Pseudotumor presentation of CMV disease: diagnostic dilemma and association with immunomodulating therapy

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Introduction

- Cytomegalovirus is a significant cause of morbidity and mortality in the immunocompromised
- Atypical presentations which may include pseudotumours or 'cancer mimics' have been described
- The aetiology of these lesions remains unclear

Methods

- The authors describe two previously unpublished cases that have arisen in the context of newer immunomodulating therapy (Table 1. case 1 & 2) and review the existing non-HIV associated CMV pseudo tumours described in the literature
- Additional cases of CMV pseudotumours were identified from the literature using a PubMed search (1980 – October 2019) of the English language medical literature applying the terms 'CMV', 'pseudotumor' and 'Inflammatory mass'. Cases associated with HIV infection were excluded

Results

- 23 cases of CMV pseudotumor described in the non-HIV setting, including two new cases not previously described are reviewed
- 48% (11/23) of patients were either organ transplant recipients or otherwise immunosuppressed
- 96% (22/23) presented with focal symptoms relating to the site of the lesion
- 78% (18/23) of all cases were found in the gastrointestinal tract
- All diagnoses were made based on microscopic findings on anatomical pathology specimens with CMV cytopathic effects identified in 100% (23/23)
- Surgical management of lesions was undertaken in 30% (7/23)
- Antivirals were administered in 57% (13/23) of cases
- After a median duration of follow up of 22 weeks, 91% (21/23) demonstrated resolution of lesions while 2 had persistent pseudotumor with signs of healing

Table 1. Characteristics of CMV Pseudotumor cases

Age, sex, site of involvement	Immunocompromised status	Clinical Presentation	Treatment	Outcome
59F, Oropharynx[1]	Pembrolizumab for recurrent SCC	3 weeks of rapidly progressive mass	Gan 28D + valgan 28D	Resolved$^{\Delta}$
52F, Vulva[2]	Renal Tx, belatacept + MMF + prednisolone	6 months of slowly progressive lesion with bleeding and pain	CMV IVIG	Resolved$^{\Delta}$
64M, Colon	Kidney Tx (CMV +/+), MMF + CyA	Months of fatigue, headache, dizziness and 7% LOW	Gan 21D then valgan 63D	Improving†
76M, Caecum	NIL	4 days of lower abdominal pain	NIL	Resolved$^{€}$
68F Rectosigmoid junction	Gliosarcoma with radiotherapy and temozolomide + dexamethasone	Abdominal pain, fevers, hematochezia	Gan for 126D	Palliated
76F, Rectum	NIL	1 week of constipation, anal and abdominal pain & bloating	Gan for 14D	Resolved$^{€}$
42M, Rectum	NIL	3 months of small volume bloody diarrhea with 13kg LOW	Gan for 21D	Resolved$^{€}$
89F Rectosigmoid junction	NIL	5 months constipation and tenesmus	NIL	Resolved$^{€}$
63M, Larynx	Nephrotic syndrome (prednisolone 35mg/day + CyA)	Rapid onset of dyspnea and stridor in context of herpes zoster opthalmicus	Gan for 24D	Resolved$^{\Delta}$
62M, Larynx	Neurofibromatosis	2 weeks of progressive SOB and stridor	NIL	Resolved$^{€}$
44M, Stomach	NIL	15 days fevers, malaise, mid-epigastric pain	NIL	Resolved$^{€}$
62M, Colon	Heart transplant (CMV +/+) CyA + AZA	12 hours abdominal pain, constipation, hematochezia	Gan 28D + CMV IVIG	Resolved$^{€}$
40M, Gastric and Small Bowel	Common variable immune deficiency	6-month history of abdominal pain, 10kg LOW with SBO	Gan 56D	Resolved$^{\Delta}$
84F, Colon	NIL	1-week abdominal pain, diarrhea, fevers	Gan 14D	Resolved$^{\Delta}$
67M, Colon	NIL	5 days abdominal pain, diarrhea, fever	Gan 14D	Resolved$^{\Delta}$
70M, Lung	Severe COPD, home oxygen dependent	Identified as part of evaluation of progressive COPD	Valgan 28D	Resolved$^{\Delta}$
70F, Caecum and sigmoid	Renal Tx, sirolimus	Asymptomatic. Routine colonoscopy post malignancy	NIL	unknown
69M, Sigmoid Colon	UC, MTX and sulfasalazine	Screening for UC	NIL	unknown
80F, Colon	NIL	Diarrhea	NIL	Resolved$^{€}$
56M, Stomach	NIL	pain	NIL	Resolved$^{€}$
49M, Lung	NIL	6 weeks of left shoulder pain and productive cough	NIL	Clinically resolved
60F, Colon	Renal Tx (CMV +/-), CyA + sirolimus + prednisolone	1 week of bloody diarrhea and bilious vomiting	Gan for unclear duration	Resolved$^{€}$
53M, Colon	Renal transplant 9 years prior (Aza + prednisolone)	8 months of intermitted epigastric pain with 2 months diarrhea	NIL	Resolved$^{\Delta}$
57F, Colon	Heart Tx (CMV +/+), CyA + Aza	24 hours of intermittent crampy abdominal pain, diarrhea and fevers	Gan 14D	Resolved$^{\Delta}$

Resolved$^{\Delta}$, Clinically resolved; Resolved$^{€}$ Endoscopically resolved; Improved† Symptoms clinically improved but repeat endoscopy not performed; Gan, Ganciclovir; Valgan, Valgancyclovir

Results

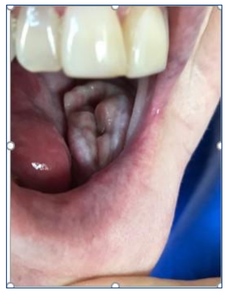

Figure 1. Oropharyngeal Pseudotumor in patient 1 pembrolizumab

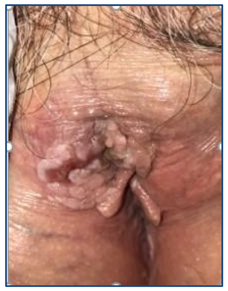

Figure 3. Slowly enlarging 6cm verrucous vulval lesion encompassing entire right labia minora, right clitoral hood and margin of right labia majora. Pathology of completely excised tissue demonstrated chronic inflammation and CMV cytopathic effect with immunostain positive.

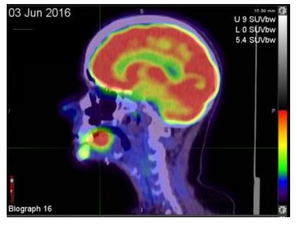

Figure 2. Sagittal images of a ^{18}F-fluorodeoxyglucose positron-emission tomography of the head and neck demonstrating an avid lesion on the left lower jaw at the site of ulcero-fungating mass from patient 1.

Conclusion

- CMV tumours are an uncommon occurrence but despite the traditionally held assumption that they affect HIV patients only, there is increasing evidence that non-HIV patients may also be affected
- Because the immunologic and viral mechanisms that govern this phenomenon are unclear, and likely heterogenous, so too is the natural history and optimal management
- The role for either antivirals or surgery is unknown, although based on this series, the prognosis of such lesions in the short to medium term would appear to be favourable
- Treatment decisions should be made on a case-by-case basis
- With the increasing adoption of immune modulating therapy to treat a variety of autoimmune, immunological and malignant conditions, it is possible these lesions may become more frequently observed in clinical practice