

**Case Report**

# Challenges in Diagnosis of Primary Classical Hodgkin Lymphoma of Parotid Gland by Fine Needle Aspiration: A Rare Case Report and Review of the Literature

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Primary Hodgkin lymphoma (HL) arising in the parotid gland is extremely rare and only accounts for 4% of primary lymphomas of the salivary glands. The nodular lymphocyte predominance HL (NLPHL) is the most common subtype. Fine needle aspiration (FNA) has a great potential in diagnosis of non-Hodgkin lymphomas (NHL), especially in combination with flow cytometry. However, it is challenging to diagnose HL by FNA due to obscuring reactive inflammatory cells and scant cellularity associated with fibrosis. Primary HL of the parotid has a good prognosis following treatment with chemotherapy and radiation. Here we report a rare case of primary classical HL (CHL), nodular sclerosis type, arising in the parotid of a 73-year old male who presented with a painless parotid mass and no lymphadenopathy at other sites. In this case, the diagnosis was made on the surgical specimen following parotidectomy. The FNA of the parotid mass prior to the surgery was misinterpreted as carcinoma mainly due to the scant cellularity, Reed-Sternberg (R-S) cells mimicking poorly differentiated carcinoma cells, and the extremely low occurrence of HL in the parotid. The patient underwent chemotherapy and radiation after parotidectomy and has been doing well. In conclusion, primary HL of the parotid is extremely rare, and it is very challenging to make a definitive diagnosis of HL by FNA. Despite the difficulties in diagnosis, primary parotid HL has a good prognosis compared to other parotid malignancy. It is important for pathologists and surgeons to be aware of this extremely rare entity.

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## INTRODUCTION

Lymphoid lesions of the parotid gland are much less common than their epithelial counterparts. Primary lymphomas arising in the parotid gland account for only 0.6-5% of tumors or tumor-like lesions of the parotid.<sup>1</sup> The majority of primary parotid malignant lymphomas are non-Hodgkin lymphomas (NHL). Hodgkin lymphoma (HL) arising in the parotid gland is extremely rare.<sup>2,3</sup>

HL is classified into nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) and Classical Hodgkin lymphoma (CHL). The latter is subclassified into four subtypes: nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depleted.<sup>4</sup> While the nodular sclerosis subtype is the most commonly diagnosed CHL, NLPHL is the most common type affecting the parotid gland.<sup>5</sup>

Fine needle aspiration (FNA) has a great potential in diagnosis of non-Hodgkin lymphomas, especially in combination with flow cytometry, thus eliminating the need

for open biopsy.<sup>6-9</sup> However, there are some limitations for diagnosing HL by FNA and flow cytometry.<sup>10,11</sup>

Treatment of lymphoma includes chemotherapy with radiation. However, a great number of patients with primary lymphoma of the parotid gland receive parotidectomy due to the difficulties of making diagnosis by FNA or open biopsy.<sup>12</sup> Patients with primary parotid HL have much better prognosis compared to those with NHL.<sup>5,12</sup> The pathologists and surgeons should be aware of this extremely rare entity.

Here we report a rare case of primary CHL, nodular sclerosis subtype, arising in the parotid of an older adult. In this case, the diagnosis was made on the surgical specimen following parotidectomy. The FNA diagnosis prior to the surgery was “malignancy, favor non-small cell carcinoma” mainly due to the morphological similarity of the large Hodgkin and Reed-Sternberg (HRS) cells and carcinoma cells on scant cytology specimens and the extremely low occurrence of HL in the parotid gland.

## CASE HISTORY

A 73 year-old male presented with enlargement of the left

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parotid area for two weeks. The mass was painless and no overlying skin changes or facial weakness were noted. No other lymphadenopathy was noted elsewhere. The patient underwent Ultrasound-guided FNA at an outside hospital with the diagnosis of suspicious for malignancy. The patient has a history of melanoma removed from his back 17 years ago with no recurrence, and he had prostate cancer and multiple skin cancers of his arm and scalp. The patient had no known autoimmune disorders.

Physical examination reveals that the left sided infra-auricular tail of parotid mass was multilobulated and the lesion was firm at the inferior edge of the conchal bowl. CT scan showed a 4.3 x 3.8 x 3.5 cm multi-lobulated solid mass (Figure 1) with ill-defined margins in the left parotid gland.

Six FNA slides from the outside hospital, including four Diff-Quik stained smear slides, one Papanicolaou stained Cyto-spin slide, and one H&E stained cell block, were reviewed by the cytopathologist. There is scant cellularity on the smear. At the low power, there are loosely cohesive cell groups in the background of blood. The groups consist of large atypical cells with abundant cytoplasm and round to oval nuclei with small prominent nucleoli. There are also single atypical large cells present (Figure 2) and some of

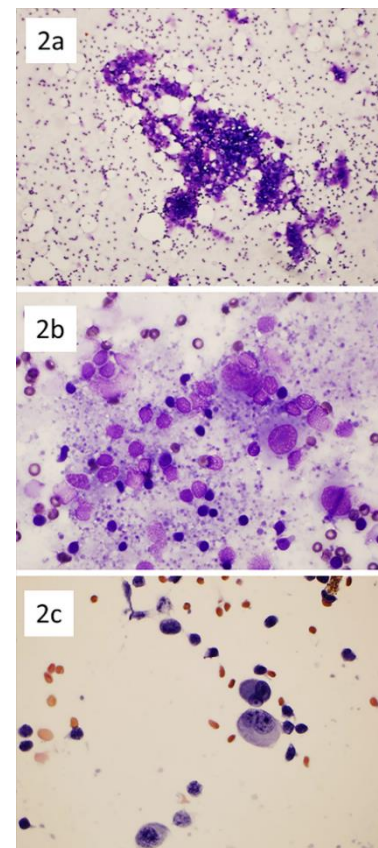
them are binucleated resembling Reed-Sternberg (R-S) cells. Few small to medium-sized lymphocytes are present in the background. The overall impression of FNA is "malignant cells present, favor non-small cell carcinoma".

The patient then underwent left parotidectomy with preservation of facial nerve. Gross examination of the parotid mass reveals a 2.5 x 1.7 x 1.5 cm gray-white poorly-circumscribed mass. Histologically, there are multiple lymphoid nodules separated by fibrous bands in the parotid gland. The nodules contain large atypical cells, small lymphocytes, histiocytes, and rare eosinophils. The atypical cells have large nuclei with irregular nuclear contour and some of them are binucleated with prominent nucleoli consistent with R-S cells. (Figure 3) Immunohistochemical stains demonstrated that the large atypical cells are positive for CD15 and CD30 with membranous and Golgi patterns and are negative for CD20, PAX5, CD45, CD3, CD4, and EMA. The tumor cells are weakly positive for Epstein Barr virus (EBV). (Figure 4) The final diagnosis is "classical Hodgkin lymphoma, nodular sclerosis type".

Following the parotidectomy, the patient underwent chemotherapy and conjunctive radiation therapy and has been doing well.

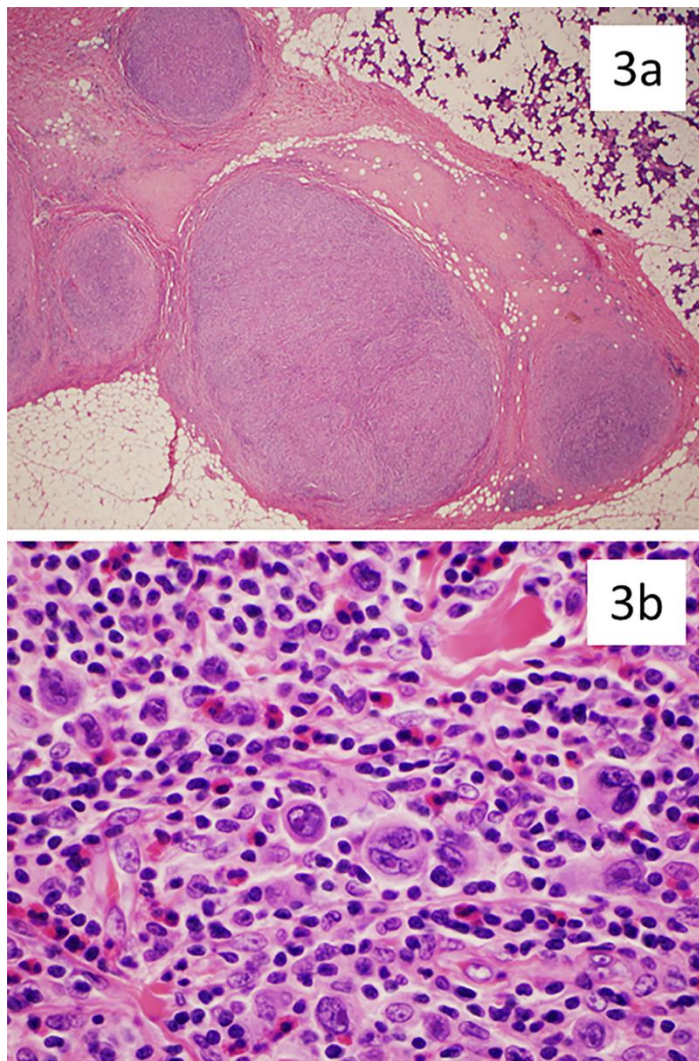


**Figure 1.** CT of the neck shows a multilobulated solid mass with ill-defined margins in the left parotid gland (arrow).



**Figure 2.** FNA cytology: (a) Loosely cohesive cell group in the background of blood (Diff-Quik, 100x). (b) Large atypical cells with abundant cytoplasm and round to oval nuclei with small prominent nucleoli (Diff-Quik, 600x). (c) Binucleated cells resembling R-S cells (Papanicolaou, 600x).



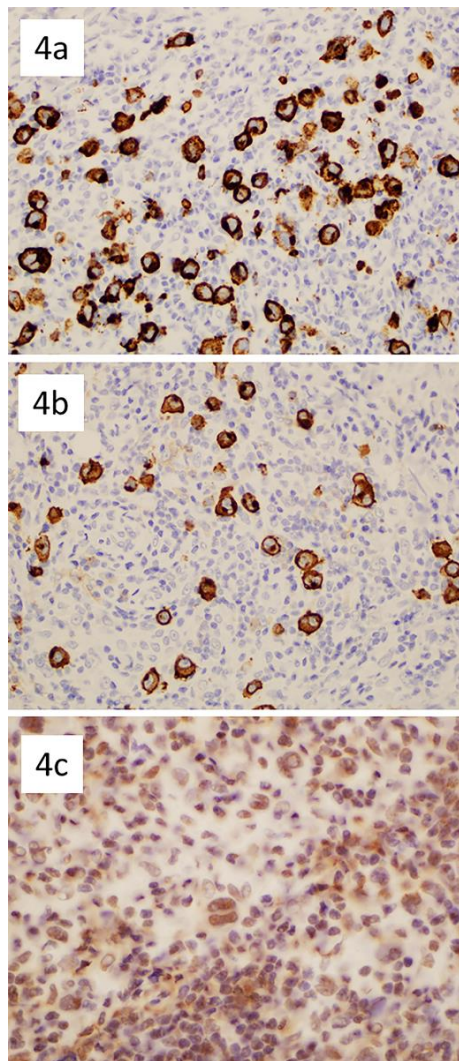


**Figure 3.** Histology specimen: (a) Multiple lymphoid nodules separated by fibrous bands in the parotid gland. (H&E, 100x). (b) Large HRS cells in the background of small lymphocytes, histiocytes, and rare eosinophils (H&E, 600x).

## DISCUSSION

Malignant lymphomas in the head and neck are the second most commonly occurring extranodal lymphomas after the GI tract.<sup>5</sup> Lymph nodes are commonly found in the parotid parenchyma because encapsulation of the gland occurs late in its formation, allowing lymph nodes to be incorporated into the substance of the gland.<sup>9</sup> Either reactive or malignant lymphoproliferative processes can occur in these lymph nodes. The presence of an underlying autoimmune disorder, such as Sjogren syndrome, is associated with an increased risk of lymphoma in the parotid.<sup>13</sup>

In general, primary parotid lymphoma is diagnosed when the initial site of disease is the parotid gland regardless of whether the neoplasm is in the parenchyma or lymphatic tissue.<sup>12</sup> The majority of primary parotid lymphomas are NHL. CHL is a monoclonal lymphoid neoplasm composed of



**Figure 4.** Immunohistochemical stains. (a) Tumor cells with positive membranous and Golgi pattern of stain for CD15 (400x). (b) Tumor cells with positive membranous and Golgi pattern of stain for CD30 (400x). (c) Tumor cells with weak positivity for EBV (600x).

mononuclear Hodgkin cells and multinucleated R-S cells residing in a background of mixed inflammatory infiltrate including small lymphocytes, plasma cells, eosinophils, neutrophils, histiocytes, and fibroblasts.<sup>4</sup> Fibrosis is a very common feature of CHL. HL predominantly occur in the lymph nodes and very rarely present as extranodal disease. Primary HL arising in the parotid are extremely rare. A few case reports are found in a literature search.<sup>2,3,5,14-16</sup> In one study, 12 of 13 cases with parotid lymphomas are NHL and there is only one case of HL.<sup>14</sup> Another retrospective study of 2140 primary parotid lymphoma cases demonstrated that HL accounts for 3.5% of the total cases.<sup>12</sup>

Here we report a case of older patient presenting with painless parotid mass. The patient had no known underlying autoimmune disorders. No lymphomas in other body sites

were identified. The patient underwent parotidectomy for definitive diagnosis. Microscopically, there are HRS cells present in the background of inflammatory cells and the HRS cells were confirmed with immunohistochemical stains (CD15+, CD30+, CD45-, CD20-).

Among primary parotid HL cases, NLPHL seems to be the most common subtype in the parotid HL, whereas CHL, nodular sclerosis subtype is the most common one in nodal HL (**Table 1**).<sup>2,3,5,14-16</sup> However, in the current case, the parotid tumor is composed of multiple fibrotic lymphoid nodules and HRS cells with typical morphological and phenotypical features of nodular sclerosis CHL.

**Table 1.** Literature review summary of primary parotid HL cases.

HL subtype	Case number	Percentage (%)
NLPHL	17	38
CHL nodular sclerosis	11	24
CHL mixed cellularity	7	16
CHL lymphocyte depleted	2	4
Unknown	8	18
Total	45	100

There are controversies regarding whether FNA can be reliably used to make diagnosis of lymphomas. Studies favoring utilizing FNA to diagnose lymphomas have shown that sensitivity and specificity of FNA with flow cytometry are 95-100% and 83-85%, respectively, for the detection of lymphomas.<sup>7,9,13</sup> Yet some people think that FNA should be avoided to utilize for diagnosing malignant lymphomas.<sup>14</sup>

It is noteworthy that majority of the lymphomas diagnosed by FNA in the above-mentioned studies are NHL. Diagnosing HL by FNA is more difficult, owing to rarity of the neoplastic cells, lack of architecture in FNA sample, and the difficulty of phenotyping the neoplastic cells in the absence of an adequate cell block. Even though the suspicious level is high, it is very challenging to make a definitive diagnosis of HL in a FNA sample. The most common causes of false negative diagnosis of HL by FNA include sampling error, obscuring reactive inflammatory cells, and scant cellularity due to fibrosis.<sup>11</sup> The difficulty of diagnosing parotid HL on cytologic examination is evident in the current case which was misdiagnosed as carcinoma due to the scant Hodgkin cells resembling carcinoma cells and the extreme rarity of this entity in the parotid.

In spite of the limitations, FNA has tremendous diagnostic potential in the initial evaluation of a parotid mass by providing a preliminary diagnosis. With this initial diagnosis, the surgeon is able to counsel the patient with some certainty, plan for the expected procedure, and, in case of a definitive diagnosis of lymphoma, avoid the unnecessary surgery and its associated morbidity.<sup>5</sup> Furthermore, recent studies have shown that the diagnosis of CHL in the lymph node using six-color and nine-color flow cytometry have high sensitivity (85.3%-88.7%) and high specificity (99.7%-100%), indicating that flow cytometry can be helpful in diagnosing

CHL, in particular in FNA and small core biopsy samples.<sup>17,18</sup>

Parotid lymphomas tend to have a more favorable prognosis than lymphomas in general. Primary parotid HL tends to have a better prognosis (5-year survival rate of 91%) than its NHL counterpart (5-year survival rate of 51%-80%).<sup>5</sup> The patient in the current case was given chemotherapy and radiation therapy after the diagnosis and he has been doing well since.

In summary, primary HL arising in the parotid gland is an extremely rare entity. FNA has potential in initial evaluation of primary lymphomas in the parotid gland. However, the relatively scant cellularity and obscuring inflammatory background make the diagnosis of HL on FNA very challenging. Because of this, many patients undergo parotidectomy to have definitive diagnosis. Despite the difficulties in diagnosis, primary parotid HL has a good prognosis compared to other parotid malignancy. Clinician and pathologists should be aware of this rare entity.

#### CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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