

## Case report

# CMV sinusitis, an overlooked diagnosis, a predisposing condition or is it a bystander? A Case report and review of the literature

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## ABSTRACT

The disease entity of cytomegalovirus (CMV) sinusitis has been uncommonly described in the literature, although other end organ debilitating diseases are frequently encountered in people with advanced Human immunodeficiency virus (HIV) infection. We herein present a case of CMV sinusitis in an patient with acquired immunodeficiency syndrome (AIDS) diagnosed by the detection of intranuclear viral inclusions and positive CMV immunostains. The patient responded to surgical debridement and targeted medical therapy. A consideration should be made to this rarely described form of CMV disease. There is heterogeneity in how the diagnosis was made in the reported cases in the reviewed literature. Unlike our patient, not all the patients had cytopathological evidence of the disease. Furthermore, some of the patients improved with surgical therapy alone raising the question of the true clinical significance of the recovery of CMV viral particles without cytopathic evidence in their corresponding diagnostic workup. On another note, the recovery of CMV in samples of patients with chronic antibiotic-resistant sinusitis may suggest a pathogenic role and necessitates adequate therapeutic interventions.

## Background

CMV reactivation and acute infections are common in severely immunocompromised people with HIV (PWH). Sinusitis is another common illness that these patients sustain. Although bacterial and fungal sinusitis is commonly described, viral sinusitis, particularly due to CMV, remains much less frequently described [1–4]. It has been hypothesized that CMV could cause sinusitis, predispose to other forms of sinusitis, or be an innocent bystander [4].

## Case presentation

Our case is that of a 40-year-old gentleman with a medical history significant for HIV, off antiretroviral therapy (ART) who presented with left eyelid redness and edema, odynophagia, dysphagia, generalized weakness, and unintentional weight loss.

His physical exam was notable for facial and periorbital edema without demarcated erythema or notable proptosis. His pupils were equal, round, and reactive to light and accommodation with normal and non-painful extraocular movement. On further exam, his nasal mucosa

appeared normal with a midline septum and no nasal discharge. He did however have a 3×3cm area of necrotic mucosal lesions at the left hemipalate with mild trismus and decreased cutaneous sensation over the V2 branch.

His laboratory workup on presentation revealed leukopenia and lymphopenia (WBC  $3.3 \times 10^3/\text{mL}$ , lymphocytes 21.9%), anemia (hemoglobin 7.7 g/dL, hematocrit 23.2%), with no noted associated renal or hepatic function abnormalities. Moreover, the CD4 + T cell count was 40 cells/mm<sup>3</sup> and the HIV RNA levels were 44,700 copies/mL. He also had an RPR of 1:2048.

A facial CT scan revealed extensive mucosal thickening in nearly all the paranasal sinuses as well as along the left nasal passage with non-enhancing mucosa of the left maxillary sinus and left inferior turbinate. It also showed diffuse superficial soft tissue swelling in the facial regions bilaterally. An MRI of sinuses confirmed these findings (Fig. 1).

A lumbar puncture was unremarkable with colorless cerebrospinal fluid (CSF), 0 red blood cells and white blood cells, glucose 64 mg/dL, proteins 26 mg/dL, lactate 1.8 mmol/L. CSF cryptococcal and streptococcal antigens were negative. CSF VDRL was negative.

A detailed ophthalmologic evaluation that included a dilated fundus

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exam revealed no abnormalities. Direct evaluation by flexible endoscopy showed bilateral mucosal edema more pronounced on the left, preventing the view of the external nasal valve. The necrotic palatal region was debrided at the bedside with noted underlying fistulous tract suggesting an orosinus communication. Tissue samples for culture and pathology were obtained. Additional laboratory workups including fungitell and galactomannan levels, which were unremarkable.

The patient underwent surgical excision of the palatal region, additional debridement, orbital decompression, excision of the inferior turbinates, and antrostomy to the maxillary sinus yielding a large necrotic and ulcerative lesion of the left hard palate extending all the way to bone. Tissue cultures grew few alpha *Streptococcus*, rare *Streptococcus anginosus*, rare *Rothia mucilaginosa*, moderate *Haemophilus* species, and rare methicillin resistant *Staphylococcus aureus* (MRSA). The anaerobic cultures grew few *Bacteroides* species and a few *Prevotella melaninogenica*.

His pathology specimens revealed signs of ulceration, acute inflammation, and necrosis, no fungal elements were identified by GMS stain in all specimens. AFB stains were also negative. Three of the 7 specimens, however, were notable for intranuclear viral inclusions and positive CMV immunostains (Fig. 2). Based on these findings, the patient was diagnosed with CMV rhinosinusitis and was started on IV ganciclovir in addition to concomitant IV broad-spectrum antibiotic therapy with vancomycin and ceftriaxone. He clinically improved on this therapy with marked decrease in his orofacial pain and swelling. He was then transitioned to valganciclovir, in addition to amoxicillin/clavulanic acid and minocycline and was discharged home on day 10 postoperatively.

## Discussion and conclusion

End organ CMV disease is determined to occur in around 6% of PWH with a CD4 + T cell counts < 50 cells/mm<sup>3</sup> [5,6].

On the other hand, the overall prevalence of sinusitis in PWH is estimated to range between 30% and 68% [7,8]. The risk factors identified in this population included delayed mucociliary transport time and nasopharyngeal lymphoid hypertrophy, particularly during the early stages of HIV infection [7]. Some reports also described increased immunoglobulin E levels in PWH with rhinosinusitis but no definite association between HIV infection and increased atopy has been established [9]. The microbiology is contingent on the level of immunodeficiency, whereby, it was not different from people without HIV when the CD4 + T cell levels are above 200 cells/mm<sup>3</sup>. As the CD4 + T cell count drops below 50 cells/mm<sup>3</sup>, pathological and radiological changes were noted to occur more often [8]. In addition, substantial concern is raised for several pathogens including *Pseudomonas aeruginosa*, which was noted in up to 15% of the cases among PWH in a review by Shah and colleagues [10] and other bacterial species (such as *Legionella pneumophila*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium avium* complex) and fungal organisms especially in the setting of associated

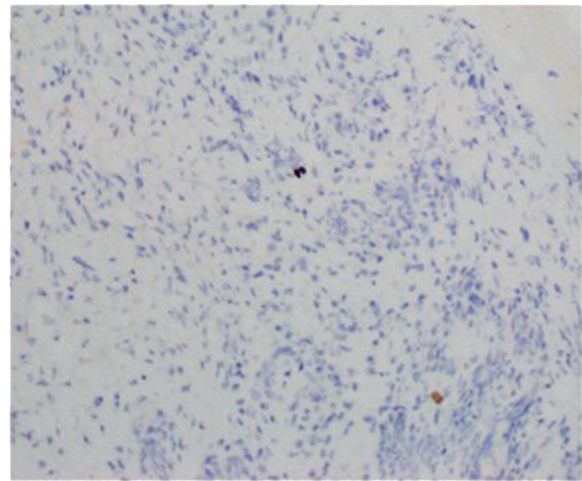


Fig. 2. Positive CMV immunostain.

neutropenia [10].

Despite the high frequency of both CMV infection and sinusitis in people with AIDS, CMV sinusitis has not been clearly defined

In a prospective study conducted on PWH with sinusitis per MRI findings and fever, 2 out of 20 sinus aspirate samples revealed CMV without detailing the course, the presence of co-infections, or the therapies given [8].

We conducted a literature review of CMV sinusitis cases reported from 1985 to 2021 in the PubMed database using the terms "CMV" and "cytomegalovirus" cross-referenced with "sinusitis." Additional sources were found following the reference citations from retrieved articles. We found 9 case reports describing the diagnosis as summarized in Table 1.

The first case of histopathologically proven CMV sinusitis was reported by Kotler et al. [11]. This case was followed by another case reported in 1995 of a histopathologically proven CMV sinusitis manifested by a heterogeneous soft tissue mass with bony erosions in a 34-year-old patient with HIV/AIDS who improved with surgical debridement and ganciclovir therapy [2]. The following year, a 4 cases case series were reported by Marks and colleagues. All 4 PWH had low CD4 + T cell counts. Only one had pathologic evidence of tissue invasion with inclusions bodies. They all underwent surgical debridement and, although all reportedly had improvement in their sinusitis syndrome, 2 of them died of pneumonia, none of them received anti-CMV therapy, and at least 2 of them received antibacterial therapy [1].

A few years later, Yoskovitch et al. reported a case of CMV sinusitis and nasal polyposis diagnosed through pathology specimens and treated with IV ganciclovir after undergoing bilateral endoscopic maxillary

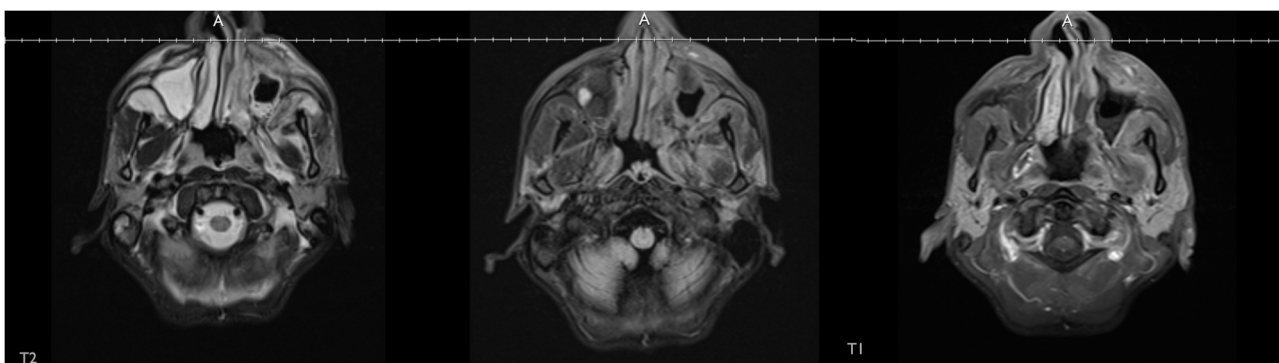


Fig. 1. MRI sinuses.

**Table 1**  
Summary of the reported cases of CMV sinusitis in the literature.

Level of immunosuppression	Duration of symptoms	Reason for admission/ related symptoms	Imaging findings	Histology / Microbiology	CMV PCR	Treatment	Outcome	Citation
AIDS	Chronic rhinosinusitis	Fever, purulent rhinitis	Xray sinuses with no abnormalities	Multiple CMV inclusions in endothelial cells	Not mentioned	Surgical debridement. Medical therapy not specified	Not mentioned	[11]
HIV/AIDs	Not specified	Facial pain and swelling	heterogeneous soft-tissue mass extending from the left maxillary antrum with bone erosion of the medial and posterior walls	Numerous CMV inclusion bodies rare colonies of <i>Pseudomonas aeruginosa</i>	Not mentioned	Surgical debridement with Ganciclovir	Symptoms Improved	[2]
HIV/AIDS (CD4 <20)	8 weeks	peri-orbital pain and fever	bilateral opacification of the maxillary, ethmoid, and sphenoid sinuses, with air fluid levels in the frontal sinuses	severe inflammation and intranuclear inclusions consistent with CMV	Not mentioned	Endoscopic sphenoidectomy with frontal sinusotomy	Symptoms improved. Died of polymicrobial pneumonia, including CMV 3 months post operatively	[1]
HIV/ AIDs (CD4 50)	Several months of Postnasal drip	fever and lower extremity weakness	bilateral opacification of all sinuses.	mucopurulent material that yielded only CMV	Not mentioned	Transnasal antral puncture; Intravenous ampicillin/sulbactam	Symptoms improved	[1]
HIV/AIDS (CD4 17)	2 weeks	nasal congestion and fever, nonproductive cough, and pleuritic chest pain	bilateral maxillary and ethmoid opacification	Intraoperative culture revealed rare <i>E. coli</i> and a heavy growth of CMV		Caldwell-Luc and nasoantral window procedures	Symptoms improved	[1]
HIV (Unknown CD4)	1 week	rapidly deteriorating vision and hearing	expansive mass in the right sphenoid sinus compressing the right orbital apex	Culture samples yielded <i>Streptococcus pneumoniae</i> , coagulase-negative <i>Staphylococcus</i> , and CMV.	Not mentioned	Endoscopic sphenoidectomy	Symptoms improved. died shortly thereafter due to pneumonia	[1]
Undiagnosed HIV infection	Chronic sinusitis, duration not specified	Not specified	CT scan showed opacification of the left maxillaris and connection between the alveolar process of the maxilla and the oral cavity	Focal, ulcerating inflammation with giant cells and viral inclusion bodies	Not mentioned	Surgical debridement with Ganciclovir and foscarnet combination therapy 4 weeks followed by maintenance therapy for 30 months	Resolved with no relapse	[13]
HIV /AIDS (Current case)	3 weeks	Left eyelid redness and edema, odynophagia, dysphagia, generalized weakness	Inflammation in the premaxillary and preseptal soft tissues	Necrotic tissue, positive CMV Immunostaining	6038 copies/mL	Surgical debridement, IV ganciclovir then oral valganciclovir with augmentin and minocycline	Clinically improved	
Renal transplant related immunosuppression lymphocyte count, $0.13 \times 10^9/L$	4 weeks	Persistent congestion with peri-orbital pain	near-complete opacification of the right paranasal and maxillary sinuses with associated maxillary wall destruction	active chronic inflammation with numerous intracellular cytomegalic inclusions immunoreacting with CMV antibodies	32,320 copies/mL	Multiple surgical debridements IV ganciclovir, IV antibiotics and methylprednisone with concomitant immunosuppression reduction then maintenance valganciclovir	Symptoms completely resolved	[14]
Relapsed CML Allogenic bone marrow transplant (10yo)	Chronic sinusitis, duration not specified	acial swelling with exquisite tenderness to palpation	near complete opacification of the paranasal sinuses, with obstruction of the ostiomeatal units. No. bony erosions.	The aerobic bacterial cultures revealed heavy growth of <i>Pseudomonas aeruginosa</i> numerous cellular inclusions consistent with CMV disease	CMV antigenemia was detected at 0.8 positive cells seen per 50,000 white blood cells	maxillary antrostomy, right total ethmoidectomy, and left myringotomy. + Ganciclovir and meropenem	Resolution of symptoms	[3]

anrostomy and nasal polypectomies. The patient had marked clinical improvement with no recurrence of the polyps [12].

In the year 2000, a case of CMV sinusitis diagnosed histopathologically was described in a 49-year-old gentleman with a long-lasting history of chronic sinusitis who sustained a traumatic fracture of the left maxillary bone. He was also diagnosed with HIV and CMV retinitis. He received surgical and medical therapy with foscarnet and ganciclovir with no reported further relapse [13].

This entity has also been reported following bone marrow transplantation [3].

and in solid organ transplant recipients whereby Gujadhur and colleagues described it in a female patient 11 months after the receipt of a renal transplant (recipient positive, donor equivocal) with numerous intracellular CMV inclusions, and negative smears and cultures for bacterial, fungal, and acid-fast organisms [14]. Morre and colleagues reported the isolation of CMV from the maxillary sinuses of an immunocompetent patient and hypothesized a superimposed acute bacterial sinusitis as precipitating the development of CMV infection [4]. These findings might suggest a role for CMV in chronic antibiotic-resistant sinusitis [15].

Despite the reported cases, there is heterogeneity in the diagnostic approach of CMV infection/disease. Although not all patients received CMV therapy, the improvement was noticeable after surgical intervention.

This review serves to present a new CMV disease entity and highlight the importance of demonstrating a cytopathologic effect to confirm end organ disease in the case of sinusitis. The presence of the virus by itself may just demonstrate shedding without associated clinical significance. An objective evaluation of treatment response is challenging as the correlation between CMV disease in the sinuses and plasma CMV DNA levels is unclear and further in-depth research is required to identify the significant and relevance and appropriate therapeutic modalities.

#### *Ethical approval*

Not applicable.

#### *Consent*

Authors were unable to obtain a consent from the patient or his next of kin due to loss of follow up.

#### **CReditT authorship contribution statement**

**Rita Wilson Dib:** Conceptualization, Writing – original draft. **Hanine El Haddad:** Conceptualization, Writing – original draft. **Ben Barnett:** Writing – review & editing. **Roberto Arduino:** Writing – review & editing.

#### **References**

- [1] Marks SC, Upadhyay S, Crane L. Cytomegalovirus sinusitis. A new manifestation of AIDS. Arch Otolaryngol Head Neck Surg 1996;122(7):789–91.
- [2] Williams JD, Kieserman SP, Tavin E. Cytomegalovirus sinusitis in a patient with acquired immunodeficiency syndrome. Otolaryngol Head Neck Surg 1995;112(6):750–3.
- [3] Rayes A, Sahni K, Hanna C, Suryadevara M, Goyal P, Cherrick I. Cytomegalovirus sinusitis in a child with chronic myelogenous leukemia following bone marrow transplantation. Pedia Blood Cancer 2011;56(7):1140–2.
- [4] Morre TD, Clement PA, Pipeleers-Marichal M. Cytomegalovirus as precipitating factor of acute bacterial sinusitis in an immunocompetent patient. A case report. Acta Otorhinolaryngol Belg 1996;50(1):37–40.
- [5] Erice A, Tierney C, Hirsch M, Caliendo AM, Weinberg A, Kendall MA, et al. Cytomegalovirus (CMV) and human immunodeficiency virus (HIV) burden, CMV end-organ disease, and survival in subjects with advanced HIV infection (AIDS Clinical Trials Group Protocol 360). Clin Infect Dis 2003;37(4):567–78.
- [6] Wohl DA, Kendall MA, Andersen J, Crumpacker C, Spector SA, Feinberg J, et al. Low rate of CMV end-organ disease in HIV-infected patients despite low CD4+ cell counts and CMV viremia: results of ACTG protocol A5030. HIV Clin Trials 2009;10(3):143–52.
- [7] Sanjar FA, Queiroz BE, Mizziara ID. Otolaryngologic manifestations in HIV disease—clinical aspects and treatment. Braz J Otorhinolaryngol 2011;77(3):391–400.
- [8] Tarp B, Fiirgaard B, Moller J, Hilberg O, Christensen T, Moller J, et al. The occurrence of sinusitis in HIV-infected patients with fever. Rhinology 2001;39(3):136–41.
- [9] Small CB, McGowan JP, Klein RS, Schnipper SM, Chang CJ, Rosenstreich DL. Serum IgE levels in patients with human immunodeficiency virus infection. Ann Allergy Asthma Immunol 1998;81(1):75–80.
- [10] Shah AR, Hairston JA, Tami TA. Sinusitis in HIV: microbiology and therapy. Curr Infect Dis Rep 2005;7(3):165–9.
- [11] Kotler DP, Scholes JV, Jacob AL, Edelheit W. Disseminated CMV. Infect JAMA 1985;253(21):3093–4.
- [12] Yoskovitch A, Cantrell H. Cytomegalovirus infection presenting as chronic sinusitis and nasal polyposis: a case report. Ear Nose Throat J 1998;77(1):35–8.
- [13] Jutte A, Fatkenheuer G, Hell K, Salzberger B. CMV sinusitis as the initial manifestation of AIDS. HIV Med 2000;1(2):123–4.
- [14] Gujadhur A, Thomson N, Aung AK, McLean C, Menahem S. CMV sinusitis in a HIV-negative renal transplant recipient. Transplantation 2014;97(9):e55–7.
- [15] Rzewnicki I, Olszewska E, Rogowska-Szadkowska D. HIV infections in otolaryngology. Med Sci Monit 2012.