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# Diagnostic Problem of Facial Malignancy in The Elderly: A rare case

## Problema diagnóstico de malignidad facial en el anciano: Un caso raro

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**SUMMARY**

**Introduction:** *Lymphoma can occur in adults and the elderly, this will affect the condition of both diagnosis and therapy. Plasmablastic lymphoma (PBL) is a subtype of diffuse large B-cell lymphoma (DLBCL), the case is rarely found and often overlaps the anatomical pathology picture similar to plasmacytoma. It is aggressive and often relapses.*
**Case Presentation:** *A 50-year-old man, complained of a lump on the right cheek extending to the left cheek and left eye. Irregular shape, hard, painful, accompanied by lumps of the right and left submandibular glands, difficulty breathing and swallowing, so a tracheostomy and gastrostomy were performed. The first anatomical pathology results in extraosseous Plasmacytoma and the second Plasmablastic lymphoma with IHC CD138 (+) CHOP chemotherapy and radiation. After chemotherapy, the patient experienced improvement.*
**Conclusion:** *Plasmablastic lymphoma is difficult to diagnose because the anatomical pathology picture overlaps with plasmacytoma in the gold standard IHC CD138 (+), which is aggressive and relapses.*

**Keywords:** *Plasmablastic Lymphoma, plasmacytoma, CD 138.*

**RESUMEN**

**Introducción:** *El linfoma puede ocurrir en adultos y ancianos, esto afectará la condición tanto del diagnóstico como de la terapia. El linfoma plasmablástico (PBL) es un subtipo de linfoma difuso de células B grandes (DLBCL), el caso rara vez se encuentra y muchas veces se superpone al cuadro de la patología anatómica similar al plasmocitoma. Es agresivo y con frecuencia recae.*
**Presentación del caso:** *Un hombre de 50 años se quejó de un bulto en la mejilla derecha que se extendía a la mejilla izquierda y al ojo izquierdo. Forma irregular, dura, dolorosa, acompañada de nódulos en glándulas*

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*submandibulares derecha e izquierda, dificultad para respirar y deglutir, por lo que se realizó traqueotomía y gastrostomía. La primera patología anatómica resulta en plasmacitoma extraóseo y el segundo linfoma plasmablástico con quimioterapia y radiación IHC CD138 (+) CHOP. Después de la quimioterapia, el paciente experimentó una mejoría.*

**Conclusión:** *El linfoma plasmablástico es difícil de diagnosticar debido a que el cuadro anatomopatológico se superpone con el plasmacitoma en el patrón oro IHC CD138 (+), el cual es agresivo y recidivante.*

**Palabras clave:** *Linfoma plasmablástico, plasmacitoma, CD 138.*

## INTRODUCTION

Lymphoma disease can occur in adults and the elderly, this will affect the condition of both diagnosis and therapy, because these cases are rare and there is often in the determination of diagnoses, the case is discussed. Plasmablastic lymphoma is a malignancy with the highest prediction in HIV-positive and immunocompetent patients such as transplantation. Several cases of Plasmablastic lymphoma are non-HIV (1). Plasmablastic lymphoma is a progressive disease, destructive and refractory of chemotherapy. This malignancy has a poor prognosis where the survival rate in HIV patients is not much different, which is about 8-15 months. The mean survival in HIV-positive patients was 10 months, 11 months in immunocompetent and HIV-negative patients, and 7 months in post-organ transplant patients (2).

## CASE PRESENTATION

The patient named Mr. P is 60 years old. The patient's address is in a Nganjuk district and works as a carpenter. The chief complaint was a lump on the right cheek. For nine months after being admitted, the patient complained of a lump on the right cheek. Initially the size of chicken eggs with hard palpation. accompanied by pain in the upper right molars. The patient went to the dentist, and it was said that the swelling was due to a perforated molar tooth. However, it did not improve after almost three months of visiting the dentist until the patient was advised to see a surgeon.

One month later, the patient went to Rumah Sakit Islam Aisyiyah Nganjuk, RSI Nganjuk (Aisyiyah Islamic Hospital Nganjuk), the doctor's surgery did a biopsy, and the results of anatomic pathology were 1 month later. After a biopsy, the patient underwent a CT scan of the tumor area. Three weeks later after that, the patient came to the division of Oncology medicine with referral and examination results from RSI Nganjuk. At that time the patient's tumor had not covered the eyes and nostrils. A review of anatomic pathology at Dr. Soetomo's hospital was carried out from the result of an anatomical pathology biopsy at Nganjuk hospital. The results showed a primary extraosseous plasmacytoma, so the patient is planned for a Bone Marrow Aspiration examination. The patient complained that the tumor was getting bigger in the eyes, nose, and mouth area. The patient complained of difficulty breathing for 1 month. The patients could only drink and eat the milk with a straw. One month ago the patient complained of weakness and increasing difficulty breathing, the patient's family was taken to the Emergency Unit Dr. Soetomo Hospital. The patient was treated by digestive surgery and the head and neck underwent a tracheostomy and gastrostomy 6 days later. After that, the patient was transferred to the internal medicine board.

During treatment at Dr. Soetomo Hospital, a control patient in Medical Oncology Room. The patient never complained of a stuffy nose, bed smell, headache, or nose bleeds. The family history of the disease is the patient's sister suffering from uterine cancer. The patient's job is an owner of a home industry, namely wooden furniture.

The patient was admitted to the Internal medicine room. The patient's general condition when received was weak with Glasgow Coma Scale (GCS) 456; BP 100/60; pulse 84x/ min; RR 20x/ min; temperature: 37 $^{o}$C. BW before the illness is 97 kg, BW now is 55 kg, height 160 cm.

On the head, there was a bumpy tumor on the right side of the face that extended to cover both eyes with an ulcer with a depth of 0.5 cm on the right cheek. There is an enlarged right submandibular lymph node measuring 6 x 6 cm, palpable hard, not mobile, and painless. There is an enlarged left submandibular lymph node

measuring 1 x 1 cm palpable hard, not mobile, and painless. A tracheostomy is attached (Figure 1). The thorax appears symmetrical and there is no retraction. Normal heart sounds, no murmurs, and gallops. Breath sounds vesicular, with no crackles and wheezing. Abdomen flat, flexible, normal bowel sounds. Attached gastrostomy, liver, and spleen were palpable. In the extremities, warm dry red acral was found.

Figure 1.

Head multi-slice CT (MDCT) result with contrast from RSI– Nganjuk (photo results not found, only photo readings are there) resulted in a solid mass of the right maxillary sinus that extends predominantly anteriorly, and destroys the right sphenoid bone. Right maxillary bone and the medial wall of the left maxillary sinus. Enlargement of the right jugular lymph node. An anatomical pathological examination was carried out from the biopsy results, it was concluded that it was a differential diagnosis of Rhabdomyosarcoma, Malignant Lymphoma, and Small Cell Carcinoma and was recommended for Immunohistochemical Examination.

Immunohistochemical was carried out at Dr. Soetomo with desmin results; negative tumor cells, and positive CD 138 on tumor cell membranes. Impression: morphologically and the location of the tumor favors a primary interosseous plasmacytoma. Fine-needle aspiration biopsy (FNAB) nodular submandibular region dextral. In Dr. Soetomo's hospital, with infiltration of plasmacytoid cells that morphologically resemble tumor cells in the cheek. Because the result of the immunohistochemistry (IHC) was Plasmacytoma (Figure 2), further investigations were carried out on the possibility of Multiple Myeloma, namely with a complete blood count, kidney function, protein electrophoresis, calcium, bone survey, and bone marrow aspiration.

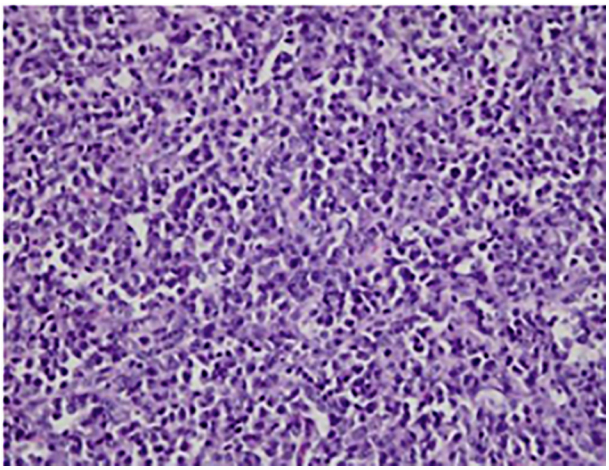

Figure 2. Fine-needle aspiration biopsy (FNAB) objective 40x.

Laboratory Examination Results showed Hb 10.8 g/dL; WBC 11.5; PLT 726 000; Albumin 3.4; BUN/creatinine serum 18/0.8; Calcium 8.2; Phosphate 3.0; Protein Bence Jones: negative; LED 71; LDH 219; HBsAg Non-Reactive; Anti HCV Non - Reactive; HIV rapid non-Reactive. Examination of serum protein electrophoresis revealed a decrease in the albumin fraction accompanied by a slight increase in the beta globulin fraction. On bone survey examination only found abnormalities in the ap/lat skull; complete fracture of the right superior mandibular ramus left mandibular body irregularity of the right mandibular bone, and multiple lytic lesions on the right and left mandibular bones. Soft tissue swelling of the right buccal region. As in other bones, there is no destruction, osteolytic or osteoblastic.

Bone Marrow Aspiration concluded a normocellular, M/E ratio of 5:1. Erythropoietic system normal impression, Myelopoiesis system normal impression with Myeloblast 4.5 %; Promyelocyte 4.3 %; Metamyelocyte 6 %; Rods 36 %; Segments 12 %; Plasma cells 1.3 %; Lymphocytes 17.8 %. Thrombopoietic system: normal impression. Bone Marrow Aspiration corresponds to the picture cells 1.3 %.

Two months after the installation of tracheostomy and gastrostomy a contrast-enhanced CT scan of the head was performed, the result showed an enhancing solid mass in the right maxillary sinus which extended medially, destroyed the medial wall of the maxillary sinus, filled the right nasal cavity. Destroyed the lamina papyracea. Filled the sinus ethmoid, destroys the lateral wall of the right maxillary sinus. Extends to the masticator space, infiltrates m. right temporal maxillaris, m. right buccinators and m. right masseter, infiltrating the right and left subcutaneous regions of the frontal region, right left maxillary and left naso-orbital right left maxillary, and left right mandibular, the mass destroys the superior wall of the right medullary sinus extending to the right maxillary sinus extending to the retro-orbital attached no m. right lateral rectus with firm boundaries pushed bulbus oculi as far as 1.5 cm, attached bulbus oculi and optic nerve with firm borders, mass destroying orbital roof extended to the right frontal sinus. Mass destroying right maxillary attached to soft palate to the right hard palate, nodules size was 0.5 cm in the left mandible, 6x6x6 cm in the right submandibular to the right and jugular, 0.7 cm in the left upper jugular, 0.7 cm in the left upper jugular 0.3 cm in the left upper jugular 0.5 cm in the left mind jugular, 0.9 cm in the right supraclavicular (AJCC staging 8th edition T4N3M0).

Thorax X-Ray: with the expression of an infiltrate in the right pericardial can be 2 differential diagnoses metastatic proses (pneumonic type), lung inflammation, no bone metastatic were seen, can't do not appear abnormal.

Follow up immunohistochemical examination was carried out on the results of the discussion of the Hematology Division with the anatomical pathology department because of the previous histopathology. The result did not support the patient's clinical manifestations. Further IHC examination showed CD 79A positive, CD 20 negative on tumor cell membranes, CD 45 positive on tumor cell membranes, and a Ki 67 proliferation index of 65 %. There was restriction for the kappa light chain, the conclusion supports a Plasmablastic Lymphoma.

The patient was diagnosed with plasmablastic lymphoma of the right maxillary region stage II BE. The patient was given the first CHOP (Cyclophosphamide, Epirubicin, Vincristine, Prednisone) chemotherapy with a dose of cyclophosphamide 1 000 mg, epirubicin 60 mg, vincristine 2 mg, and methylprednisolone 3x16 mg for 5 days. Before chemotherapy, the patient was in good general condition. During chemotherapy, the patient did not experience any side effects of chemotherapy drugs such as nausea, vomiting, urticaria, fever, and anaphylaxis. The chemotherapy went well for about 2 hours. The patient was then given an NS infusion of 1 500 mL. 24 hours, ranitidine injection 50 mg/12 h, and methylprednisolone tablet 3x16 mg. The patient's condition after chemotherapy was good.

On day 3$^{rd}$ after chemotherapy, the tumor on the patient's face seemed to have shrunk with the size of the tumor, at first was barely able to open the left eye, but now it can be opened. The patient did not complain of nausea and vomiting. The general condition of the patient is good with GCS 456; Blood pressure 120/70 mm/Hg; Pulse 80x/m; RR 20 x/m; Temperature 36.8 ºC. Laboratory results: Hb 11.2; WBC 6 400; Plt 209 000; SGOT 22; SGPT 22; BUN 15; SK 0.8; Uric acid 4.8; Sodium 138; Potassium 4.0; Chloride 100; Calcium 8.6.

On 5 the day after chemotherapy, the tumor on the patient's face seemed to be getting smaller with the remaining tumor size only on the forehead with a diameter of 5 cm and on the right cheek with a diameter of 10 cm. The patient a left eye can be opened and can see with vision OS 6/60. OD 2/6-. The patients did not complain of nausea and vomiting. the general condition of the patient is good with GCS 456, blood pressure 120/70, pulse 80x/m, RR20x/m, temperature 36.8 ºC. Laboratory results of the patient the days after chemotherapy with Hb 11, 0; WBC 6330; Plt 199 000; SGOT 24; SGPT 22; BUN

15; Creatinine serum 0.8; Uric acid 4.8; Sodium 138; Potassium 4.8; Chloride 100; Calcium 8.4.

On the 7th day after chemotherapy, the tumor on the patient's face got smaller with the remaining tumor on the right cheek with a diameter of 10 cm. The patients can see, eat through the mouth, and speak, and enlargement of the right submandibular lymph nodes began to shrink to a size of 3x3 cm. Enlargement of the left submandibular gland was not palpable. The patient didn't complain of nausea and vomiting. The general condition of the patient is good with GCS 456, blood pressure 120/70, pulse 80x/m, RR20x/m, temperature 36.8 ºC, Laboratory results of the patient the days after chemotherapy with blood Hb 11.8; WBC 6 700; Plt 214 000; SGOT 20; SGPT 19; BUN 15; Creatinine serum 0.8; Uric acid 4.3; Sodium 138; Potassium 4.0; Chloride 100; Calcium 8.5. The patient was planned outpatient with the second schedule of chemotherapy two weeks later.

After the second and third chemotherapy, the lump got smaller with a final diameter of 6 cm. The patients can see, speak, and eat smoothly. There were no side effects from chemotherapy drugs. However, after the fourth and fifth chemotherapy, new lumps began to appear at the side of the old tumor. The longer lump got bigger with a diameter of 4 cm and almost closed the patient's right eye. The patient was planned to receive adjuvant radiotherapy. After completing 8 cycles of chemotherapy plus adjuvant radiotherapy, the new tumor disappeared with the old tumor shrinking to 4 cm in size and there were no side effects from chemotherapy with radiotherapy. Namely dry mouth that the patient could tolerate (Figure 3).

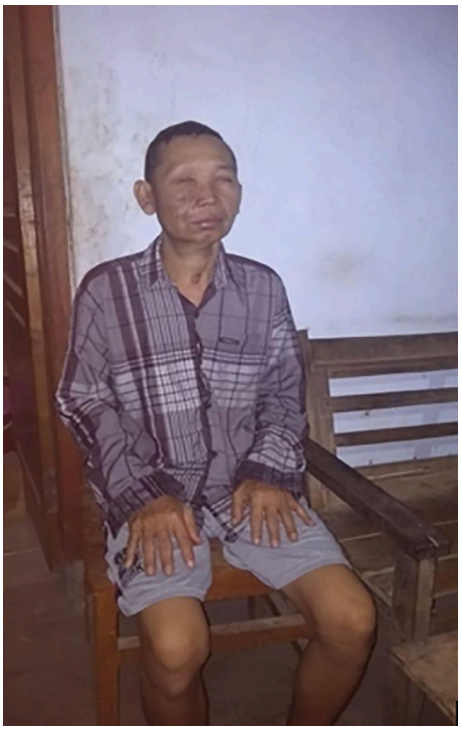

Figure 3. After 8 cycles of chemotherapy and adjuvant radiotherapy.

## DISCUSSION

The diagnosis of the head and neck malignancy can be established through anamnesis, physical examination, and supporting examination, and supporting examination with the gold standard in the form of anatomical pathology biopsy results. The general history of patients with suspected malignancy is an appearance of a lump that is getting bigger and bigger, facial asymmetry, headache, oral manifestations, sometimes fever, and weight loss. Head and neck malignancies are more common in men than women 4:1 ratio, Risk factors for head and neck malignancies include smoking, alcohol consumption, exposure to industrial gases, wood dust, leather industry tanning fluids, and the Epstein Barr virus. Exposure to industrial gases and minerals as well as wood dust is a particular risk factor for the incidence of sinonasal malignancies (3). The commonly affected lymph nodes were cervical (78 %), Axillary (46.6 %), and mediastinal glands (21.8 %) (3).

Patients generally come with complaints of lymph in the oral cavity or sinonasal area then the patient comes to the dentist which does not improve with treatment. This tumor is clinically purplish in color with clear borders. Lymph node involvement is common with the most predilection being in the neck area. Investigations that can help are CT scans and often there is the destruction of the facial bones and the tumor extends to the ethmoid sinus, orbit, and masticator muscle (4).

From the patient's history, it was found that the lump was getting bigger and bigger for about 9 months before the was admitted to the hospital. The lump started from the right cheek the size of a chicken egg until when it came it experienced facial asymmetry and there were lumps on the oral cavity in the buccal and palate areas. The patient's work history as an owner of wooden furniture is often exposed to wood dust and wood tanning paint. There was a weight loss of 12 kg over 9 months. There were no complaints of fever, stuffy nose, frequent nosebleeds, and ringing in the ears before. Considering the results of the anamnesis, it can be assumed that the type of tumor is of sinonasal origin.

The patients found facial asymmetry. enlarged submandibular neck lymph nodes, airway obstruction due to shifting of the nasal bones, lumps in the palate and buccal area, and swallowing disorders. In the patient, rhinoscopy and indirect laryngoscopy were not possible because the tumor had invaded almost the entire face.

In the patient, the results of a CT scan from RSI Nganjuk were a solid mass of the right maxillary sinus that extended predominantly anteriorly, destroying the right sphenoid bone, the right maxillary bone, and the medial wall of the left maxillary sinus. Right jugular lymph node enlargement. The most common types of head and neck malignancies are squamous cell carcinoma, lymphoma, and adenocarcinoma, squamous cell carcinoma most often arises in the oral cavity and oropharynx, whereas lymphoma often arises from the sinonasal tract and tonsils. Neck lymph node involvement is common in lymphoma. Definitive diagnosis of the tumor type was carried out by anatomical pathology biopsy followed by immunohistochemistry (5).

Anatomical pathology examination was carried out from the biopsy results, it was concluded that it was a malignant round cell tumor with a differential diagnosis of Rhabdomyosarcoma, malignant lymphoma, and small cell carcinoma and it was recommended for immunohistochemistry examination from Nganjuk Hospital. The results of the immunohistochemical examination at the general hospital of Dr. Soetomo with desmin results negative on tumor cells, and positive CD 138 on tumor cell membranes (Figures 4 and 5).

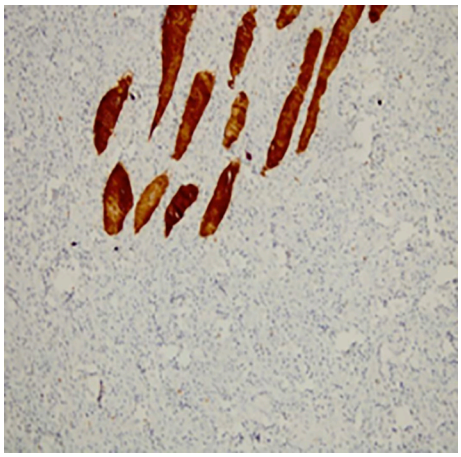

Figure 4. Desmin Staining Preparation.

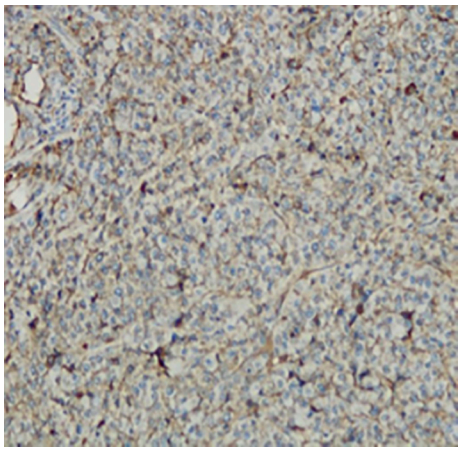

Figure 5. Preparation Antibody Desmin 138.

Impression morphologically and the location of the tumor favors a primary extraosseous plasmacytoma. One type of lymphoma that is difficult to diagnose is Plasmablastic lymphoma. The diagnosis of Plasmablastic lymphoma can overlap with that of Plasmacytoma both can occur in the upper respiratory tract and oral cavity. From protein electrophoresis, 14 %-25 % of cases of plasmacytoma found monoclonal components while the rest were normal. In Plasmablastic lymphoma, no abnormalities were found on protein electrophoresis. Kidney function, calcium, and blood laboratory result are within normal limits. Other important radiological

examinations included anatomical pathology, chest X-ray, and bone survey (6).

Both Plasmablastic lymphoma and Plasmacytoma show a strong positive CD138 on immunohistochemical examination with light chain restriction, which could be either Kappa or Lamda chains. In Plasmacytoma, if bone marrow aspiration is performed, the plasma cells are less than 5 % without forming a clone. There is almost no bone marrow involvement in Plasmablastic lymphoma. From the results of the biopsy, Plasmacytoma can be found in plasma cells that form a clone. Expression of B-cells was not found in Plasmablastic lymphoma or Plasmacytoma which was shown to be CD 20 negative. Expression of CD 79a can still be found in Plasmablastic lymphoma, while CD 45, a marker got that identification of hematopoietic or lymphoid neoplasm, can be underexpressed or weakly positive.

Almost all lymphoid cells are reactive to CD 45 The indicator of cell proliferation namely Ki 67 which increased by 75 %-905, indicated Plasmablastic lymphoma (7-9).

The results of the patient's bone marrow aspiration obtained cellularity with plasma cells at 1.3 %. Further immunohistochemistry results showed positive CD 79a(-), CD 20(-) on the tumor cell membrane, positive CD 45 on the tumor cell membrane, Ki 67 proliferation index 65 %, Kappa and Lamda had light chain restriction for Kappa. The conclusion supports a Plasmablastic lymphoma. The low Ki 67 results in these patients may be due to the immunocompetent status of the patients so that the proliferation of tumor cells is not specific staging for Plasmablastic lymphoma. Tumor staging was performed according to the ann arbor criteria for Lymphoma (3).

In this patient, the primary tumor was in the maxillary sinus with right and left submandibular lymph node involvement and systemic symptoms. Such as weight loss of 15 kg within 9 months so this patient was diagnosed with Plasmablastic lymphoma dextral maxillary region stage IIBE.

The presence of CD 45 expression is reported to provide a better prognosis but there is no standard therapy for Plasmablastic lymphoma it is a rare case. Several cases were reported using CHOP (cyclophosphamide, Vincristine, Doxorubicin, Prednisone). In which CHOP was considered suboptimal therapy.

The National Comprehensive Cancer Network® (NCCN) guideline recommends more aggressive therapy such as EPOCH (Etoposide, Vincristine, and doxorubicin, with bolus cyclophosphamide and prednisone). CODOX-MIVAC (Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate, alternating with ifosfamide, etoposide (Cyclophosphamide, Vincristine, Doxorubicine, Ethrotexate) and cytarabine. However, some cases with EPOCH therapy did not provide a better benefit than CHOP (10).

The Response to chemotherapy in the patient is a partial response, where the tumor rapidly shrinks within 2-3 weeks after chemotherapy, The patient also received 35 cycles of adjuvant radiotherapy with good results (partial response).

## CONCLUSION

We report a 50-year-old man with Plasmablastic lymphoma in the right maxillary region, Plasmablastic lymphoma is a malignancy that is difficult to diagnose because it overlaps with (plasmacytoma and lymphoma. This disease often attacks the oral cavity and upper respiratory tract, Plasmablastic lymphoma are common in HIV and non – immunocompromised patients, in this case, Plasmablastic lymphoma is destructive to bone and invasion of other tissue.

The gold standard was obtained from anatomic pathology and immunohistochemistry biopsy examinations. There is no standard therapy for Plasmablastic lymphoma, CHOP chemotherapy is still considered suboptimal but chemotherapy that is more aggressive than CHOP such as EPOCH has also been reported to have not increased median survival. Plasmablastic lymphoma has a poor prognosis where the median survival is between 8-15 months. Giving adjuvant radiotherapy can improve the response to therapy in the patient.

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## Conflicts of Interest

The authors declare no conflict of interest.

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