

# **Granulomatous Appendicitis, Dermatitis, and Encephalopathy: A Unique Case of Immune-Related Adverse Events in a Woman With Breast Cancer Treated With Pembrolizumab**

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## **Introduction:**

The introduction of immune checkpoint inhibitors has revolutionized the treatment of multiple malignancies. Despite their efficacy, side effects due to reactivation of immune cells and tumor specific T cells, have produced a unique spectrum of adverse events known as immune-related adverse events (irAE). We present a case of a woman with breast cancer who developed multiple irAEs involving granulomatous appendicitis, dermatitis, and encephalopathy from pembrolizumab.

## **Case:**

71 year old woman with breast cancer (T2-3, N0, M0) completed 4 cycles of chemotherapy and 3 cycles of immunotherapy presented with malaise, nausea, emesis, and diarrhea along with auditory and visual hallucinations. Abdominal CT demonstrated dilated and thickened appendix with adjacent inflammatory changes. Her gastrointestinal (GI) symptoms did not improve with conservative treatment, so she underwent laparoscopic appendectomy with appendix pathology demonstrating no perforation, but severe inflammatory changes with gangrene with eosinophils, lymphocytes and poorly formed epithelioid granulomas. Her symptoms persisted despite antibiotics and surgery, however she was discharged with concern her delirium was hospital-induced. Her encephalopathy marginally improved and developed a new diffuse rash, so represented to the hospital. Given her persistent encephalopathy, she underwent a lumbar puncture which showed no evidence of infection, and a punch biopsy of the skin. She was started on high dose steroids for concern of irAE. Her encephalopathy, diarrhea, and dermatitis rapidly improved over the next 72 hours. Punch biopsy showed dermatitis with basal vascular changes and dyskeratotic keratinocytes with predominantly lymphohistiocytes and admixed neutrophils consistent with irAE. She was discharged home on a prednisone taper and at her follow-up, symptoms had completely resolved and was able to perform all ADLs independently.

## **Discussion:**

With the expanding use of immunotherapy, increasing numbers of immune-related adverse events have been documented. While there have been few case reports of appendicitis associated with immunotherapy, our patient's appendix pathology showed inflammatory infiltrates composed of eosinophils, lymphocytes, and a poorly epithelioid granuloma, which appears to be the first documented case.

Granulomatous appendicitis occurs in 0.1-2.0% in cases of appendicitis and are commonly associated with other etiologies. In our case, optimal treatment regimens have not been established. This may include high dose corticosteroids, pausing or stopping immunotherapy, or surgical removal. This case highlights the importance of continuing to understand the potential side effects of immunotherapy as it becomes more common in cancer treatment as well as potential treatment options for these adverse events as we continue to see them.