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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A B S T R A C T

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 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 ×10³/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/mm³ 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 left hemipalate with mild trismus and decreased cutaneous sensation over the V2 branch.

A detailed ophthalmologic evaluation that included dilated fundus
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 betablates, and antrostomy to the maxillary sinus yielding a large necrotic transional debridement, orbital decompression, excision of the inferior turbinates, and nasal polyposis diagnosed through pathology specimens and treated with IV ganciclovir after undergoing bilateral endoscopic maxillary

discussion and conclusion

End organ CMV disease is determined to occurs in around 6% of PWH with a CD4 + T cell counts < 50 cells/mm³ [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/mm³. As the CD4 + T cell count drops below 50 cells/mm³, 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 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
### 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; Facial pain and swelling | X-ray 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               |                 | Numerous CMV inclusion bodies; rare colonies of *Pseudomonas aeruginosa* | Not mentioned | Surgical debridement with Ganciclovir | Symptoms improved | [2] |
| HIV/AIDS (CD4 < 20)        | 8 weeks               | Periorbital 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 sphenoethmoidectomy with frontal sinusotomy | Symptoms improved | [1] |
| HIV/AIDS (CD4 50)          | Several months of Postnasal drip | Fever and lower extremity weakness nasal congestion and fever, nonproductive cough, and pleuritic chest pain | Bilateral opacification of all sinuses; bilateral maxillary and ethmoid opacification | Mucopurulent material that yielded only CMV; Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Transnasal antral puncture; Intravenous ampicillin/sulbactam Caldwell-Luc and nasoantral window procedures | Symptoms improved | [1] |
| HIV/AIDS (CD4 17)          | 2 weeks               | Fever and lower extremity weakness nasal congestion and fever, nonproductive cough, and pleuritic chest pain | Bilateral opacification of all sinuses; bilateral maxillary and ethmoid opacification | Culture samples yielded *Streptococcus pneumoniae*, coagulase-negative *Staphylococcus*, and CMV. Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Endoscopic sphenoethmoidectomy | 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 *Streptococcus pneumoniae*, coagulase-negative *Staphylococcus*, and CMV. Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Endoscopic sphenoethmoidectomy | Symptoms improved | [3] |
| 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 | Culture samples yielded *Streptococcus pneumoniae*, coagulase-negative *Staphylococcus*, and CMV. Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Endoscopic sphenoethmoidectomy | Resolved with no relapse | [13] |
| HIV/AIDS                   | 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 | Culture samples yielded *Streptococcus pneumoniae*, coagulase-negative *Staphylococcus*, and CMV. Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Endoscopic sphenoethmoidectomy | Symptomatic improvement | [1] |
| HIV/AIDS                   | 1 week                | Chronic sinusitis, duration not specified | Not specified | Culture samples yielded *Streptococcus pneumoniae*, coagulase-negative *Staphylococcus*, and CMV. Intraoperative culture revealed rare *E. coli* and a heavy growth of CMV | Not mentioned | Endoscopic sphenoethmoidectomy | Symptoms improved | [1] |
| HIV/AIDS                   | 3 weeks               | Left eyelid redness and edema, odynophagia, dysphagia, generalized weakness | Near-complete opacification of the right maxillary sinus with associated maxillary wall destruction | Active chronic inflammation with numerous intracellular cytomegaly 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] |
| Renal transplant related immunosuppression lymphocyte count, 0.13 × 10⁹/L | Chronic sinusitis, duration not specified | Periorbital pain with persistent congestion | Near-complete opacification of the right maxillary sinus with associated maxillary wall destruction | Active chronic inflammation with numerous intracellular cytomegaly 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 | Acral swelling with exquisite tenderness to palpation | Near complete opacification of the maxillary sinuses, with obstruction of the ostiomeatal units. No bony erosions | The aerobic bacterial cultures revealed heavy growth of *Pseudomonas aeruginosa*; numerous cellular inclusions consistent with CMV disease | CMV antigenemia was detected at 0.8 positive cells seen per 50,000 white blood cells | Resolution of symptoms | [3] |
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antrostomy 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.

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