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Pancreatic Mixed Acinar-Neuroendocrine Carcinoma: a Single Institutional Genomic Characterization Report

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BACKGROUND

Pancreatic mixed acinar-neuroendocrine carcinomas are a rare distinctive entity with histologic and immunohistochemical features of pancreatic acinar cell carcinoma and pancreatic neuroendocrine tumor and pose diagnostic challenges. Very few cases have been described in the literature. Genomic information about these tumors remains unknown. We identified two cases of mixed acinar- neuroendocrine carcinoma from our database since January 2020 who had full genomic information available including germline and NGS assays.

METHODS

Two patients were identified from the Dartmouth Pathology database since January 2020 with a biopsy proven diagnosis of pancreatic mixed acinar neuroendocrine carcinoma. Genomic characterization was done using the Illumina TruSight Tumor 170 (TST170) sequencing assay which detects gene variants across 170 gene targets in nucleic acids extracted from FFPE tissue samples. Sequencing was performed on the NexSeq 500 system which is designed to examine single nucleotide variants, small deletions, small insertions, amplifications, fusions and splice site variants across 170 genes.

RESULTS

Two patients identified from the database had tumors in the head of the pancreas. Results are summarized in the following table.

Table 1. Histopathologic and NGS characteristics of pancreatic mixed acinar neuroendocrine carcinoma patients.

Age in years/ sex	Tumor site	Type of pathology	Pathology IHC identification	Ki 67	MMR	Other hereditary syndrome	Presentation	Treatment	NGS assay results	Patient status
66/M	Pancreatic head mass	EUS guided biopsy of pancreatic head	Tumor cells positive for trypsin, synaptophysin, chromogranin, INSM1 and CKAE1/3; negative for beta catenin (negative nuclear stain)	50%	Proficient	Germline Invitae did not show any actionable mutations but a variant of uncertain significance (VUS) in the DIS3L2 gene, specifically c.2605G>A (p.Glu869Lys), was detected	Metastatic to liver and regiuonal lymph nodes.	Poor ECOG PS. No treatment	FGFR1-TACC fusion, BARD1 insertion	expired
30/M	Pancreatic head mass	EUS guided biopsy of pancreatic head Whipple with Bilroth II reconstruction	tumor cells positive for trypsin and synaptophysin and are negative for ISL1,	10%	Proficient	Familial adenomatous polyposis (FAP)	Localized tumor. Final pathology stageing per AJCC: pT2N0	Resection and adjuvant chemotherapy with FOLFIRINOX	DDR2, APC, CSF1R, PTCH1 substitutions.	alive

CONCLUSIONS

Mixed acinar neuroendocrine carcinomas of the pancreas are very aggressive neoplasms. As usually seen in GEP NENs, our patient with a higher Ki 67 index had poor prognosis as compared to the patient with the G2 tumor. The NGS results of FGFR1-TACC fusion, BARd1 mutation has been documented in brain tumors and breast cancers respectively. Similarly, DDR2 mutation has been identified as one of the actionable mutations in squamous cell carcinoma of lungs. Significance of these mutations identified in this rare tumor is yet unknown. Our search of Dartmouth pathology database is ongoing to identify more cases in the last 10 years and to complete genomic analysis on these cases.

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