

Diarrhoea in a Melanoma Patient

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Received date: August 08, 2017; Accepted date: August 30, 2017; Published date: August 31, 2017

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Abstract

Case report of a female with malignant melanoma, developing diarrhoea following administration of Pembrolizumab. Macroscopic investigation was normal, but histology was in keeping with lymphocytic colitis secondary to drug related injury, which is the first to be described with this immunotherapy.

Keywords: Lymphocytic colitis; Diarrhoea; Immunotherapy; Melanoma

Clinical Presentation

A 53 year old female presented to gastroenterology with a history of diarrhoea, with loose stools and frequency of up to six times a day. This was associated with nausea, vomiting and weight loss. Her past medical history included malignant melanoma, which had been excised in 2013. Recurrence was found in the previous wound site in 2015.

She had been commenced on Pembrolizumab in October 2015 following staging CT showed multiple lung metastases. She was not on any other regular medications. She had not previously suffered from diarrhoea or gastrointestinal upset. Past medical history was otherwise unremarkable. Flexible sigmoidoscopy and colonoscopy were macroscopically normal. Histology from biopsies taken is shown in Figure 1.

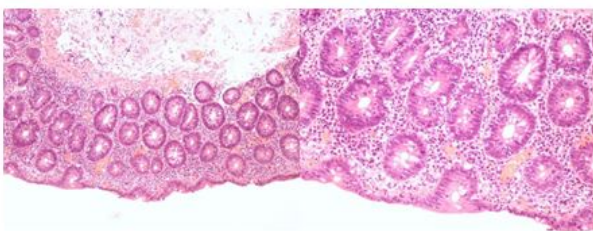


Figure 1: Histology slides from colonic biopsies.

Question: What is the diagnosis?

The diagnosis is lymphocytic colitis secondary to Pembrolizumab. The biopsies show diffuse increase in lamina propria chronic

inflammatory cells, raised numbers of intraepithelial lymphocytes and no increased thickness of the subepithelial collagen plate. Additionally, there are acute inflammatory cells and cryptitis which is not typical of lymphocytic colitis, but indicative of injury secondary to monoclonal antibody damage. She was commenced on prednisolone and improved.

Pembrolizumab is a humanized antibody that targets the programmed cell death 1 receptor (PD-1), used to treat metastatic melanoma. It is an example of a checkpoint inhibitor immunotherapy, which, though effective, is associated with a variety of side effects including diarrhoea. Diarrhoea is less common with PD-1 blockade than with other immunotherapies. Management involves excluding an infective cause. Proven colitis is treated with cessation of the drug, anti-motility agents and steroids. Infliximab is recommended in severe cases.

Conclusion

There are very few reported cases of colitis secondary to pembrolizumab. The KEYNOTE-001 trial, assessing the efficacy and safety of pembrolizumab, reported an incidence of 20% of diarrhoea, however only 4 cases of proven colitis out of 411 patients on pembrolizumab in the trial [1]. To date, there is one other published case of colitis with pembrolizumab, however they describe a collagenous colitis, in contrast to this example of lymphocytic colitis [2].

References

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