

Ocular sarcoidosis as a rare immune-related adverse affect of nivolumab therapy

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Learning Objectives

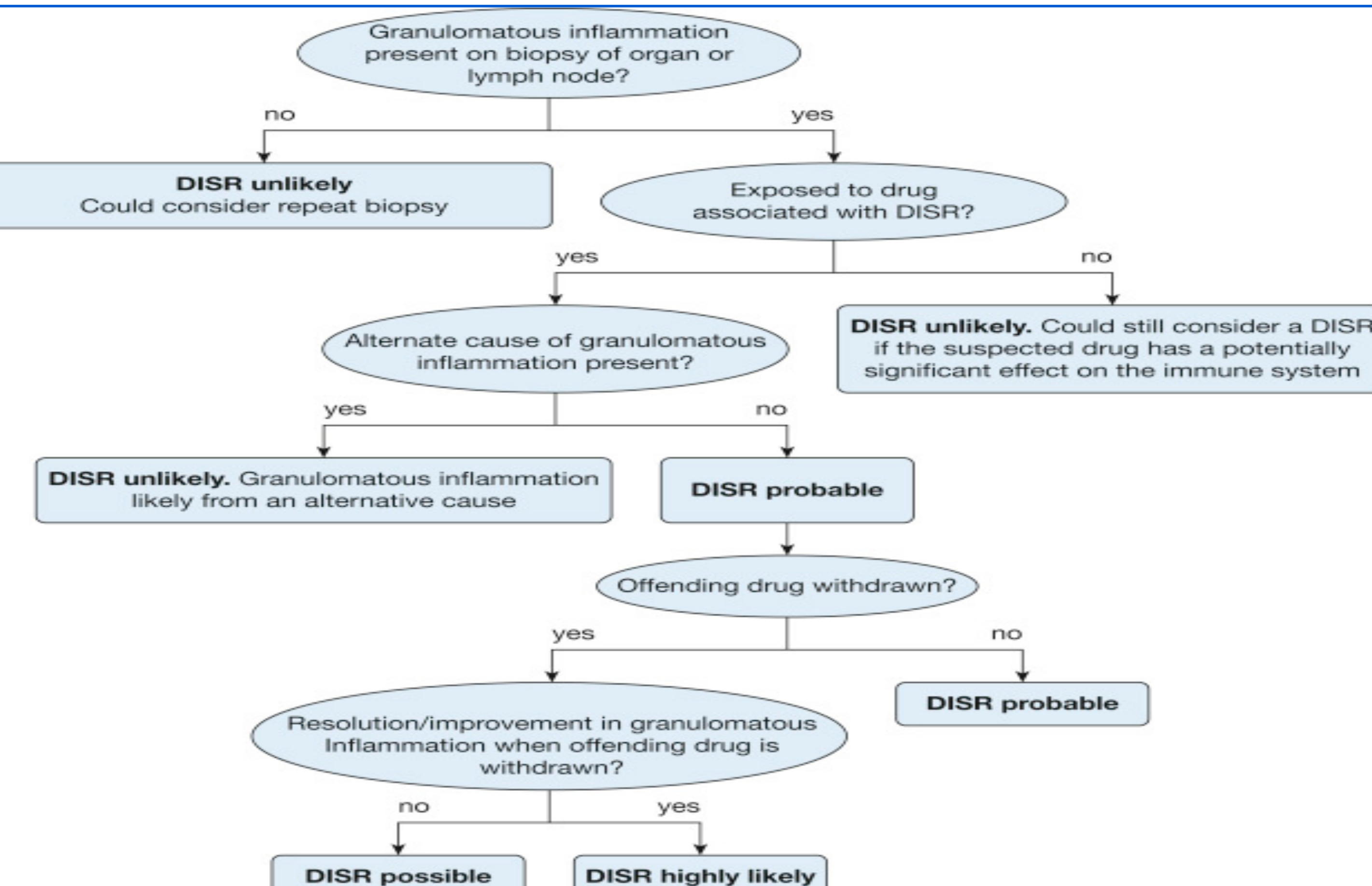
- 1. Recognition and monitoring of ocular sarcoidosis as a rare but potential immune-related adverse effect (irAE) of nivolumab immunotherapy.

Background

Nivolumab is a fully humanised monoclonal immunoglobulin that inhibits programmed death-ligand 1 (PD-L1) from binding to programmed cell death protein 1 (PD-1) on activated T-cells, resulting in immune checkpoint blockade. The downside to novel cancer immunotherapy agents is their association with immune-related adverse effects (irAEs), with reports of sarcoidosis/sarcoidosis-like syndromes as a rare side effect.²

Establishing a diagnosis

Drug-induced sarcoidosis-like reactions (DISR) are clinically indistinguishable from sarcoidosis. In order to determine whether the sarcoidosis is drug-induced, a temporal relationship between the onset of the drug must be established, and alternative causes for granulomatous inflammation must be excluded.¹⁴ The development of anterior uveitis, choroidal granulomas, and pulmonary granulomatous inflammation consistent with sarcoidosis after the introduction of nivolumab immunotherapy, alongside the lack of prior systemic inflammatory disease are strong indicators of a diagnosis of DISR.



Imaging findings

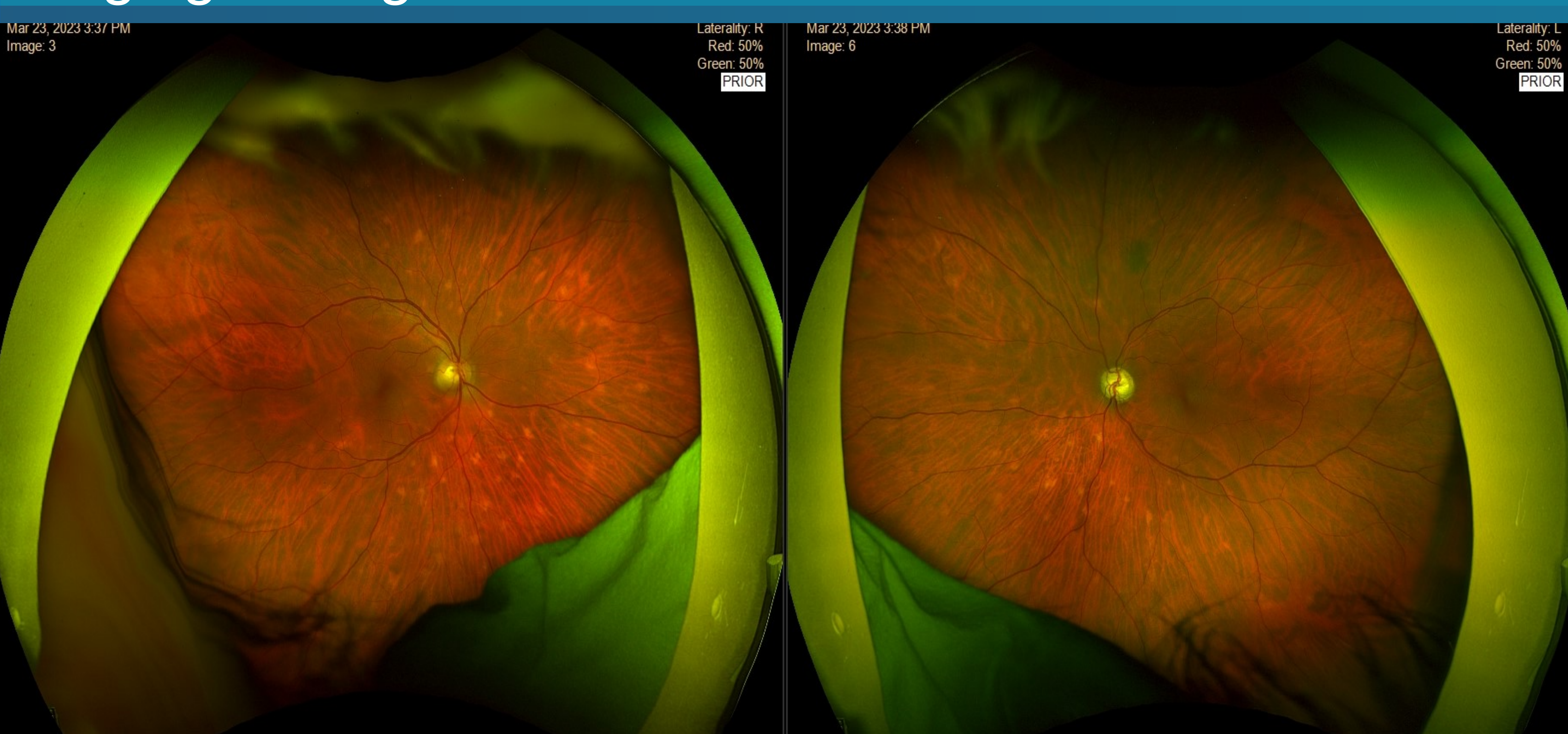


Figure 1. Fundus photography demonstrates numerous pale, creamy, round lesions throughout the fundus, suggestive of choroidal granulomas.

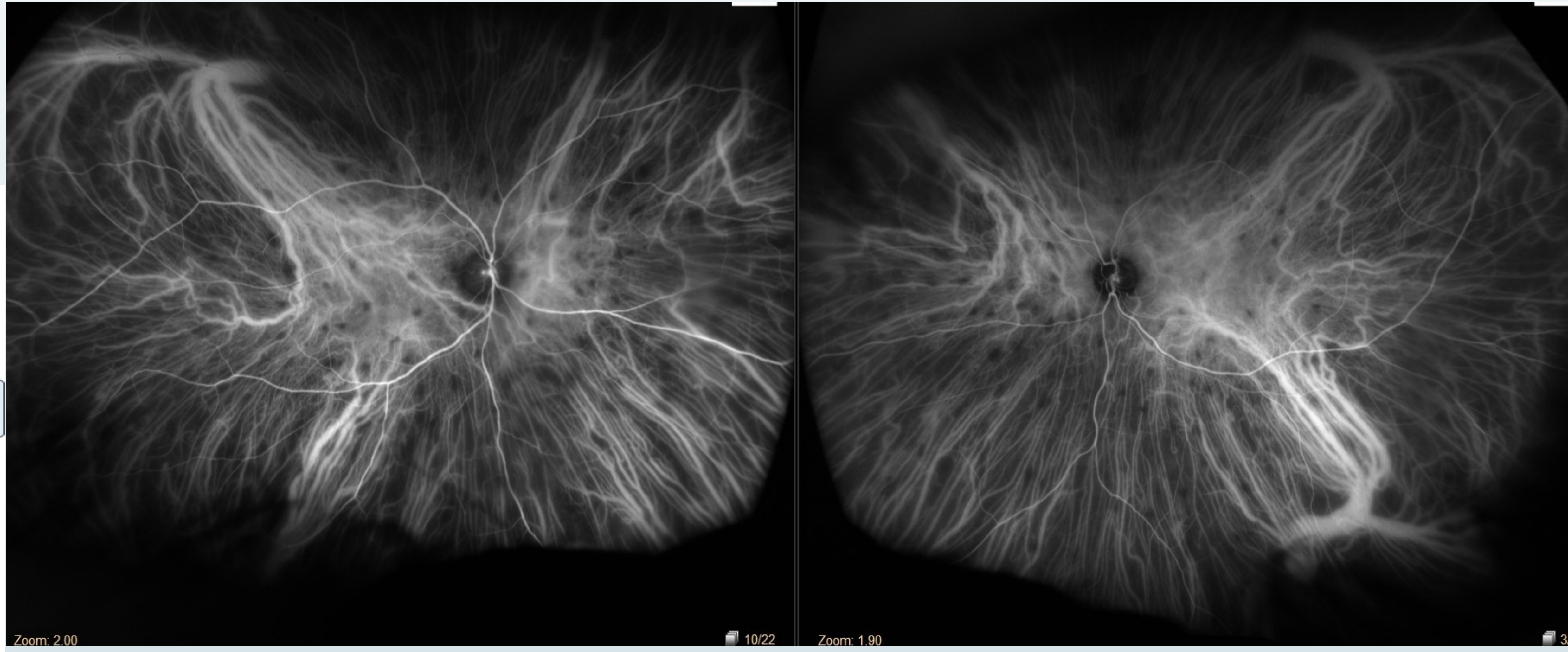


Figure 2. Indocyanine green (ICG) angiography illustrates hypofluorescent spots suggestive of choroidal granulomas.

Discussion

The advent of immune checkpoint inhibitors (ICIs) such as nivolumab has played a crucial role in the management of metastatic malignancies, due to their high affinity for the programmed death protein 1 (PD-1) receptor. As a result, nivolumab prevents the pathological dampening of the T lymphocyte immune response from abnormal programmed death-ligand 1 (PD-L1) expressing tumour cells.⁵ Ocular side effects of immune checkpoint inhibitors are uncommon (1%), with the most common manifestations including uveitis (1%), keratoconjunctivitis sicca (1-24%), and inflammatory orbitopathy.⁶ Notably, nivolumab has been reported as having the highest association with ocular myasthenia gravis with myositis.⁷ In very rare cases, sarcoidosis/sarcoid-like reactions have been documented in individuals treated with nivolumab monotherapy,⁸ however these reactions are most commonly associated with the use of ipillimumab in the treatment of melanoma and present as cutaneous or pulmonary sarcoidosis.⁹ Ocular sarcoidosis is a particularly rare phenomenon in individuals undergoing nivolumab therapy.

Take-home points

Awareness of ocular sarcoidosis as a potential complication associated with nivolumab treatment allows for synergistic efforts to be made between ophthalmologists and oncologists to manage drug-induced ocular inflammation, resulting in potentially reducing the likelihood of sight-threatening complications and improving patient outcomes.

References

