C-9

Anti-apoptosis as a therapeutic strategy in Neuroendocrine neoplasms (NEN): A case report

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BACKGROUND

The expression of BCL-2, an anti-apoptotic protein, has been implicated in the aggressive behavior of NENs. Dysregulation of BCL-2 expression, controlled by the pRb1-E2F1 axis, has been linked to the development of various cancers, including NENs. Studies have shown that higher BCL-2 expression is associated with poorer survival outcomes in NEN patients.

METHODS

We report a unique case of a patient with a pancreatic neuroendocrine tumor who had an unexpected response to venetoclax as part of a regimen to treat chronic lymphocytic leukemia (CLL).

RESULTS

A 69-year-old woman with CLL that is IgVH unmutated, and has a complex karyotype, del13q on FISH panel, as well as TP53, SF3B1, and NOTCH1 mutations required treatment due to fatigue and progressive lymphadenopathy. On imaging she had bulky retroperitoneal lymphadenopathy and a pancreatic tail mass that was 3.6 x 4.9. This mass was presumed due to her CLL and was 3 x 3.7cm five years earlier. She enrolled in a clinical trial for CLL with acalabrutinib, rituximab, and venetoclax.

A CT scan done 6 weeks in treatment when she had only received acalabrutinib and rituxumab showed improved retroperitoneal lymphadenopathy but progression in pancreatic tail lesion to 5.5 x 4.1cm. Venetoclax was subsequently started as planned for the study. A repeat scan 4 weeks into venetoclax revealed decrease in size of the pancreatic tail lesion to 4.2 x 3.0 cm, along with continued decrease in lymphadenopathy. As the mass was unlikely to be her CLL, an upper GI endoscopic ultrasound and fine needle aspiration of the pancreatic tail lesion was performed which revealed a well-differentiated neuroendocrine tumor. The Ki-67 was not estimable due to scant specimen. A Gallium-68 dotatate PET (Ga-PET) scan showed increased uptake in the pancreatic tail, peripancreatic lymph nodes and liver consistent with metastatic disease. The liver lesions were subsequently noted on triple phase imaging of the liver.

Venetoclax was discontinued after one year of therapy as specified in the CLL trial. Subsequent imaging showed continued shrinkage in the pancreatic tail lesion to a nadir of 2.8 x 3.2 cm; seen on a scan performed 4 weeks after discontinuation of venetoclax. The pancreatic tail lesion and liver metastasis remained stable for approximately 18 months after stopping venetoclax.

Subsequently, the patient experienced progression in two satellite nodules adjacent to the pancreatic tail lesion. A Ga-PET scan confirmed disease progression in the pancreatic tail, peripancreatic lymphadenopathy, and increased multifocal liver activity compared to scans from three years prior. She ultimately achieved a complete remission with undetectable minimal residual disease for her CLL.

CONCLUSIONS

We report the first known case of a response to venetoclax in a neuroendocrine tumor. BCL-2 pathway inhibition should be investigated as a therapeutic strategy in NENs.

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