Sinonasal Plasmablastic Lymphoma: A Systematic Review

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Abstract

Objective Plasmablastic lymphoma (PBL) is a type of non-Hodgkin's B-cell lymphoma associated with human immunodeficiency virus and Epstein–Barr virus, commonly located in the oral cavity or gastrointestinal tract. Sinonasal involvement is rare, and there is no consensus on treatment.

Data Sources Peer-reviewed published articles served as data sources.

Review Methods A systematic review was conducted of the PubMed database for all cases of sinonasal PBL between 1978 and 2023 with the phrase "plasmablastic lymphoma." Studies not written in English and that did not separate individual cases of sinonasal PBL from aggregated data were excluded. Age, sex, immune status, treatment, and outcomes were collected.

Conclusion PBL is a rare malignancy in the sinonasal region usually treated with chemotherapy. It most commonly occurs in immunocompromised adults but has also been diagnosed in immunocompromised children and in immunocompetent adults. It is aggressive and has a poor prognosis.

Implications for Practice PBL is a recently described entity with few cases of the sinonasal anatomic variant in the literature. Sinonasal PBL was most frequently treated with chemotherapy alone, closely followed by chemoradiation. The most common chemotherapy regimen utilized in the literature is cyclophosphamide, doxorubicin, oncovin/vincristine, and prednisone, which is also the most common chemotherapy regimen in nonsinonasal PBL. A second commonly used regimen is cyclophosphamide, vincristine/oncovin, doxorubicin/adriamycin, and dexamethasone. However, no treatment has emerged as superior to others with regard to survival. Further data are needed to better understand this rare disease.

Keywords
- plasmablastic lymphoma
- sinonasal lymphoma
- non-Hodgkin's lymphoma
- diffuse large B-cell lymphoma
- sinonasal neoplasm

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Introduction

Plasmablastic lymphoma (PBL) is a rare and highly aggressive form of non-Hodgkin's B-cell lymphoma that was first described in 1997.[1] Typically, PBL is extranodal and is most commonly seen in the oropharyngeal area, followed by the gastrointestinal tract, lymph nodes, and skin.[1–3] PBL most commonly presents in males and can occur at any age, although it very rarely presents in children.[4–9] Additionally, PBL is commonly associated with human immunodeficiency virus (HIV) and Epstein–Barr virus (EBV). It presents with an aggressive clinical course, frequent relapse, and poor prognosis.[1] PBL in HIV-positive patients often presents with more advanced disease than in immunocompetent patients.[5,10,11] Respective of immune status, median overall survival is generally less than 12 months.[4,7]

PBL often presents as tumors in extranodal sites, notably in the oral cavity and/or gastrointestinal tract, with immunosuppressed posttransplant patients showing a higher incidence of nodal and skin involvement.[4] Upon PBL presentation, more than 65% of HIV-positive patients, 50% of posttransplant patients, and 25% of seemingly immunocompetent patients demonstrate Ann Arbor stages III and IV.[2] In HIV-positive patients, bone marrow involvement has been shown in up to 40% of patients.[4]

PBL is a rare disease with no widely accepted evidence-based therapies. The most commonly used PBL treatment regimen is a combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP).[10] However, guidelines established by the National Comprehensive Cancer Network (NCCN) on AIDS-related B cell lymphomas recommend more aggressive therapy such as dose-adjusted etoposide, vincristine, and doxorubicin with cyclophosphamide and prednisone (DA-EPOCH).[4,12,13] Neither CHOP nor more intensive treatment regimens like DA-EPOCH have been demonstrated to be superior over the other when comparing overall survival.[14]

There exists a paucity of PBL cases that are reported in the sinonasal region, and there is no compilation in the literature of sinonasal PBL. Here we gather all reported cases of

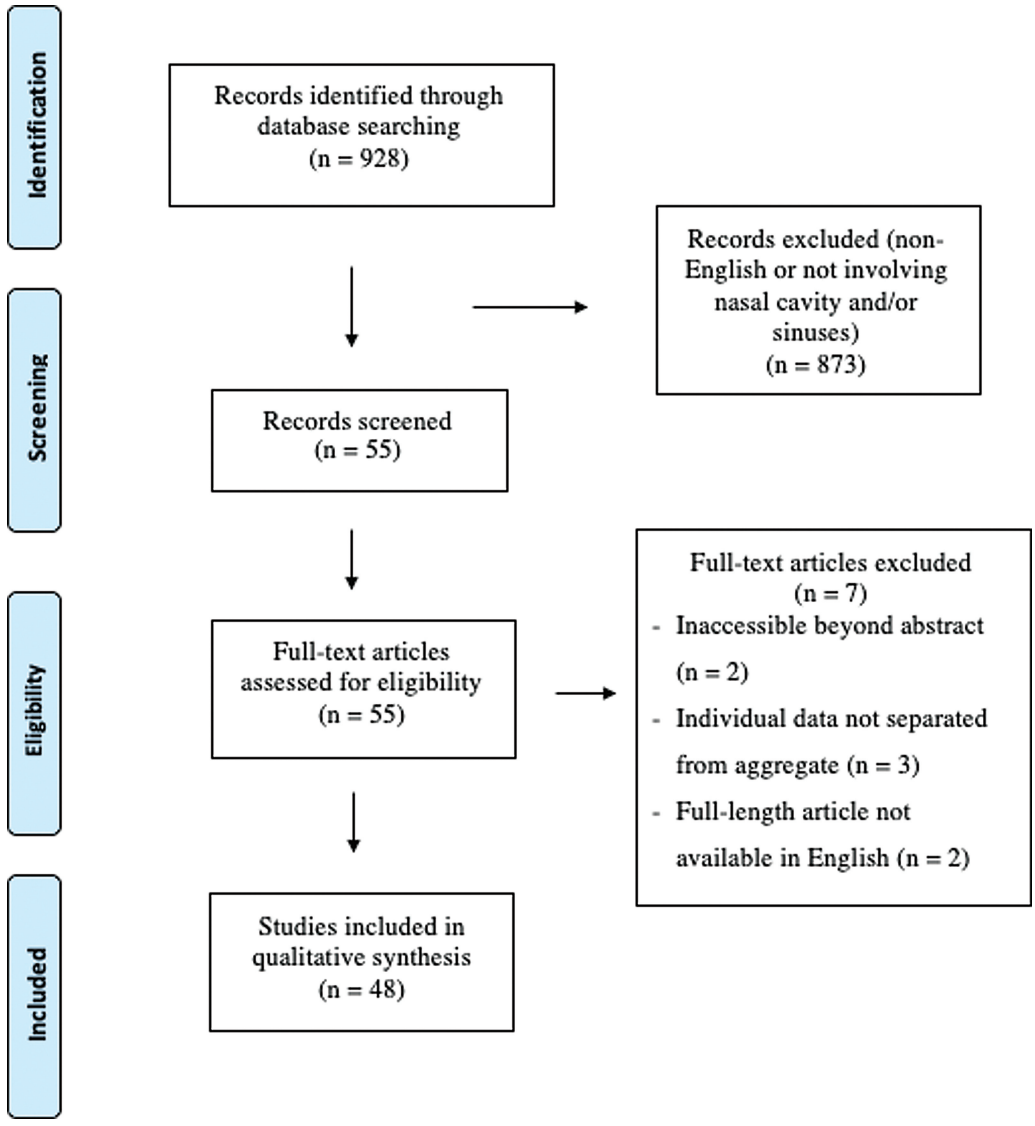

Fig. 1 Preferred reporting items for systematic reviews and meta-analyses showing article selection process.

sinonasal PBL and analyze them as a cohort to present a comprehensive review of this rare disease.

Methods

A systematic review of the literature was conducted by doing a comprehensive search of PubMed for all cases of sinonasal PBL. The search was performed with the query of "plasmablastic lymphoma," which returned 928 articles. Exclusion criteria included articles not written in English. Of the 928 studies, 55 assessed PBL in the nasal cavity and/or nasal sinuses. Two studies were excluded for being inaccessible beyond their abstracts, and three studies with 29 cases were excluded as individual data could not be separated from aggregated data. Two studies were excluded because the full-length article was not available in English. After these studies were excluded, 48 studies presenting case reports or case series of sinonasal PBL between the years of 1978 and 2023 resulted in 73 individual cases. From these 48 articles, patient information including age, sex, immune status, treatment regimen, staging, and outcomes were collected. The article selection process is depicted in ►**Fig. 1**.

Results

Final analysis of the literature search included 73 individual cases of sinonasal PBL from 48 studies (►**Table 1**).[3,7,8,15–59] Age ranged from 6 to 91 years. Five patients were missing sex information, six had no reported immune system status, 41 were without staging information, and nine without treatment status. Individual cases were mostly male 80.9% (55/68). The majority were immunocompetent (42/67, 62.7%). Twenty-six individuals were immunocompromised. In total, 35.8% (24/67) were HIV positive, one of the 67 (1.5%) had been on prolonged steroids for eosinophilic granulomatosis with polyangiitis and chronic rhinosinusitis with polyps, and one (1.5%) was an organ transplant recipient. Of those with staging, 43.8% (14/32) were diagnosed with advanced stage disease, including 40.6% (13/32) who presented with stage IV disease. Of those 13 patients with stage IV disease, two patients had distant metastasis, one to the liver and one to the central nervous system.

►**Table 2** shows the treatment regimens reported in the literature. A total of 84.4% (54/64) received chemotherapy, with 21 patients additionally receiving radiation. Ten (15.6%) underwent surgical resection. Of these 10 patients, two also received chemotherapy (3.1%), another two underwent radiation, and four (6.4%) underwent both chemotherapy and radiation. Five individuals (7.8%) received definitive radiation alone. The most common chemotherapy regimen (►**Table 3**) was CHOP, which 37.7% of chemotherapy patients (20/53) received. The second most common chemotherapy regimen was cyclophosphamide, vincristine/oncovin, doxorubicin/adriamycin, and dexamethasone (CVAD), which was given to nine patients (17.0%). EPOCH was another common regimen, and 6 (11.3%) of patients received this. One patient spontaneously regressed without treatment and remained in remission 4 years later.

Of the 13 patients diagnosed with stage IV disease, only four were still alive at time of follow-up. Follow-up ranged from 12 days to 53 months. One patient spontaneously regressed without treatment. Overall, prognosis for all patients varied from death within 12 days (2 patients) to no evidence of disease at 15 years. Overall mortality rate by time of follow-up was 23.0% (14 of 61 patients with a reported follow-up status had expired at time of follow-up). Two of the 73 patients were lost to follow-up, and 10 other individual cases did not comment on follow-up status.

Discussion

PBL is an aggressive and rare form of lymphoma that most frequently presents in the oropharynx of individuals with HIV and EBV and is characterized by frequent relapse and poor prognosis. PBL is rarely described in the sinonasal region, and the literature is lacking. To our knowledge, this is the largest analysis of the literature and includes 73 cases of sinonasal PBL with individualized data.

As PBL is a rare disease, and even rarer in the sinonasal region, there is no widely accepted evidence-based treatment of PBL. From this systematic review, the most common treatment used for sinonasal PBL was chemotherapy, with the most common regimen being CHOP. This regimen has been documented as the most widely used treatment regimen for PBL regardless of site of involvement.[2] Castillo et al found that in HIV-positive patients undergoing CHOP, overall response rate was 77%, but overall survival was still low at 14 months, with the high mortality of PBL attributed to a high relapse rate, chemotherapy-resistant disease, and concomitant infections.[60] The NCCN therefore recommends a more intensive treatment approach, specifically suggesting DA-EPOCH, for AIDS-related B cell lymphomas according to their guidelines.[2,13] However, as shown in previous studies by Castillo et al,[10,60] and Dodero et al,[61] neither CHOP nor more intensive treatment like DA-EPOCH have been shown to definitively increase overall survival when compared with the other. Various clinical trials are being conducted to assess for treatment efficacy of large B-cell lymphomas such as PBL. Clinical trial NCT05389423 is studying DA-EPOCH with pomalidomide with or without rituximab for HIV-associated lymphomas, including PBL. The use of DA-EPOCH in combination with daratumumab, a monoclonal antibody that targets CD38-expressing cells, which are present in high levels in PBL, is being studied through clinical trial NCT04139304. Other clinical trials include NCT04676360 testing belantamab mafodotin in relapsed or refractory PBL, and NCT04915248 on the use of a combination of daratumumab, dexamethasone, and bortezomib for relapsed or refractory PBL. Results for these clinical trials are pending.

Immunocompromised status, including that measured by HIV status, affects PBL prognosis. Counterintuitively, despite HIV being highly associated with the development of PBL, the possible reversibility of immune system compromise through antiretroviral therapy (ART) may allow HIV-positive patients to have more favorable outcomes. Chemotherapy has been found to generate a better response in HIV-positive

Table 1 Cases of sinonasal plasmablastic lymphoma reported in the literature

Paper	Age	Gender	Immunocompromised	Presentation	Stage	Surgery	Chemo	Radiation	Outcome
Chicuellar et al 2022	72	F	No	Unilateral left nasal obstructive symptoms, ipsilateral facial pain and numbness for 3 mo, no B symptoms, left maxillary sinus PBL	–	–	Velcade/bortezomib + etoposide, prednisone, vincristine, oncovin (V-EPOCH), cyclophosphamide, doxorubicin hydrochloride ×2 cycles with additional high-dose methotrexate ×3 cycles	Radiation to local site	Significant disease progression with treatment strategy reevaluation at time of writing
DiBlasi et al 2022.	57	M	No	Benign nasal polyposis treated with endoscopic sinus surgery (ESS), polypectomy, recurrent nasal airway obstruction (NAO) and anosmia 1.5 y later progressing to left NAO and intermittent night sweats	IV (involved 8th rib, sub-trochanteric left hip)	ESS, polypectomy b/l for diffuse polyps in bilateral sinuses, followed by 2nd ESS and polypectomy, postradiation 3rd ESS with repeat polypectomy for recurrent polyposis	2 mo postop: 6 cycles of DA-EPOCH and 2 treatments of intrathecal methotrexate (MTX)	4 mo after chemo: consolidation intensity-modulated radiation to left maxilla (hyper-metabolic on PET/CT)	Alive, followed q6-12 mo, with peripheral neuropathy of hands and feet
Lee et al 2022	61	M	No	3 wk of epistaxis, nasal airway obstruction—left nasal cavity mass	–	–	–	–	Spontaneous regression without treatment, in remission 4 y later
Rapiti et al 2022	13	F	HIV+	Nasopharynx	IV (liver)	–	CHOP	–	Lost to follow-up
Rapiti et al 2022	32	M	HIV+	Ethmoid sinus	IV (CNS)	–	CHOP	–	–
Sabry et al 2022	59	M	Extended period of steroids for eosinophilic granulomatosis with polyangiitis and chronic sinusitis with polyps	2 wk of left frontal sinus pain and swelling—left paranasal sinus mass extending into left orbit and left anterior cranial fossa	–	Endoscopic excision of left sinonasal mass, left anterior and posterior ethmoidectomies, left middle meatal antrostomy, left middle turbinectomy, left sphenoidotomy, left frontal sinusotomy/empyema and pneumocephalus requiring burr hole drainage and 3 craniotomies	Cyclophosphamide, etoposide, oncovin, prednisone (CEOP) and intrathecal methotrexate, weekly rituximab x4; postradiation 2nd cycle of R-CEOP and high dose MTX; 3rd R-CEOP and MTX/refractory and started on lenalidomide, bortezomib, dexamethasone (RVD) for 5 cycles, then lenalidomide maintenance	VMAT for 4000 cGy in 20 fractions over 4 wk	In remission at 3 y
Cai et al 2021	63	M	No	Left epistaxis—left maxillary sinus mass	–	0	Bortezomib, cyclophosphamide, epirubicin, vindesine, prednisolone (V-CDOP) x5 followed by autologous hematopoietic stem cell transplantation and lenalidomide-based maintenance therapy	Local radiotherapy to nasopharyngeal regions 30 Gy in 15 fractions over 3 wk	Progression-free survival at 22 mo
Castillo et al 2021	79	M	No	Left cheek bulging and facial numbness—left maxillary sinus mass	I	–	Bortezomib, cyclophosphamide, doxorubicin, vincristine, prednisone (V-CHOP) x4/rapid progression: daratumumab, lenalidomide, and dexamethasone x2 cycles/persistent disease: IV pembrolizumab x4 cycles—started radiation, continued pembro with radiation, stopped at 18 cycles	Post-pembro: adjuvant radiotherapy 30 Gy	Complete response 43 mo after diagnosis (22 mo after last dose of pembro)
Lasrado et al 2021	53	M	No	Right NAO with epistaxis—right maxillary sinus mass	–	Diagnostic nasal endoscopy and biopsy	Chemotherapy	–	–
Mariani et al 2021	17	M	No	Large lobulated mass extending from right nasal septum into oral cavity, 2nd mass in anterior left nasal sidewall—collision tumor (right tumor) comprising both plasmacytoma and nasopharyngeal angiofibroma, also with L2 spine lesion PBL	–	Excision of both nasal masses	–	Proton radiotherapy for L2 lesion	–

Table 1 (*Continued*)

Paper	Age	Gender	Immunocompromised	Presentation	Stage	Surgery	Chemo	Radiation	Outcome
Modi et al 2021	6	M	HIV+	Gum hypertrophy, breathlessness, abdominal distension, found to have soft tissue swelling of right obit, right nasal cavity, hard palate, and maxillary alveolus	–	–	Chemotherapy	–	Currently on follow-up
Ando et al 2020	64	M	HIV+	Nasal bleeding—bilateral nasal cavity lesion	–	–	EPOCH, salvage ifosfamide, carboplatin, etoposide (ICD), followed by bortezomib, cyclophosphamide, dexamethasone (CyBorD) x2, changed to lenalidomide and dexamethasone due to peripheral neuropathy for 2 y	–	Partial response at 2 y
Furlan et al 2020	78	F	No	Maxillary sinus	–	–	R-CHOP x6 cycles	–	Asymptomatic at 6 mo
Li et al 2020	42	M	No	Nasopharynx	II	–	Gemcitabine + oxaliplatin (GEMOX)	Involved-field radiotherapy	Alive and complete remission at 10 mo
Li et al 2020	69	M	No	Nasal cavity	I	–	CHOP	No	Alive and complete remission at 79 mo
He et al 2020	69	F	No	Left NAO due to nasal cavity mass	–	–	Chemotherapy	Radiation	Alive at 18 mo
He et al 2020	26	M	No	Dry eyes—inferior nasal concha, maxillary sinusitis	–	–	–	Radiation	Alive at 71 mo
He et al 2020	64	M	No	Mild rhinorrhagia—mass in left nasal cavity	–	Extensive resection of nasal neoplasm	–	–	Alive at 2 mo
Mai et al 2020	57	M	HIV+	Sinonasal mass	–	–	EPOCH	–	Alive at 34 mo
Mai et al 2020	47	M	HIV+	Nasal mass, maxillary mass	–	–	Hyper-CVAD	–	Alive at 60 mo
Miao et al 2020	64	M	HIV negative	Nasal cavity	II	–	CHOP	–	–
Miao et al 2020	66	M	HIV negative	Nasopharynx	I	–	CHOP	–	–
Shakri et al 2020	56	F	No	Right-sided epistaxis requiring transfusion	–	Endoscopic exam under anesthesia, biopsy, tumor debridement	6 cycles of hyperfractionated CVAD	–	Disease-free 18 mo posttreatment (including 2 PET/CT's)
Shwe et al 2020	33	M	No	Intermittent epistaxis with prolonged bleeding, left nasal cavity mass with post-chemotherapy cutaneous involvement	–	–	DA-EPOCH with intrathecal methotrexate; after cutaneous involvement: weekly bortezomib	–	–
Yap et al 2020	91	M	No	Posterior nasal space	IE	–	–	Radiation only	Complete response at 37.5 mo
Perkins et al 2019	–-	M	No	12 mo of left nasal congestion—solitary polypoid left nasal septal mass	I	En bloc removal from the nasal septum	Etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone (EPOCH) x1 cycle and rituximab, switched (due to neutropenic fevers) to CVAD, and rituximab	–	–
Rodrigeus et al 2019	37	M	HIV+	Left cheek swelling—left maxillary sinus mass	–	–	EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) x6 cycles	–	Undergoing chemo still at time of writing
Gibbs et al 2017	76	M	No	(History of T2N2bM0 left hypopharyngeal squamous cell	–	–			No recurrence 2 y out

(*Continued*)

Table 1 (*Continued*)

Paper	Age	Gender	Immunocompromised	Presentation	Stage	Surgery	Chemo	Radiation	Outcome
				carcinoma), epistaxis—R maxillary sinus mass				Definitive radiation (180-4500 cGy) to R sinus	
Rafei et al 2017	49	M	HIV+	Nasopharyngeal mass	–	–	DA-EPOCH with intrathecal MTX, hydrocortisone, and liposomal cytarabine via lumbar puncture and ommaya reservoir, chemo x6 cycles	Palliative radiation up to 1,500 cGy, interrupted by DA-EPOCH	Free of disease for 12 y
Wang et al 2017	53	M	HIV+	Epistaxis, left maxillary sinus mass	–	–	Hyper-CVAD	–	Lost to follow-up
Yan et al 2017	27	M	No	Nasal obstruction, epistaxis—nasal cavity tumor	–	Resection	–	Radiation	Alive and no evidence of disease at 70 mo
Koizumi et al 2016	51	M	HIV+	Sinus	–	–	EPOCH + dexamethasone, high-dose cytarabine, cisplatin (RT DHAP)	Radiation	Died of disease at 4.3 mo
Koizumi et al 2016	52	M	HIV+	Sinus	–	–	Best supportive care	–	Died of disease at 2.8 mo
Koizumi et al 2016	39	M	HIV+	Sinus	–	–	CHOP	–	Alive at 26.9 mo, complete response
Koizumi et al 2016	43	M	HIV+	Sinus, bone	–	–	CHOP	–	Died of disease at 13.3 mo
Pinnix 2016	–	–	–	Right maxillary sinus	–	–	R-CHOP x6 cycles	IMRT 39.6 Gy	NED
Pinnix 2016	–	–	–	Right nasal cavity, maxillary sinus	–	–	Hyper-CVAD x4 cycles	IMRT at 41.4 Gy	NED
Pinnix 2016	–	–	–	Right nasal cavity	–	–	Hyper-CVAD x4 cycles	IMRT at 39.6 Gy	NED
Pinnix 2016	–	–	–	Left ethmoid sinus	–	–	DA-EPOCH x6 cycles	Volumetric modulated arc therapy at 41.4 Gy	NED
Segal et al 2016	44	M	No	Nasopharyngeal branchial cleft cyst	–	Endoscopic resection of nasopharyngeal cyst	Conservative treatment by hematologist	–	No evidence of disease at 1.5 y
Elyamany et al 2015	59	F	No	Nasopharynx	IV	–	Cyclophosphamide, adriamycin, vincristine, prednisolone, rituximab (R-CHOP)	Radiotherapy	Died of disease at 12 mo
Loghavi et al 2015	26	F	No	Stuffy nose—nasal cavity tumor	–	–	Hyper-CVAD x3	Radiation	Alive with no e/o disease at 59.9 mo
Loghavi et al 2015	61	M	No	Epistaxis—right nasal septum	–	–	–	Radiation	Alive w/ no e/o disease at 44.8 mo
Sachsman et al 2015	66	–	–	Base of skull and paranasal sinuses	IV	–	CHOP x6 cycles + gitoxin, then intrathecal MTX	Consolidative proton treatment, 36 Gy (RBE) in 1.2 fx BID	Died of 2nd cancer at 53 mo
Ambrosio et al 2014	74	M	--	Right maxillary sinus solitary mass infiltrating oral cavity	–	Surgical excision after chemoradiation	Bortezomib, melphalan, prednisone (VMP scheme)/relapse after CXRT: bortezomib, cyclophosphamide, dexamethasone with minimal response, switched to 3rd line therapy with lenalidomide, cyclophosphamide, and	50 Gy radiotherapy	–

Table 1 (*Continued*)

Paper	Age	Gender	Immunocompromised	Presentation	Stage	Surgery	Chemo	Radiation	Outcome
							dexamethasone/after surgical resection liposomal doxorubicin and cytosine arabinoside, added bendamustine/continuous lenalidomide treatment with rituximab x3 and acyclovir		
Morisco et al 2014	40	M	HIV+	Nasal	–	–	–	–	Alive at 191 mo
Morisco et al 2014	–	F	No	Nasal	–	–	–	–	Alive at 12.8 mo
Yasuhara et al 2014	50	F	No	Left maxillary sinus tumor with intraoral manifestation	II	–	CHOP x4	–	Complete remission at 9 mo after chemo
Pather et al 2013	14	M	HIV+	Left nasal, maxillary, and orbital mass	II	–	BFM '86 B NHL protocol	–	Death at 15 mo
Saraceni et al 2013	24	M	No	Chronic sinusitis for 2 mo, left face numbness, and asymmetry- involved maxillary sinus	IIE		6 cycles of hyperfractionated CVAD (odd cycles x3), alternating with high doses of methotrexate and cytosine arabinoside (even cycles ×3), intrathecal methotrexate, and cytosine arabinoside with each of the 6 cycles	Postchemo consolidation radiation by intensity-modulated radiation therapy (IMRT) for a total dose of 45 Gy	Alive at time of writing, complete remission of 4 y
Liu et al 2012	67	M	No	Nasal cavity	III	–	CHOP	–	partial response, alive at 26 mo
Liu et al 2012	64	M	No	Nasal cavity	I	–	CHOP	RT	complete response, alive at 55 mo
Liu et al 2012	86	M	No	Nasal cavity	IV	–	50% CHOP	–	died of unrelated disease at 1 month
Liu et al 2012	60	M	No	Nasal cavity	I	–	CHOP	–	under therapy, alive at 1 month
Liu et al 2012	50	M	No	Nasal cavity	II	–	Dexamethasone, etoposide, ifosfamide, carboplatin (DeVIC)	RT	complete response, alive at 12 mo
Liu et al 2012	45	M	No	Nasal cavity + bone + LN	IV	–	Cyclophosphamide, bortezomib, dexamethasone (CVD)	–	under therapy, alive at 2 mo
Liu et al 2011	60	F	No	Nasal cavity	IV	–	Hyper-CVAD x4	received radiation	died of disease at 36.5 mo
Liu et al 2011	66	M	No	Sinus	IE	–	CHOPx6	received radiation	alive and no evidence of disease at 23.9 mo
Liu et al 2011	59	M	No	Nasal cavity	IE	–	CHOPx6	received radiation	alive and no evidence of disease at 15.5 mo
Suzuki et al 2010	84	M	No	2 mo of left face pain, left maxillary tumor infiltrating left nasal cavity and upper oral cavity	IIA	–	–	involved-field radiation therapy of 30Gy/20 fractions and limited local field radiation of 20Gy/10 fractions (total 50 Gy)	new right chest wall tumor with lymphoma infiltration 3 mo after radiation
Kim et al 2009	72	F	No	Paranasal sinus	IA	–	Chemotherapy	–	alive at 6 mo
Morley et al 2009	49	M	HIV+	6-mo toothache, intermittent nasal discharge and facial swelling, left	–	–	CHOP protocol, repeat intrathecal chemotherapy (methotrexate, RSE, hydrocortisone);	–	died within 3 mo of presentation

(*Continued*)

Table 1 (*Continued*)

Paper	Age	Gender	Immunocompromised	Presentation	Stage	Surgery	Chemo	Radiation	Outcome
				maxillary sinus mass with 2nd lesion in ipsilateral ethmoid air cells			dexamethasone, cytarabine, cisplatin chemotherapy (DHAP), systemic melphalan and methylprednisolone; weekly prednisolone, mitoxantrone, cyclophosphamide, etoposide, bleomycin, vincristine chemo (PMitCEBO) for 3 wk		
Ustun et al 2009	38	M	HIV+	Paranasal sinus mass	IVA	steroid	–	–	partial response, died on hospital day 12
Chetty et al 2003	23	F	HIV+	Anosmia and right NAO—maxillary sinus tumor	–	–	CHOP x2	–	alive at 7 mo
Reid-Nicholson et al 2008	40	M	HIV+	Sphenoid sinus	–	–	–	–	Died 12 d after admission from hematemesis complications
Dong et al 2005	44	M	HIV+	Nasopharynx (adenoid)	–	–	50% CHOP intrathecal methotrexate	–	died of disease at 1 month
Colomo et al 2004	65	M	HIV+	Maxillary sinus	IV	–	–	–	alive at 19 mo
Colomo et al 2004	35	M	HIV+	Maxillary sinus	IV	–	–	–	Alive with disease at 16 mo
Colomo et al 2004	30	M	Posttransplant	Maxillary sinus	IV	–	–	–	dead at 19 mo
Colomo et al 2004	35	M	HIV+	Maxillary sinus	–	–	–	–	–
Colomo et al 2004	86	F	No	Maxillary sinus	IV	–	–	–	dead at 4 mo
Schichman et al 2004	41	M	HIV+	Nasal fullness, left nasal polyp, and right frontal bone mass displacing frontal lobe treated with radiation, followed by testicular mass and left tibia mass treated with removal of testicular mass and radiation to leg followed by VAD x2 complicated by plasmacytoma in scapula treated with radiation complicated by left arm lesion	–	removal of testicular mass	After radiation to tibia: vincristine, dexamethasone, Adriamycin (VAD) x2/for left arm lesion, was placed on CHOP (vincristine, adriamycin, prednisone, cytoxan) and due to resistance started on EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) and intrathecal MTX x6	1st treatment radiation: 30.4 Gy in 19 fractions to nose and frontal bone/tibia mass treated with 30 Gy in 15 fractions over 21 d/scapula treated with 30 Gy in 15 fractions over 28 d	–
Nguyen et al 2003	42	M	No	Rapid onset otalgia and hearing loss, nasal obstruction for 3 mo	IEA	–	3-mo courses of hyper-CVAD, intrathecal methotrexate with each chemo cycle	Postchemo consolidative locoregional radiation: 40 Gy to right nasal cavity, ethmoid, and maxillary sinuses and 36 Gy to bilateral superior cervical areas	No recurrence at 6 mo

Abbreviations: BFM, Berlin–Frankfurt–Munster protocol; CDOP, cyclophosphamide, epirubicin, vindesine, prednisolone; CEOP, cyclophosphamide, etoposide, oncovin/vincristine, and prednisone; CHOP, cyclophosphamide, doxorubicin, oncovin/vincristine, and prednisone; CVAD, cyclophosphamide, vincristine/oncovin, doxorubicin/adriamycin, and dexamethasone; CVD, cyclophosphamide, bortezomib, dexamethasone; DA-EPOCH, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; DeVIC, dexamethasone, etoposide, ifosfamide, carboplatin; EPOCH, etoposide, prednisone, oncovin/vincristine, cyclophosphamide, and doxorubicin; GEMOX, gemcitabine and oxaliplatin; IMRT, intensity-modulated radiation therapy; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

Note: "–" denotes no data reported.

Table 2 Types of treatment for sinonasal plasmablastic lymphoma

Treatment regimen	Number of patients (%)
Surgical resection alone	2 (3.1%)
Surgery + chemotherapy	2 (3.1%)
Surgery + radiation	2 (3.1%)
Surgery + chemoradiation	4 (6.3%)
Chemotherapy alone	26 (40.6%)
Chemoradiation	21 (32.8%)
Radiation alone	5 (7.8%)
Supportive care	2 (3.1%)
Total	64 (100%)

Table 3 Specific chemotherapy regimens used to treat sinonasal plasmablastic lymphoma

Chemotherapy regimen	Number of patients (%)
CHOP	20 (37.7%)
CVAD	9 (17.0%)
EPOCH	6 (11.3%)
BFM	1 (1.9%)
DeVIC	1 (1.9%)
CVD	1 (1.9%)
GEMOX	1 (1.9%)
Unspecified regimen	4 (7.5%)
Multiple combinations of regimens	10 (18.9%)
Total	53 (100%)

Abbreviations: BFM, Berlin–Frankfurt–Munster protocol; CDOP, cyclophosphamide, epirubicin, vindesine, prednisolone; CEOP, cyclophosphamide, etoposide, oncovin/vincristine, and prednisone; CHOP, cyclophosphamide, doxorubicin, oncovin/vincristine, and prednisone; CVAD, cyclophosphamide, vincristine/oncovin, doxorubicin/adriamycin, and dexamethasone; CVD, cyclophosphamide, bortezomib, dexamethasone; DA-EPOCH, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; DeVIC, dexamethasone, etoposide, ifosfamide, carboplatin; EPOCH, etoposide, prednisone, oncovin/vincristine, cyclophosphamide, and doxorubicin; GEMOX, gemcitabine and oxaliplatin.

patients compared with HIV-negative patients, possibly attributed to the effect of ART on strengthening the immune system.[11] Indeed, having a higher CD4 count is a favorable prognostic factor in PBL,[40] whereas immunosuppression is a negative prognostic factor in HIV-negative individuals.[50] Better survival in EBV-positive and HIV-positive patients has been noted compared with EBV-negative and HIV-negative patients, possibly attributed to a similar mechanism in which initiation of ART allows better virological control.[7] However, this is controversial as Florindez et al[62] concluded that HIV status had no effect on survival in PBL. Morscio et al[7] found no significant difference in the incidence of PBL before and after the initiation of ART, implying that HIV, as a cause of immunosuppression, is still implicated in the development of PBL.

Regardless of HIV status, prognosis of PBL remains poor with a median overall survival < 12 months, and those with HIV initially present with more advanced disease.[2,4] In our study, almost half of sinonasal PBL patients presented with advanced stage disease, which is slightly lower than but still on par with that seen in the literature,[10,11,62] and remains consistent with aggressive disease. In patients with limited-stage (stage I or II) PBL in the head and neck region, the use of involved site radiotherapy may impart a survival benefit.[21,41] However, despite the achievement of complete remission with PBL treatment, most patients experience relapse of disease with a median progression-free survival period of 6 months.[12]

A limitation of this study stems from its retrospective nature, the limited number of sinonasal region cases of PBL in the literature, and the variation in reporting of these individual cases. These factors collectively diminish the power of the study. Additionally, though 55 studies were identified that described sinonasal PBL, some abstracts could not be accessed and others did not differentiate individualized data from aggregate data, limiting the validity and generalizability of our findings. Furthermore, there are no published randomized controlled trials of treatment regimens for PBL, much less that specifically targeting the sinonasal region.

Implications for Practice

PBL is a rare malignancy in the sinonasal region associated with immunosuppression, marked by diverse treatment approaches and high mortality. In fact, the most common stage at presentation was stage IV, demonstrating its aggressive course and late diagnosis. This review reveals the most common treatments used, but no regimen has been found to best treat sinonasal PBL. Most cases are treated with chemotherapy alone, followed by chemoradiation. The NCCN recommends DA-EPOCH for AIDS-related B cell lymphomas. However, the most common chemotherapy regimen utilized in the literature for sinonasal PBL is consistent with the most common chemotherapy used in PBL: CHOP. The second most commonly prescribed chemotherapy regimen is CVAD. Additional research is needed to determine optimal treatment for sinonasal PBL, but the rarity of this condition poses a challenging undertaking for treatment and control of disease.

Authors' Contributions
S.C. contributed to study design, data acquisition and interpretation, and manuscript writing; H.C. was involved in data acquisition and interpretation as well as manuscript writing; S.S. participated in data acquisition and interpretation along with manuscript writing; and M.W. contributed to study design, data acquisition and interpretation, and manuscript writing.

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None declared.

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