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Background

- Serous adenocarcinoma of the uterine cervix (USCC)** is an exceptionally rare and aggressive cervical cancer subtype, accounting for approximately 0.4% of cervical malignancies.
- Because of its rarity, treatment recommendations are extrapolated from studies of more common cervical cancer histologies.
- Immune checkpoint inhibitors have demonstrated efficacy in recurrent and metastatic cervical cancer, but evidence supporting their use in metastatic USCC is limited.
- This case highlights the potential role of pembrolizumab in achieving durable disease control while minimizing treatment-related toxicity.

Case

- A 45-year-old woman with uterine didelphys initially presented with cervical and vaginal lesions interpreted as adenocarcinoma. Following expert pathology review, she was diagnosed with FIGO stage IIA2 serous adenocarcinoma of the cervix.
- She underwent radical hysterectomy with bilateral salpingo-oophorectomy. The patient declined adjuvant therapy and remained disease free for five years before presenting with metastatic recurrence involving the chest wall and buttock.
- Molecular testing demonstrated:
 - PD-L1 CPS = 50
 - HER2 negative
 - Microsatellite stable
 - Low tumor mutational burden
- She initially received three cycles of the KEYNOTE-826 regimen. Treatment was discontinued because of grade 3 chemotherapy-induced peripheral neuropathy. Pembrolizumab monotherapy was continued.
- Early PET/CT demonstrated a mixed response; however, continued therapy resulted in progressive reduction in metastatic disease.
- The patient has now completed 24 cycles of pembrolizumab without treatment-related adverse events and continues to demonstrate durable clinical benefit.

Clinical Course and Treatment Timeline

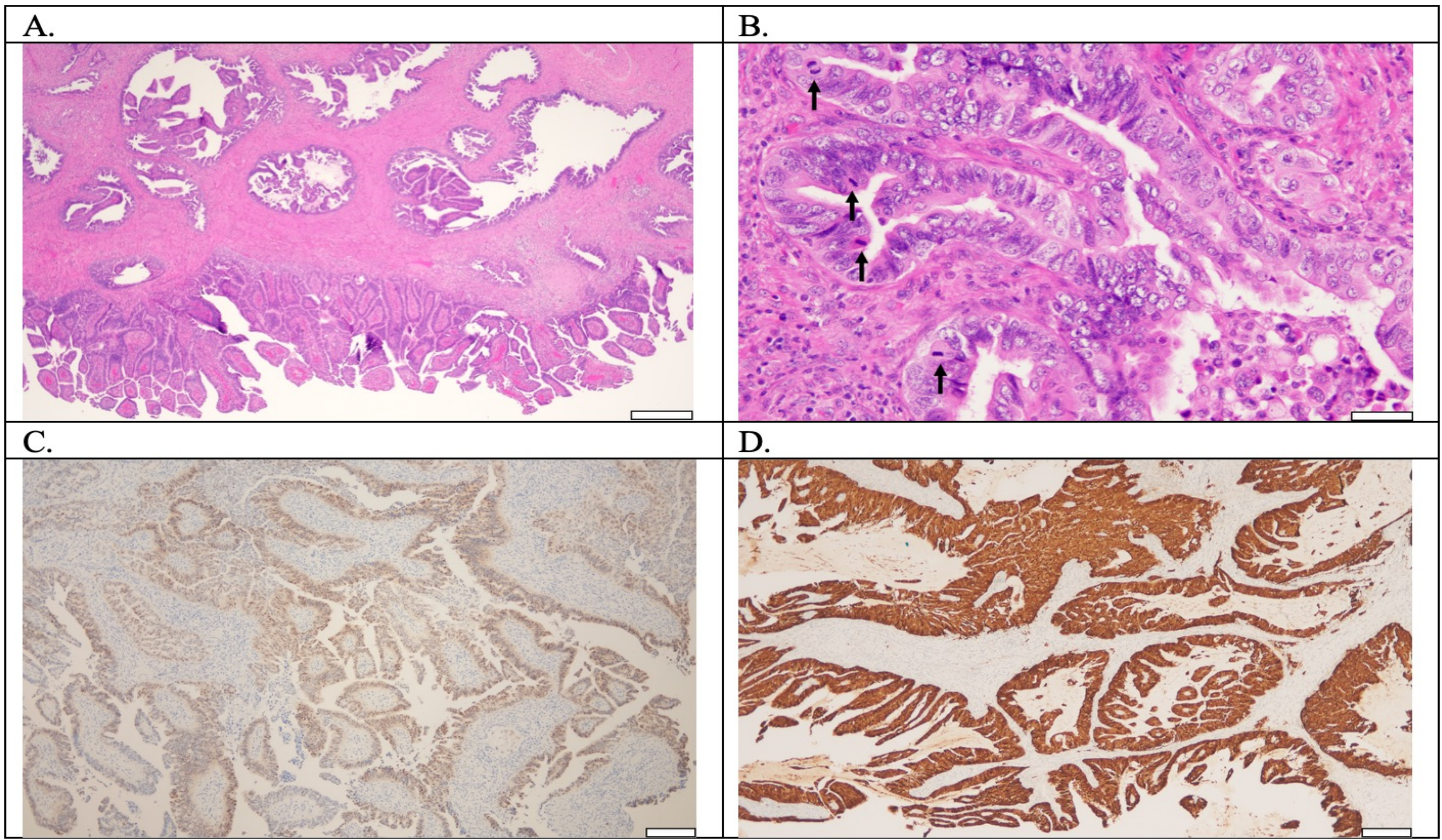


Figure 1. A. Hematoxylin and eosin (H&E) section demonstrating both prominent papillary and irregular glandular growth. Magnification 20x; Scale bar 500 µm. B. H&E section demonstrating marked cellular atypia, nuclear pleomorphism and enlargement, loss of polarity, and multiple mitotic figures (arrows). Magnification 200x; Scale bar 50 µm. C. In situ hybridization probe stain for HPV High Risk 16/18, positive in the cells of interest. Magnification 40x; Scale bar 200 µm. D. Immunohistochemical staining for p16, strong and diffusely positive in the cells of interest. Magnification 40x; Scale bar 200 µm.

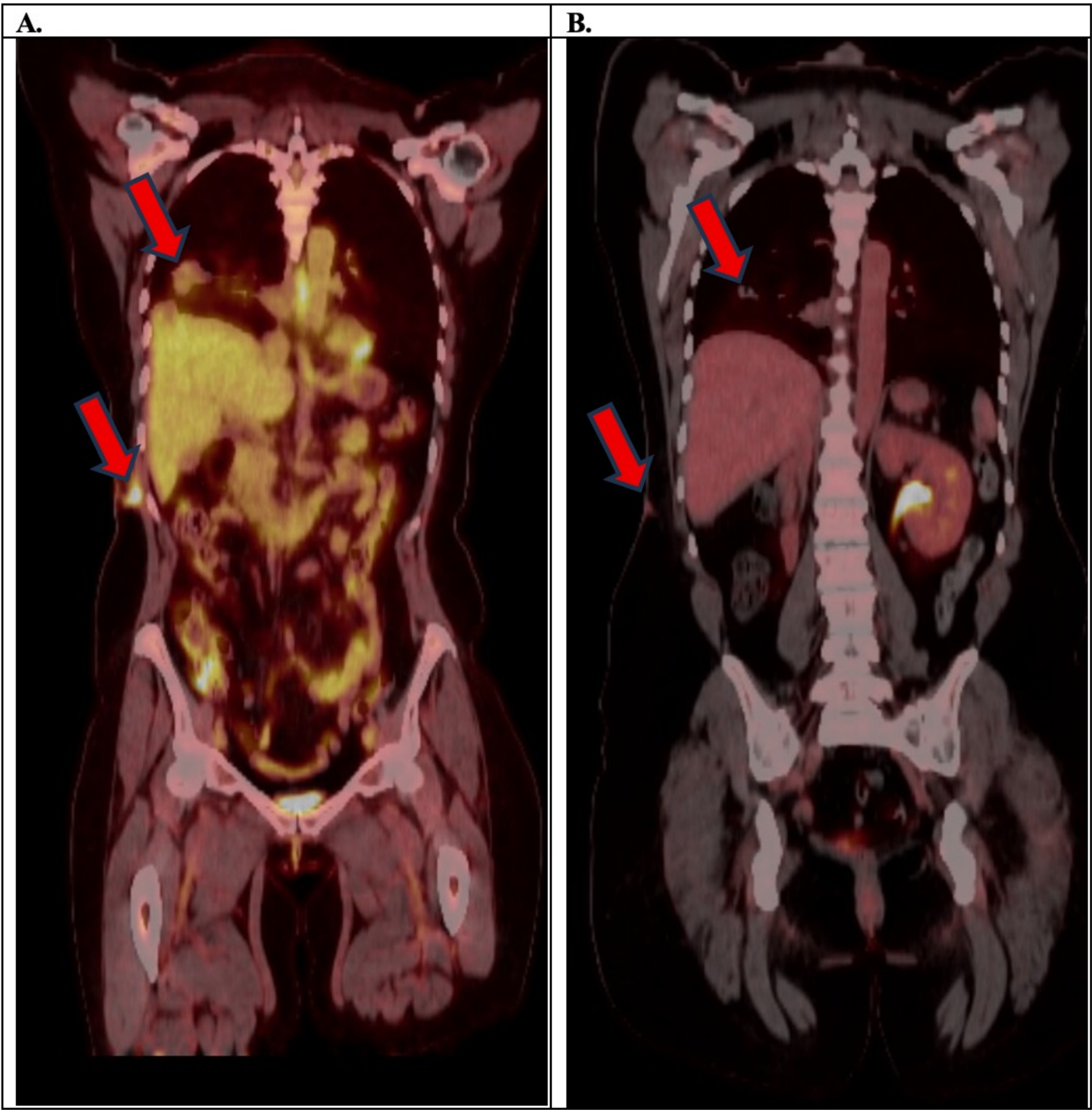


Figure 2. PET-CT showing response to single agent pembrolizumab. A. PET-CT obtained at the completion of three cycles of KEYNOTE-826 regimen with red arrows showing a right lower lobe and right chest wall metastatic implant. B. PET-CT obtained after cycle 19 of maintenance pembrolizumab showing marked decreased in the right lower lobe and right chest wall metastatic implant.

Discussion

- Metastatic USCC remains one of the rarest cervical malignancies, and evidence guiding systemic therapy is extremely limited.
- This case demonstrates prolonged clinical benefit with pembrolizumab despite an initial mixed radiographic response. Importantly, treatment was well tolerated and avoided additional chemotherapy-related toxicity.
- These findings suggest that, in clinically stable patients with high PD-L1 expression, continuation of immune checkpoint inhibition beyond early mixed imaging findings may be appropriate.
- Further investigation is needed to better define the role of pembrolizumab in this rare histologic subtype.

Take-Home Message:

- Durable Response to Pembrolizumab in Metastatic PD-L1-Expressing USCC**
 - High PD-L1 expression may identify patients who derive substantial benefit from pembrolizumab
 - Early mixed radiographic findings should not necessarily be considered treatment failure, particularly in clinically stable patients