

## Introduction

Cancer treatments are continuously updating with new therapies to optimize survival. Cyclin-dependent kinase inhibitors (CDK4/6) have demonstrated promising responses in ER+ breast cancers. This is a case presenting a newly recognized side effect of ileitis with concomitant colitis with palbociclib (PAL) treatment.

## Case Presentation

- A 30 year-old female with biopsy confirmed stage IV ER+, PR+, HER2- ductal carcinoma with metastases to the liver and bone, developed abdominal pain, diarrhea, and hematochezia 2 months into therapy with letrozole and palbociclib.
- 6 months into treatment, colonoscopy showed diffuse colitis with congestion, erythema, and shallow ulcerations scattered through the entire colon, and several superficial aphthous ulcerations in the ileum.
- C. difficile testing was negative and biopsies revealed nonspecific ileitis and colitis.
- There was concern for inflammatory bowel disease (IBD) vs drug induced enteritis/colitis.
- Palbociclib and letrozole were held and the patient was started on prednisone 60 mg QD taper with resolution of symptoms after 1 month.
- Given concern for disease progression, PAL alone was restarted 1 month later with return of symptoms within 1 month.
- This led to hospital admission and PAL was stopped.

## Diagnosis and Case Continued

Labs at presentation of hospitalization:

- WBC **1.84 TH/uL**; Hgb **7.6 g/dL**; Plt **24 TH/uL**; ALT **450 U/L**; AST **221 U/L**; Alk phos **223**; Tbili wnl; ESR **49 mm/hr** ; CRP **45 mg/L**; LDH **4211 U/L**
- Infection was ruled out.
- Colonoscopy was performed and showed erythema, friability, congestion, erosions and ulceration in the terminal ileum (TI) compatible with ileitis (Image 1) as well as patchy erythema, edema, erosions, and ulcers throughout the colon with skip lesions and sparing of the rectum.
- Biopsies were taken and reported as normal TI and colon.
- Once PAL was discontinued indefinitely, patient had complete resolution of symptoms within weeks.



Image 1: Erythema, friability, congestion, erosions, and ulceration in the terminal ileum

## Discussion

- CDK4/6 inhibitors are now a first line treatment for metastatic hormone receptor positive breast cancer.
- There are no current reports of CDK4/6 induced ileitis.
- These symptoms can mimic inflammatory bowel disease clinically.
- It is important for gastroenterologists to assess the severity of inflammation with endoscopy and biopsies while ruling out infection prior to initiation of high-dose glucocorticoids.
- As CDK4/6 inhibitors become used more as the first-line treatment of metastatic HR-positive breast cancer, more cases of GI related toxicities may emerge.
- Our patient was on palbociclib for 9 months before presenting with new onset ileitis with colitis, making our case unique.

## Conclusions

Cyclin-dependent kinase inhibitors should be considered in the differential as a cause of ileitis/colitis in patients who develop new onset symptoms of hematochezia, diarrhea, and abdominal pain.

## References

1. Turner, N. C., Ro, J., André, F., Loi, S., Verma, S., Iwata, H., Harbeck, N., Loibl, S., Huang Bartlett, C., Zhang, K., Giorgetti, C., Randolph, S., Koehler, M., Cristofanilli, M., & PALOMA3 Study Group (2015). Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. *The New England journal of medicine*, 373(3), 209–219. <https://doi.org/10.1056/NEJMoa1505270>
2. Malik, A. A., Abbas, H., Oo, Z. M., & Lim, Z. (2021). CDK4/6 inhibitor-induced colitis: a case report and review of the literature. *BMJ case reports*, 14(7), e242766. <https://doi.org/10.1136/bcr-2021-242766>
3. Azhar, A. M., Abbas, H., Zin, M. O., & Lim, Z. (2021). CDK4/6 inhibitor-induced colitis: A case report and review of the literature. *BMJ Case Reports*, 14(7). doi:http://dx.doi.org/10.1136/bcr-2021-242766
4. Spring, L. M., Zangardi, M. L., Moy, B., & Bardia, A. (2017). Clinical Management of Potential Toxicities and Drug Interactions Related to Cyclin-Dependent Kinase 4/6 Inhibitors in Breast Cancer: Practical Considerations and Recommendations. *The oncologist*, 22(9), 1039–1048.