to solve mysteries that otherwise would be difficult for even Sherlock Holmes to tackle!

At Perthera, we are dedicated to helping physicians and patients have access to the latest and most complete information in their decision-making process.

ABOUT PERTHERA

Perthera is the leading Therapeutic Intelligence Company advancing precision medicine through our Perthera Report, which precisely matches cancer patients with multiple therapeutic options ranked by strength of clinical and scientific evidence.

The Perthera Report does this through an integration of the patient's multi-omic findings and treatment history by our leading-edge Therapeutic Intelligence Engine, with the conclusions reviewed and approved for every-patient by our real-time physician and scientific tumor board.

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