

Aftermath of induced inflammation: acute periaortitis due to nivolumab therapy

Ashish K Roy, Harshavardhan R Tathireddy, Moni Roy

OSF Saint Francis Medical Center, Peoria, Illinois, USA

Correspondence to

Dr Ashish K Roy,
aashishkumarroy@gmail.com

AKR and MR contributed equally.

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DESCRIPTION

A 57-year-old man with medical history of left upper lobe metastatic squamous cell carcinoma of lung and seizures due to brain metastasis was admitted with acute-onset low back pain. Patient also had a known history of infrarenal aortic and left common iliac artery aneurysm stable on regular surveillance CT over the past 3 years with the most recent CT scan 1 month prior to presentation showing no signs of inflammation around the infrarenal aneurysmal aorta as seen in [figure 1](#). Positron emission tomography 1 year prior to presentation did not show signs of inflammation in the region of aortic aneurysm as shown in [figure 2](#). For his metastatic lung cancer, he was initially started on carboplatin and gemcitabine therapy but unfortunately had progression of cancer in left lung on the regimen. Subsequently, he was placed on nivolumab therapy. After being on the medication for 9 months, patient presented with acute low back pain that started about 1 hour after completion of nivolumab infusion. Pain was described as sharp, 10/10 in intensity, radiating across the back, no associated nausea, vomiting, diaphoresis, fever, chills or urinary symptoms. The pain resolved after administration of methylprednisolone sodium succinate injection 60 mg once with no recurrence of symptoms during hospital stay and on 1-month follow-up. CT showed stable diameter of infrarenal abdominal aortic aneurysm and unchanged intimal flap involving the left iliac artery without extension into the distal aorta consistent with chronic



Figure 2 Positron emission tomographic image done 1 year prior to presentation showing left upper lobe malignancy with metastatic adenopathy and T1 vertebral skeletal metastasis. No increased uptake noted around infrarenal aortic aneurysm.



Figure 1 Coronal CT image showing fusiform dilation of infrarenal aorta 1 month prior to presentation with back pain.

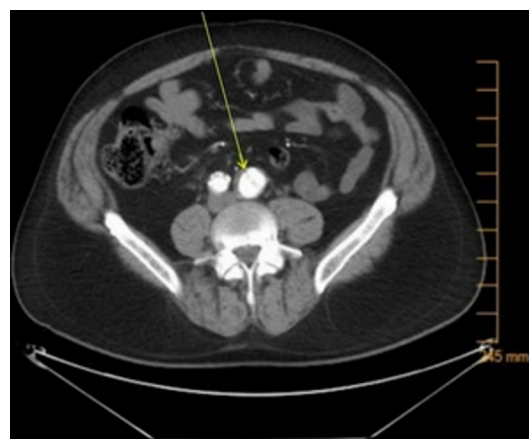


Figure 3 Axial CT image showing intimal flap in the left common iliac artery (downward arrow).



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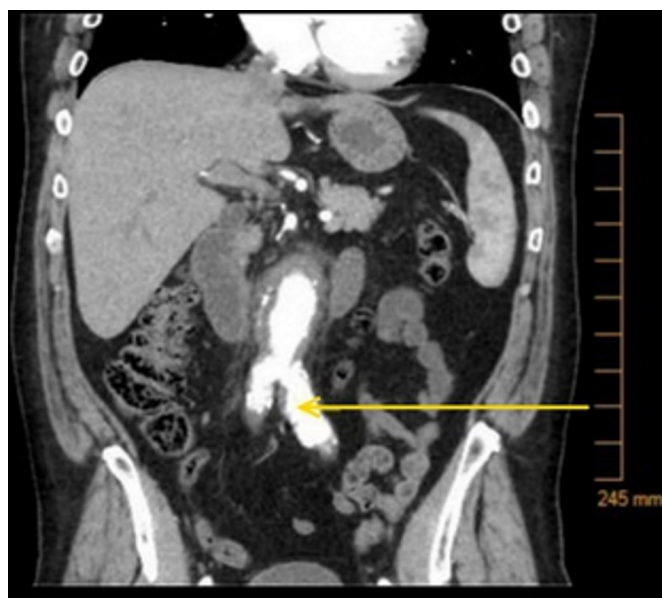


Figure 4 Coronal CT image showing linear filling defect within left common iliac artery aneurysm consistent with a chronic intimal flap (left arrow) and fusiform dilation of infrarenal abdominal aorta.

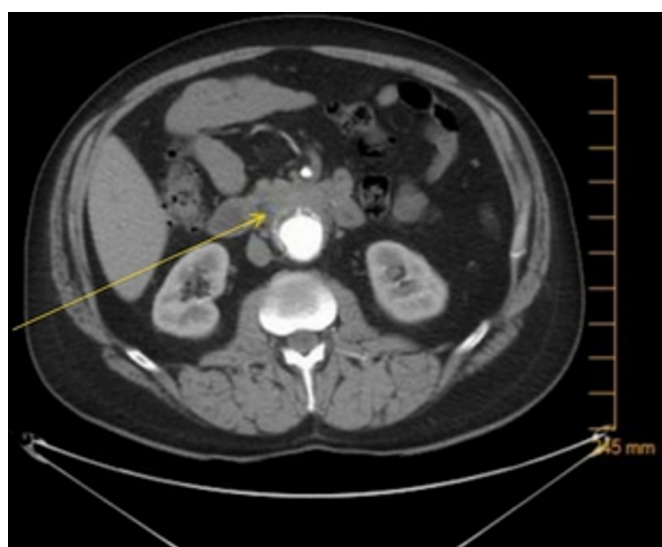


Figure 5 Axial CT image showing periaortic soft tissue thickening involving the distal infrarenal abdominal aorta (right arrow).

dissection as shown in figures 3 and 4 and these changes were noted on prior CT scan as well. A new finding on the CT was increase in periaortic soft tissue thickening involving distal infrarenal abdominal aorta consistent with acute periaortitis as shown in figure 5. Laboratory studies to rule out other possible infectious and autoimmune causes of acute periaortitis were obtained as shown in table 1. Infectious aetiology was ruled out and patient was started on oral prednisone taper for 4 weeks. The acute onset of back pain, starting immediately after nivolumab infusion, elevated inflammatory markers and resolution of pain after administration of high-dose steroid was consistent acute inflammatory process most likely due to nivolumab therapy. An aortic biopsy in this setting of acute inflammation was not undertaken due to the risks of procedure. A decision was made to treat conservatively with steroid taper and holding nivolumab infusion after discussion with oncologist and rheumatologist. Repeat CT scan done 8 weeks after stopping nivolumab therapy showed interval decrease in soft tissue thickening along the anterior aspect of abdominal aortic aneurysm as shown in figure 6.



Figure 6 Axial CT image showing interval decrease in soft tissue thickening along the anterior aspect of abdominal aortic aneurysm.

Table 1 Laboratory testing to rule out infectious and autoimmune aetiology of periaortitis

Test	Normal range	Result
Erythrocyte sedimentation rate	0–15 mm/hour	31 mm/hour
C-reactive protein	<0.50 mg/dL	4.43 mg/dL
Antinuclear antibody screen	Negative	Negative
Antineutrophilic cytoplasmic antibodies	<1:20 titre	<1:20
Blood culture (bacterial)	Negative	Negative after 5 days
Blood culture (fungus)	Negative	Negative after 1 week
Rapid plasma reagin (RPR) screen	Non-reactive	Non-reactive
Hepatitis A IgM antibody	Non-detected	Non-detected
Hepatitis B core antibody	Non-detected	Non-detected
Hepatitis B surface antigen	Non-detected	Non-detected
Hepatitis C antibody	<0.79 signal/cut-off ratio	0.54
HIV 1 and 2 antibody antigen screen	Non-detected	Non-detected

Nivolumab is human IgG4 anti-PD1 immune checkpoint antibody that has recently emerged as a therapy for metastatic non-small cell lung cancer.^{1,2} This being a newer class of medication the side effect profile is currently under study. The mode of action (MOA) is activation of immune response against cancer cells and the MOA for this drug class is the best explanation for reported side effects of immune-mediated pneumonitis, hepatitis and gastritis to name a few. El-Refai *et al* recently reported that more than 25% of patients with lung and renal cancer had a coexisting autoimmune condition that is at risk of worsening with immune checkpoint inhibition.³ In our patient, no history of autoimmune disorder was present. Our patient did have a known history of atherosclerotic aneurysm and chronic dissection of infrarenal aortic segment, which in itself is a result of

chronic inflammation in the arterial wall with formation of atherosclerotic plaque. CT scan of abdomen 1 month prior to onset of symptoms did not show significant fat stranding around the aneurysmal aorta. It is very likely that the immune checkpoint inhibitor leads to a state of acute or chronic inflammation, leading to periaortitis. The safety of this class of medication is still to be studied and the risk versus benefit of the medication has to be assessed on case to case basis.

Contributors AKR and MR wrote the initial manuscript and performed literature review. AKR, MR and HRT performed the final manuscript designing. All authors read and approved the manuscript prior to submission.

Competing interests None declared.

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Learning points

- ▶ Nivolumab is a human IgG4 anti-PD1 immune check point antibody that acts by activation of immune response against cancer cells.
- ▶ Acute periaortitis is a possible side effect of nivolumab in patients with underlying chronic atherosclerotic aneurysm and dissection.

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