

The “Prochronous Metastases” Theory

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Context It is known that metastatic process is an early event in the life of a pancreatic ductal adenocarcinoma (PDAC). As soon as cancer cells (cells which became able to pass the basal lamina) are present in the pancreatic gland, maybe that is the moment since the disease should be considered as systemic. A recent study on mouse models revealed that not only PDAC cells can move through basal lamina, but even pre-cancerous cells (pan-IN cells) could do it. This outstanding report gives rise to new possible explanations of some clinical scenarios not fully understood to this day. **Case report** We report the case a of 70-year-old man who underwent splenectomy for a solid mass of uncertain origin. Pathology revealed a metastasis from undifferentiated adenocarcinoma, biliopancreatic origin was suspected. Extensive

sonography, endoscopy, EUS, conventional and nuclear imaging were carried out. No proofs or clues of the primary cancer were found. However, enlarged lymph nodes were visible in the liver hilum, lesser omentum and interaortocaval region. Explorative laparotomy was performed and a small cancer of the pancreatic tail with nodal and peritoneal metastases was found. **Conclusion** We theorize that PDAC could first arise in distant organs and only later in the pancreas. If pan-IN cells can pass through the basal lamina and reach systemic blood-stream, they could dedifferentiate in distant organs. Could such pan-IN “metastases” give birth to pancreatic cancer before “pancreatic” pan-IN proceed to PDAC? We already deal with synchronous and metachronous metastases; what if really exist prochronous metastases?