

A case of autosplenectomy associated with T-cell checkpoint inhibitor treatment

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DESCRIPTION

A 77-year-old Caucasian man presented to the oncology service with de novo v-raf murine sarcoma viral oncogene homolog B (BRAF), wild-type metastatic melanoma and widespread disease involving; subcutaneous fat, lymph nodes, bone and spleen with no history of autoimmunity. At diagnosis, the spleen was measured within normal limits on CT. In November 2013, he commenced treatment on a phase-III randomised double-blinded clinical trial (CA209-067) and received combination checkpoint inhibitor therapy with ipilimumab and nivolumab.

Radiological mixed response was observed after three months, with a partial response in all target lesions (RECIST V.1.1 criteria) but an increase in the size of the non-target splenic metastasis consistent with pseudoprogression. In conjunction, splenic enlargement was demonstrated (figure 1).

After seven months of immunotherapy, he achieved a complete radiological response to treatment with an accompanying reduction in splenic size (figure 2). Subsequent imaging demonstrated a persistent reduction in splenic size and by June 2015, only a spleen remnant remained (figure 3). Functional hyposplenism was demonstrated with Howell-Jolly bodies and Acanthocytes on the peripheral blood film (figure 4).

His treatment was complicated by a range of immune-related adverse events (irAE) including hypophysitis, nephritis and colitis. Although steroid dependant, he remains in radiological remission with an excellent performance status. In the absence of alternative autoimmune pathology, we hypothesise that this is a case of checkpoint inhibitor-induced autosplenectomy, the first reported case of a new rare irAE.

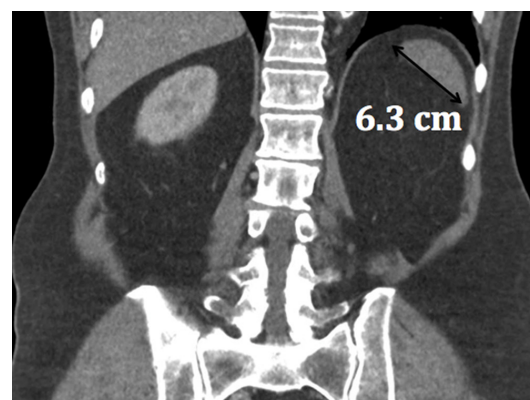


Figure 2 Coronal abdominopelvic CT demonstrating a reduction in the splenic length to 6.3 cm.



Figure 3 Coronal abdominopelvic CT with residual splenic remnant.

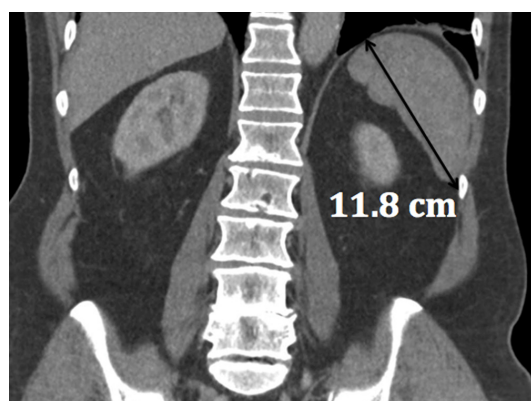


Figure 1 Subsequent restaging coronal abdominopelvic CT demonstrating an increased splenic length of 11.8 cm.

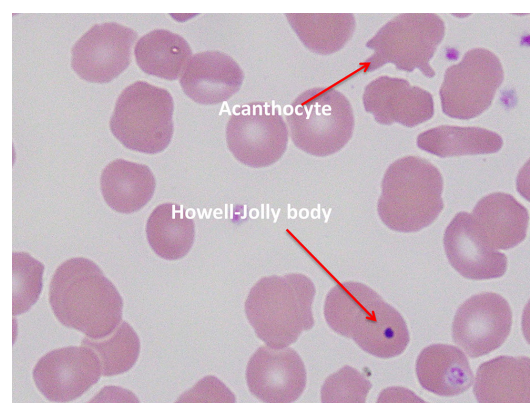


Figure 4 Blood film demonstrating signs of hyposplenism with Acanthocytes and Howell-Jolly bodies.

With increasing use of checkpoint inhibitor's in oncology, clinical vigilance for rare irAE associated with these agents is required.



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Learning points

- ▶ Checkpoint inhibitors are a form of immunotherapy that have revolutionised the management of melanoma and provide benefit across a spectrum of malignancies.
- ▶ These new agents bring with them unique immune-related adverse events (irAE).
- ▶ Adverse events associated with checkpoint inhibitors are common, particularly with combination therapy (55% grade 3–4 severity¹) and can be potentially fatal.
- ▶ Rare immune-related adverse events are increasingly being recognised, they can be inflammatory or autoimmune and impact almost any organ.
- ▶ As checkpoint inhibitors become part of routine clinic practice, it is paramount that all clinicians providing primary and supportive care to oncology patients develop knowledge and experience with these agents and their potential toxicities.

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