Clinical Case Report

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^{18}F-FDG PET/CT for staging and response assessment of primary parotid MALT lymphoma with multiple sites involvement

A case report

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Abstract

Rationale: Mucosa-associated lymphoid tissue (MALT) lymphoma is an extranodal low-grade B cell lymphoma that generally exhibits an indolent clinical course. Currently, the application of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) in MALT lymphoma is still controversial. Herein, we reported a case of using ^{18}F-FDG PET/CT for staging and response assessment of primary parotid MALT lymphoma with multiple sites involvement. As far as we know, there are no similar case reports have been published before.

Patient concerns: A 71-year-old woman, who received mass resection twice during the past 2 years due to the repeatedly relapse of facial painless masses and diagnosed as reactive lymphoid hyperplasia by pathologic tests. However, the pathological diagnosis was then changed to primary parotid MALT lymphoma after left parotidectomy operation because of a new mass found in her left parotid. Four months later, the right eyelid of the patient swelled with a blurred vision. Then, ^{18}F-FDG PET/CT scan was performed for staging, and the imaging results showed an abnormal increase of ^{18}F-FDG uptake in multiple sites including bilateral ocular adnexal, lungs, pleura, occipital subcutaneous tissue, left kidney, and lymph nodes.

Diagnoses: The patient was diagnosed as primary parotid MALT *lymphoma* with Ann Arbor stage of IVA based on the ^{18}F-FDG PET/CT findings.

Interventions: The patient received 4 cycles of chemotherapy, followed by a partial metabolic remission (PMR), which was determined by interim ^{18}F-FDG PET/CT, and finally additional 2 cycles of chemotherapy.

Outcomes: The follow-up study illustrated that the patient had been alive and doing well at 12 months after chemotherapy.

Lessons: Although MALT lymphoma normally localizes in the primary organs, the involvement of multiple organs and lymph nodes is possible. The use of PET/CT demonstrated significant clinical values in the accurate staging and response assessment of ^{18}F-FDG-avid MALT lymphoma. It is potentially useful for indicating the progress and transformation of MALT lymphoma, and guidance in localization of pathological biopsy. It is also helpful for clinicians to choose reasonable treatment strategy and improve the prognosis of patients.

Abbreviations: ^{18}F-FDG = ^{18}F-fluorodeoxyglucose, CT = computed tomography, HL = Hodgkin lymphoma, MALT = mucosa-associated lymphoid tissue, MRI = magnetic resonance imaging, NHL = non-Hodgkin lymphoma, OS = overall survival, PET/CT = positron emission tomography/computed tomography, PMR = partial metabolic remission, R-CVP = rituximab combined with cyclophosphamide, vinorelbine and prednisone, SUVmax = maximum standard uptake value.

Keywords: ^{18}F-FDG, MALT lymphoma, parotid, PET/CT

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1. Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma is an extranodal low-grade B cell lymphoma accounted for 7% to 8% of non-Hodgkin lymphoma (NHL).[1] The most common site of occurrence is gastrointestinal tract (50%), followed in order by salivary glands, lung (14%), head and neck (15%), ocular adnexa (12%), skin (11%), thyroid (4%), and breast (4%).[2] Parotid gland involvement accounts for 80% of salivary MALT lymphoma with higher incidence in women than in men.[3] MALT lymphoma is considered as an indolent clinical course, which usually localizes within the primary organ for a prolonged period.[4] But the dissemination is not rare, which approximately one-third of patients suffering from disseminated diseases including multiple mucosal sites.[5–8] The diagnosis of MALT lymphoma is primarily achieved by pathologic examination. Various recommendations for staging procedures have been published recently.[9–11] Currently, computed tomography (CT) and magnetic resonance imaging (MRI) are the recommended imaging modalities, yet positron emission tomography/computed tomography (PET/CT) is not suggested as clinical routine for patients with MALT lymphoma in these guidelines. Although ^{18}F-FDG PET/CT has been widely used in the diagnosis, staging, response assessment and prognosis of Hodgkin lymphoma (HL) and ^{18}F-FDG-avid NHL,[10,12] the application of PET/CT in MALT lymphoma is still controversial. Some early studies considered that the PET/CT produced false-negative diagnosis due to low uptake of ^{18}F-FDG for low-grade malignant tumors.[13,14] Nevertheless, many recent studies have shown that nongastric MALT lymphoma was more aggressive with high recurrence rate.[7] The positive rate of ^{18}F-FDG PET/CT was also significantly higher than that of gastric MALT lymphoma.[15,16] Herein, we reported a case of primary parotid MALT lymphoma with multiple organs and lymph nodes involvement detected by PET/CT, after which the interim PET/CT was performed after 4 cycles of chemotherapy for the treatment response assessment. This report illustrated the values of PET/CT in MALT lymphoma offering important implications for future clinical practice and research.

2. Case report

A 71-year-old woman was referred to our hospital with repeated relapse of facial painless masses during the past 2 years. Initially, the patient was diagnosed as reactive lymphoid hyperplasia for twice and treated with local resection. However, the symptom of medium textured, immobile, painless mass with normal temperature was presented soon after a new mass found in her left parotid region. The cervical contrast-enhanced CT revealed a mass of $20\times20\times5$ mm in the left parotid gland with a clear boundary between the mass and its surrounding tissue. Then the patient received the left parotidectomy since no obvious abnormalities were observed in the routine laboratory examination. The pathological examination of left parotid gland (Fig. 1) revealed that parotid tissue was replaced by small- to medium-sized lymphocytes with lymphoid follicles. Immunohistochemical staining demonstrated that the abnormal cells were positive for CD20, CD79α, CD43, CD3, CD21, CD23, Bcl-2, Kappa and negative for TdT, CyclinD1, Lambda. The Ki-67 index was 25%. These findings were consistent with the symptom of MALT lymphoma. However, no further examination was conducted to stage the patient by that time.

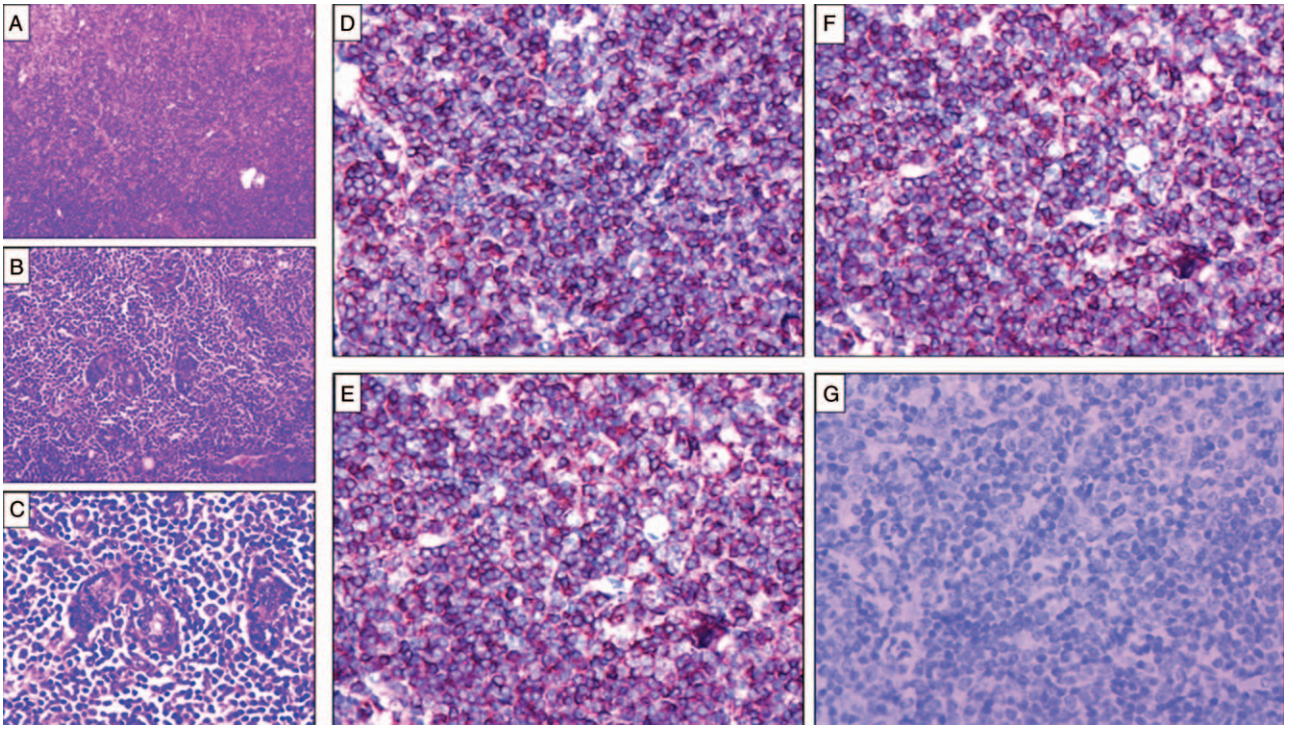

Figure 1. Pathological examination of left parotid. H&E staining (A, 100× magnification) and (B, 200× magnification) showed parotid tissue replaced by small to medium-sized lymphocytes. H&E staining (C, 400× magnification) showed lymphoid follicles were identified. Immunohistochemical staining demonstrated that the abnormal cells were positive for CD20 (D, 200× magnification), CD79a (E, 200 × magnification) and Kappa (F, 200× magnification), and negative for Lambda (G, 200 × magnification). H&E = hematoxylin and eosin.

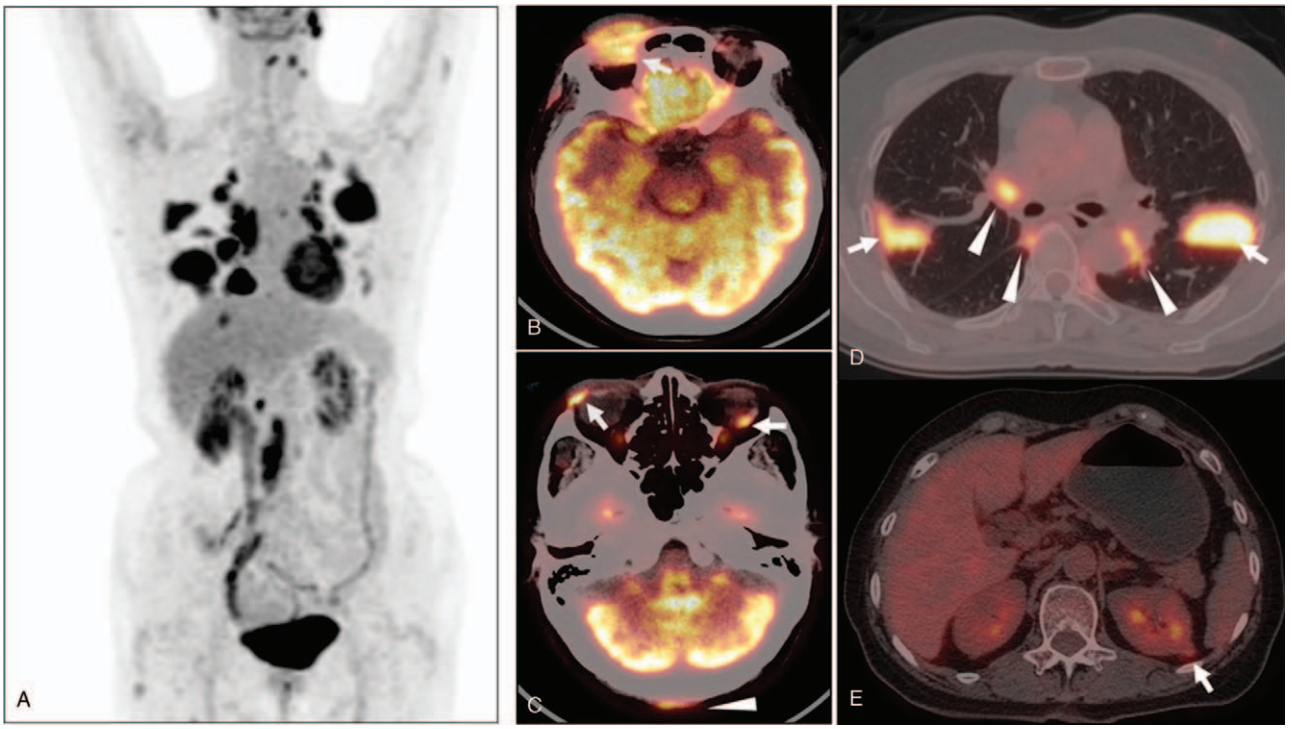

Figure 2. ^{18}F-FDG PET/CT (before chemotherapy). Coronal MIP image (A) showed multiple foci of intense ^{18}F-FDG uptake in lungs and lymph nodes in cervical, hilar and retroperitoneal. Fused PET/CT demonstrated intensive ^{18}F-FDG uptake in bilateral ocular adnexal (B and C, arrows), occipital subcutaneous (C, arrowhead), lungs and hilar lymph nodes (D, arrows and arrowheads, respectively), and left kidney (E, arrow). ^{18}F-FDG = ^{18}F-fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography, SUVmax = maximum standardized uptake value, MIP = maximum intensity projection.

After the surgery, the patient did not receive any other treatment until swelled right eyelid and blurred vision appeared 4 months later. Hence, the patient underwent ^{18}F-FDG PET/CT for determining stage (Fig. 2). Many abnormalities where the increased ^{18}F-FDG uptake were observed: hot spots in bilateral ocular adnexal with maximum standard uptake value (SUVmax) of 5.6 to 8.9; pulmonary consolidations in both lungs with SUVmax of 4.8 to 9.4; thickening region of bilateral pleura with SUVmax of 2.5 to 5.4; a nodule in occipital subcutaneous with a SUVmax of 6.9; a small nodule in left renal with a SUVmax of 3.6; multiple enlarged lymph nodes in cervical, hilar and retroperitoneal with SUVmax of 8.2 to 9.2. The patient was then staged as IVA (Ann Arbor staging classification) since no B symptoms were presented.

In the later phase, the patient received 4 cycles of R-CVP regimen chemotherapy (Rituximab combined with cyclophosphamide, vinorelbine, prednisone). One month after finishing the fourth cycle of chemotherapy, the interim PET/CT was performed for the treatment response assessment. According to the Lugano classification,[13] partial metabolic remission (PMR) was determined. The images (Fig. 3) showed that multiple lesion foci in the lungs, pleura and hilar lymph nodes shrunk with decreased uptake of ^{18}F-FDG. The ^{18}F-FDG uptake of the lesions in the ocular adnexal, occipital subcutaneous nodule, left kidney, lymph nodes of cervical and retroperitoneal disappeared. Then another 2 cycles of chemotherapy were performed. For the follow-up study, the patient was alive and doing well at 12 months after the treatment. The timeline of the patient's diagnosis and treatment course is demonstrated in Figure 4. Ethical approval is not necessary, as this article is a retrospective case report and we did not intervene in the treatment of the patient. The written consent was obtained from the patient for publication of this case report and accompanying images.

3. Discussion

MALT lymphoma is a unique type of lymphoma with marked differences from other indolent B cell lymphomas. It arises from extranodal sites normally devoid of lymphoid tissue, but these sites can acquire lymphocytes in states of inflammation. Infections, autoimmune diseases, chronic inflammation could result in MALT lymphoma.[5] It is common to have a history of Sjogren syndrome or sialadenitis in salivary MALT lymphoma.[17] Salivary MALT lymphoma has an excellent prognosis, and patients with Sjögren syndrome have a better survival rate.[18] The patient we reported had no symptoms of Sjögren syndrome, but a history of facial masses with repeated relapses and was initially diagnosed with reactive lymphoid hyperplasia. Therefore, we deduced that the occurrence of MALT lymphoma in the patient may be related to chronic inflammatory stimulation.

There is no clear consensus for the treatment of MALT lymphoma. In general, the treatment strategy should consider the lesion site, stage, and clinical characteristics of individuals. Surgical resection or radiotherapy may be considered if the lesion is localized, while chemotherapy can be performed if the lesions are systemic disseminated.[5,19,20] Rituximab was proven to be effective, producing a more than 70% response rate in MALT lymphoma irrespective of the disease site.[21–22] Thus, an accurate staging was required for MALT lymphoma to assess the extent of the disease for treatment strategy. The patient in this report did not undergo systemic diagnosis initially but was treated as a local

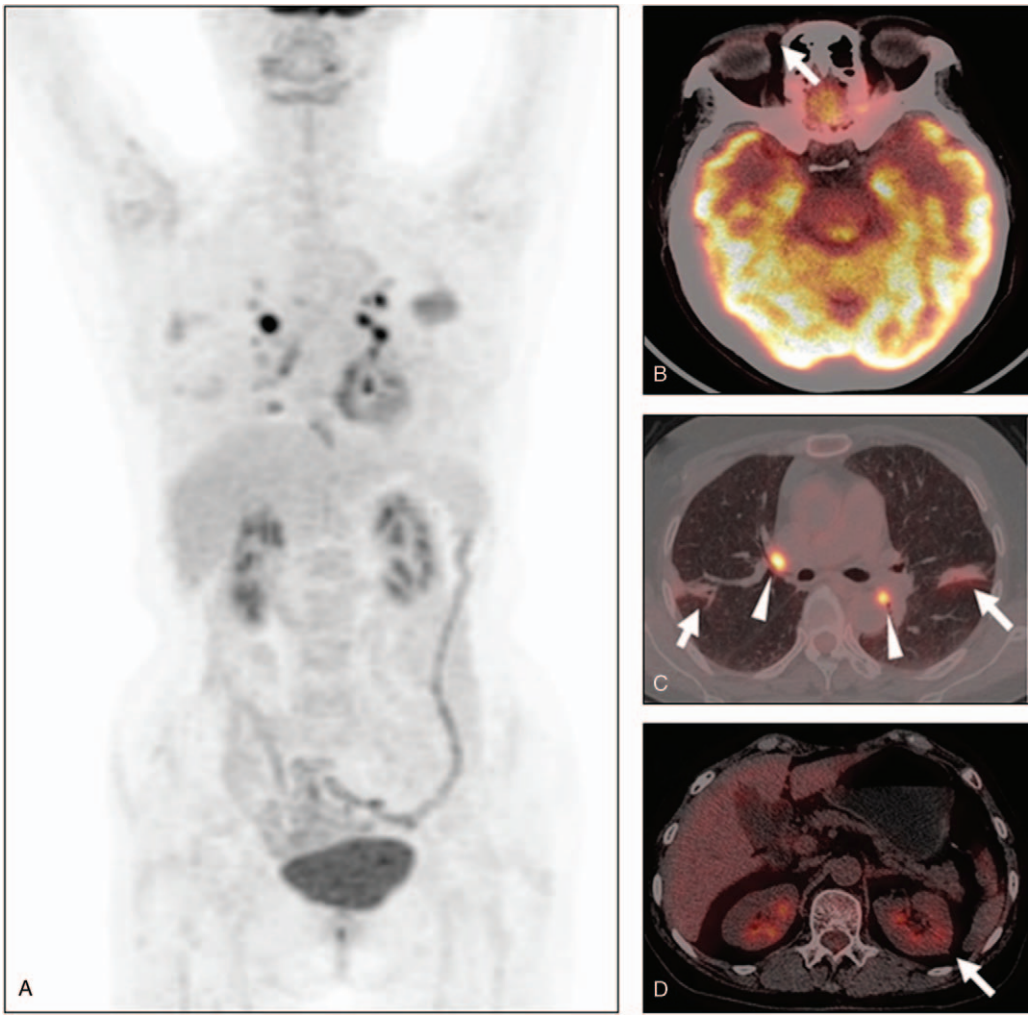

Figure 3. Interim ^{18}F-FDG PET/CT (after 4 cycles of chemotherapy). Coronal MIP image (A) showed significant remission of all lesions. The ^{18}F-FDG uptake of the lesions in the ocular adnexal (B, arrow), left kidney (D, arrow) disappeared. Multiple foci in the lungs and hilar lymph nodes (C, arrows and arrowheads, respectively) shrunk with decreased uptake of ^{18}F-FDG. ^{18}F-FDG = ^{18}F-fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.

lesion. To review this case, it was not clear whether the distant dissemination occurred in the earlier time. Then, PET/CT scan was performed and the images showed abnormal increased ^{18}F-FDG uptake in bilateral ocular adnexal, lungs, pleura, occipital subcutaneous tissue, left kidney and multiple lymph nodes with Ann Arbor staging IVA. As a result, the treatment strategy was changed to chemotherapy. And partial metabolic remission was determined by interim PET/CT after 4 cycles of chemotherapy. Then the patient continued to have another 2 cycles of chemotherapy. At 12-month after the above treatment, the patient was presently alive and doing well. Thus, we believe that PET/CT plays an important role in accurate staging and response assessment after chemotherapy. Only a few previous cases of primary parotid MALT lymphoma with other tissues involvement have been studied in the literatures.[23–26], which the reported involvement sites were usually located in the head and neck. There has not been such a report similar to ours may be due to the previous limited approaches of examinations in evaluating extranodal disease involvement, for example, CT, MRI scans and biopsy, which highlights the advantages of PET/CT imaging described in our report.

In addition, some literatures indicated that few MALT lymphoma transformed into diffuse large B-cell Lymphoma (DLBCL).[27,28] Qi et al[29] reported the MALT lymphoma patients with an SUV≥10 had a higher incident rate of large cell transformation and inferior overall survival (OS). The patient in this report was diagnosed as MALT lymphoma in her parotid gland, but the PET/CT findings presented as extreme invasiveness. It was difficult to determine transformation as it was impossible to biopsy all the lesions. We recommended this patient to be followed up regularly with ^{18}F-FDG PET/CT after treatment, to monitor progress and transformation by observing the changes of ^{18}F-FDG uptake. Then, the pathological biopsy can be conducted as a guidance.

From this case study, we believe that PET/CT has significant values in accurate staging and response assessment of ^{18}F-FDG-avid MALT lymphoma. It is potentially useful for indicating the progress and transformation, and for guidance in localization of pathological biopsy, and is also helpful for clinicians to choose reasonable treatment strategy improving the prognosis of patients. Besides the absence of pathological examination of all lesions, the limitations of this article lie in that the report

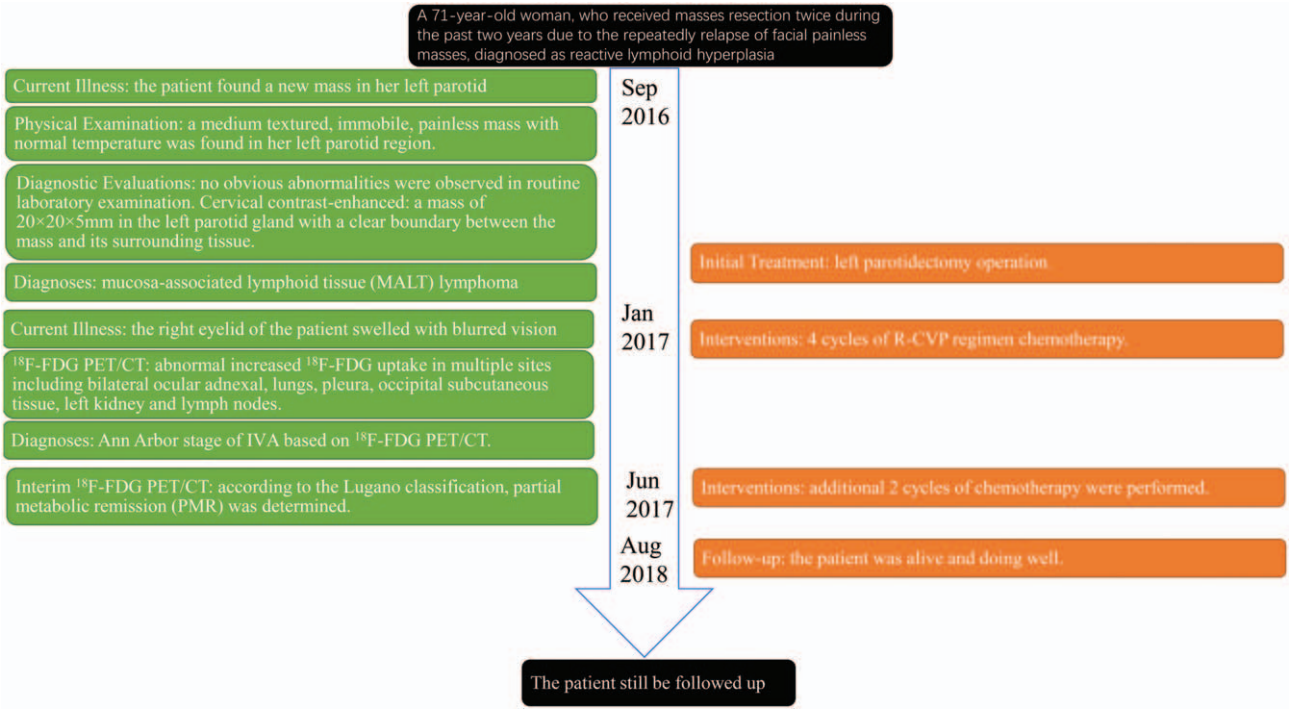

Figure 4. The timeline of the patient's diagnosis and treatment course.

contains only one patient. Future study needs more cases to summarize the general characteristics of primary parotid MALT lymphoma with multiple sites involvement.

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