A Unique Case of HER2-Positive Adenocarcinoma of the Small Bowel

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Introduction

- Duodenal adenocarcinoma is a rare malignancy with a poor prognosis. The optimal chemotherapy regimen remains largely unclear. Unlike other GI cancers, this malignancy rarely harbors HER2 amplification or overexpression.
- Our case is of a patient with HER2-positive stage III duodenal adenocarcinoma with a positive response to trastuzumab.

Case Presentation

- Patient is a 59-year-old male with a history of Crohn's disease on infliximab who had presented with abdominal pain and was found to have a small bowel obstruction.
- After failing conservative management, he underwent a partial small bowel resection with lysis of adhesions.
- *A 3.5 cm jejunal mass with lymphovascular invasion and negative margins was identified and biopsy was positive for adenocarcinoma.*
- His preliminary pathology was consistent with T3NxM0 adenocarcinoma of the small intestine.
- He was started on a six month course of Capecitabine adjuvant therapy. This was prematurely discontinued due to severe diarrhea and hand-foot-mouth syndrome.
- Patient was followed with repeat CEA levels and CT scans.
- He had a recurrence thirteen months following his surgery with an increased CEA of 16.6 and a positive PET scan showing focal thickening of the small bowel with mesenteric masses and lymph nodes extending toward the mesentery.
- Upper endoscopic ultrasound was performed with fine needle biopsy which was **positive for metastatic adenocarcinoma**.
- Patient was then started on FOLFOX [leucovorin, 5-Fluorouracil (5- FU), oxaliplatin] chemotherapy with subsequent transition to maintenance 5-FU & leucovorin.
- Due to disease progression, he was transitioned to FOLFIRI regimen (irinotecan, leucovorin, and 5-FU).
- He then underwent **next generation sequencing** which identified **ERBB2 (HER2) amplification**.
- He was started on targeted therapy against ERBB2 with fam-trastuzumab-deruxtecan-nxki.
- Due to GI intolerance, he was switched to Trastuzumab plus Pertuzumab which he has tolerated well.
- Repeat imaging has shown a complete clinical response.
- **His CEA has returned back to normal levels from a peak of 30.7 as seen in Table 1.**
- Patient has had sustained improvement over twelve months with improving fatigue, anorexia and performance status.

CEA Trend (Normal reference range: (0-5)	
August 2021	28
September 2021**(HER2 initiation)**	30.7
October 2021	9.6
December 2021- January 2023	1.6-1.9

Table 1: CEA (carcinoembryonic antigen) levels during treatment course

Discussion

- Trials to determine optimal treatment regimens for duodenal adenocarcinoma have been limited due to its low incidence. As a result, patients are frequently treated with either colorectal or gastric cancer drug regimens.(1)
- 15% of gastric cancers have shown HER2 overexpression. However, **duodenal cancers seem to rarely harbor HER2 amplification**.(2)
- In HER2-positive breast cancer, trastuzumab has shown a survival advantage and is currently the standard of care.
- The addition of trastuzumab to cisplatin and 5-FU or capecitabine in patients with HER2-positive gastric tumors confirmed a better overall survival (13.5 vs. 11.1 months, p = 0.0048) when compared to chemotherapy alone.(3)
- However, the role of trastuzumab in HER2-positive metastatic duodenal cancer still needs to be further studied.

Conclusion

- In our case we saw significant improvement after targeted therapy against HER2 in duodenal adenocarcinoma which traditionally has a poor prognosis.
- Through our poster, we want to encourage the use of **next generation sequencing** in metastatic disease to allow for targeted therapy which could result in better outcomes.

References

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