

# A Case of Nivolumab induced Vulval Lichen Sclerosus: Further support for a drug induced pathology

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Programmed cell death-1 receptor (PD-1) inhibitors, such as Nivolumab and Pembrolizumab, inhibit immune check points, leading to disruption of T cell activation and an enhanced immune response. Consequently, cutaneous immune-related adverse events have been reported with the use of these drugs, including lichen sclerosus<sup>1</sup>. This case report and literature review provide further support for a link between PD-1 inhibitors and lichen sclerosus.

## Case Report

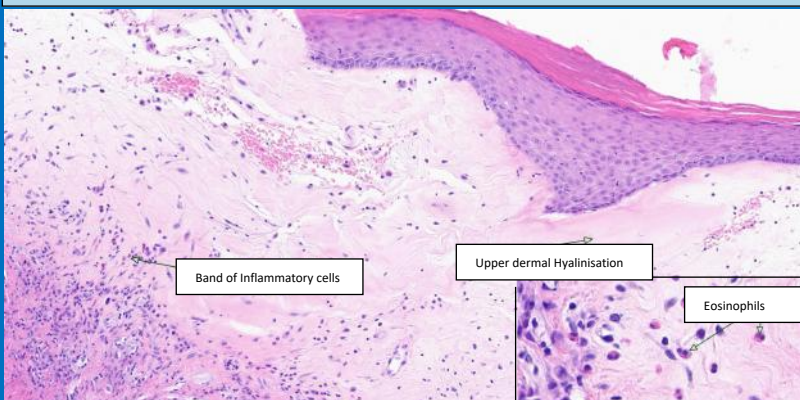
- 64-year-old female
- Commenced on Nivolumab for unresectable stage IIIC metastatic melanoma
- Tolerated well for almost two years
- Developed vulval and perianal itching which significantly worsened following her most recent Nivolumab infusion
- Her Nivolumab treatment ceased after receiving two years of therapy
- Responding well to standard topical steroid regime for vulval lichen sclerosus

## Clinical Presentation



Photograph after 4 weeks of topical treatment. Classical 'figure of eight' vulval and perianal inflammation, pallor and atrophy with superficial erosions in the perianal skin.

## Histology



Band like inflammation with upper dermal hyalinisation and additional plasma cells and eosinophils within the inflammatory infiltrate, suggestive of a drug induced pathology.

## Literature Review

- Literature search using Medline revealed 10 publications describing 11 cases of LS following PD-1 inhibitor treatment
- Mostly genital disease with 4 extragenital
- Seven had melanoma.
- The remaining had bladder, lung or endometrial cancer
- One was known to have pre-existing vulval lichen sclerosus which worsened with nivolumab<sup>2</sup>
- No other cases commented on presence of any underlying autoimmune disease
- Onset of symptoms in relation to PD-1 inhibitor commencement ranged from 3 months to 2 years

Reference	Location	PD-1 inhibitor	Duration of treatment before symptom onset	Malignancy
Miraglia E. et al	Genital	Nivolumab	5 Months	Melanoma
Jafari S. et al	Extragenital	Nivolumab	2 years	Melanoma
Andres Lenciana J. et al	Genital	Nivolumab	4 Months	Bladder Cancer
Williams E. et al E	Extragenital - Flare	Nivolumab		Melanoma
Wernham A.G.H. et al	Genital	Nivolumab	4 months	Melanoma
Di Meo N. et al	Extragenital	Nivolumab	3 months	Melanoma
Geisler A. et al	Genital	Pembrolizumab	2 years (started after completion)	Endometrial Cancer
Veronesi G. et al	Extra Genital	Nivolumab	4 months	Melanoma (Uveal)
Trojanova-Slavkova S. et al	Genital	Pembrolizumab		Melanoma
Rovers J. et al	2 Cases Genital	2 Cases Pembrolizumab		2 Cases with Lung Cancer

- **Five cases mentioned histological findings**
- **None described the presence of eosinophils as was seen in our case**
- **A drug related pathology is more likely based on this finding**
- **Our case provides further support for an association between PD-1 inhibitors and lichen sclerosus**

### References

1. Haanen JBAG. et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2018; 29: iv264–iv266.
2. Williams E. et al Extragenital lichen sclerosus is an immune-related adverse event with nivolumab. *Pigmentation and melanoma abstracts* 819.