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Original Research Article

Study of Extra-Nodal Lymphoproliferative Malignancy Presented As Isolated Parotid Gland Swelling

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Abstract: Primary parotid lymphomas are a rare entity. The clinical presentations as well as the investigations primarily available are non-specific and often lead to delay in diagnosis and treatment. Our primary aim is on the diagnostic and management of such cases. Ours is a retrospective analysis of the cases of primary malignant lymphoma diagnosed after surgery and their management. Out of 10 cases 9 patient were diagnosed with NHL while 1 case was of CML. After surgery patients were sent for radiotherapy and chemotherapy. All the cases responded well without any recurrence. Primary parotid lymphomas have good prognosis with minimal morbidity, although diagnostic modality pose a challenge, therefore one must keep it as differential for parotid swellings.
Keywords: Parotid, lymphoma, salivary gland tumour, Non-hodgkin

INTRODUCTION

Tumours of salivary gland are relatively uncommon and represent less than 2% of all head and neck neoplasms. The major salivary glands are the parotid, submandibular and sublingual glands. Minor salivary glands are found throughout the mucosa of the upper aero-digestive tract with highest density found within the palate. About 85% of salivary gland neoplasms arise within the parotid gland. Among the lymphoproliferative [1] disorders the head and neck area is the most common in both nodal and extra-nodal form[2,3], constituting 0.3% of all reported malignancy[4].

Primary lymphomas of the salivary gland are rarely observed. Primary malignant lymphomas constitute 1.7-3.1% of all salivary gland neoplasms and 0.6-5% of tumors and tumor-like lesions ofthe parotid gland[5]. Non-Hodgkin and Hodgkin lymphoma are the most frequently observed head and neck tumors after squamous cell carcinoma and thyroid carcinomas[6]. In the head and neck region, 23% of non-Hodgkin lymphomas and 4% of Hodgkin lymphomas are located extranodally[7]. For the primary parotid gland lymphoma the overall incidence is about 0.3% of all tumours, 2-5% of salivary gland neoplasm and 5% of extranodal lymphomas[8-10].

Like other extranodal sites, the non-Hodgkin's lymphomas predominate over Hodgkin's disease in salivary tissue[11],and have been found to be of relatively low malignancy[12]. Extranodallymphomas, as a group, have been found to have a better survival rate than the others[13]. Salivary gland lymphomas are no exception, and in fact,have been found to have a prolonged survival rate evenin comparison to other extranodal sites[14].

The main treatment modality of parotid lymphoma is radiotherapy and chemotherapy depending on the extent and staging. Surgery is done as a diagnostic tool as none of the investigation including FNAB can conclusively detect the lesion.

The aim of our study is the retrospective investigation of patients who presented with parotid masses and underwent surgery with the diagnosis of primary parotid lymphoma, and to evaluate the histopathology, and clinical course including treatment and outcome, in the light of the related literature.

MATERIAL & METHODS

In our study we conducted a retrospective chart review of 10 patients during duration of 10 years,managed for parotid gland surgery and were found to be NHL on histopathology except one which came out to be CML, also confirmed on bone marrow

analysis and immunohisto-chemistry. These patients who presented with a swelling of the parotid as their first symptom, who did not have a previous diagnosis of lymphoma and who later on were confirmed histologically post surgically as a parotid gland lymphoma were included in the study.

The patients' age, sex, type of surgery, and histopathology results were assessed. The files of those who were diagnosed with parotid lymphoma were evaluated in detail. The age, sex, histopathological subtype and cell type, disease grade, applied therapies, histopathology results and the survival of these patients were recorded.

All patients underwent complete head and neck evaluation and a pre-operative CT with contrast study. All cases underwent Superficial Parotidectomy with informed consent and specimen sent for histological study. The patients were staged according to Ann-Arbor staging system. Postoperative recovery was uneventful and facial nerve function was intact.After histopathological confirmation the patients were sent for Radiotherapy and/or chemotherapy.

RESULTS

Among the 10 cases, 5 were male and 5 female, age presentation varied from 13 yrs of the youngest male to 60 yrs of the oldest female. All the cases presented with hard and firm swelling not associated with pain. On clinical examination the swelling was not fixed to the deep structure, no features suggestive of seventh nerve palsy and no clinically palpable cervical lymph nodes. The FNAB, done in all the cases were all negative for malignant lymphatic invasion. In 1 case the cytological examination revealed mononuclear and inflammatory cells and a diagnosis of a chronic parotiditis was made, in one case it suggested a benign lymphoepithelial lesion; and in the remaining one case gave an inconclusive result. One of the cases was found to be immune-suppressive, HIV positive.

Table 1: Patient data

Patient	Age/Gender	Extra-parotid involvementon CT	Fine needle aspiration	Diagnostic procedure
1	13/M	No	Yes	Superficial Parotidectomy
2	45/F	No	Yes	Superficial Parotidectomy
3	40/M	No	Yes	Superficial Parotidectomy
4	60/F	No	Yes	Superficial Parotidectomy
5	35/M	No	Yes	Superficial Parotidectomy
6	26/F	No	Yes	Superficial Parotidectomy
7	42/M	No	Yes	Superficial Parotidectomy
8	46/F	No	Yes	Superficial Parotidectomy
9	48/M	No	Yes	Superficial Parotidectomy
10	47/F	No	Yes	Superficial Parotidectomy

After diagnosis, all cases were sent for Radiotherapy and Chemotherapy with CHOP or R-CHOP protocols (cyclophosphamide 750 mg/m2, doxorubicin 50 mg/m2, vincristine 1.4 mg/m2, prednisone 100 mg for 5 days every 14 days). All patients received conformal external beam RT to the parotid bed.
Median follow up was for one year.

DISCUSSION

Primary lymphomas of the salivary glands are rare and account for 4.7% of lymphomas at all sites [15]. A non-Hodgkin lymphoma of a salivary gland may appear as a painless, progressively enlarging mass [16-19]. Therefore, it is rarely suspected before biopsies or surgical removal. MALT lymphomas developing within the salivary glands may be related to chronic lymphoid hyperplasia. Lymphoma is a very common malignancy and the second most common neoplasm of the head and neck after squamous cell carcinoma. Most of the non-Hodgkin's lymphomas arise primarily in the lymph nodes (71.9%), while only 29.1% are primarily extra-nodal. Primary parotid lymphoma accounts for only 0.87% of all NHL cases (3.1% of extra-nodal NHLs) [20-22].This type of malignancy constitutes 0.2–0.8% of malignant tumors in the parotid gland. [23] Batsakis assessed that the propensity of parotid gland to be involved by NHL is related to the anatomy of the gland, rich in lymph nodes and lymphoid tissue [12]. Non-Hodgkins lymphoma of the parotid gland may be classified as extranodal if the origin is from the mucosa associated lymphoid tissue (MALT) or nodal if the true origin is from lymph node within the gland[31].

The population known to have a much higher incidence of primary lymphoma of the parotid is the one with autoimmune diseases, the strongest correlation being with Sjogren syndrome [24-26]. In patients with primary Sjögren's syndrome, the risk of lymphomas has been reported as 4.3-6% and 80% of these are MALT lymphomas. None of our patients hada history of concurrent autoimmune disease. Autoimmune disorders affecting salivary glands may predispose to uncontrolled proliferation of lymphatic tissue. Sjogren's

syndrome is associated with 6.5 fold increase in the risk of NHL, 250 fold increase in the risk of parotid gland NHL and a dramatic 1000 fold increase in the risk of parotid gland MALT lymphoma.

There is controversy in the literature regarding whether the parotid is truly primarily involved or whether it arises in intra-glandular lymph nodes.

Hyman and Wolff proposed criteria for the diagnosis of primary parotid lymphoma:a) involvement of the salivary gland as the first clinical manifestationof disease; b) histologic proof that lymphosarcomainvolves the salivary gland parenchyma, rather than beingconfined to soft tissue or a lymph node in the area; c) architecturaland cytologicconfirmation of the malignant natureof the infiltrate.

In common with previous reports and series, the majority of lymphomas (73%) arose within the parotid gland, although the proportion found within the minor glands was much greater. This bias towards the parotid favours the concept that these lesions arise primarily in lymphnodes within the gland, **as** nodes are more plentiful within the parotid than other salivary glands[27]. However, it is clear from all studies that non-Hodgkin's lymphomas predominate and that Hodgkin's disease arising primarily in salivary tissue is exceptionally uncommon.

The most common presentation of parotid lymphoma is as a painless mass indistinguishable from other non-malignant or other more common epithelial tumors. This is the reason why the diagnosis is commonly overlooked and patients are often subjected to unnecessary procedures and a delay in diagnosis. In most cases the facial nerve is not jeopardized [28]. Diagnosing parotid lymphoma can be a difficult task, as evidenced by the unnecessary tests conducted before correct diagnosis is made [29]. Both from our experience and from the review of the literature, FNA is not diagnostic and therefore should be avoided whenever a high index of suspicion for lymphoma arises in the differential diagnosis (e.g., B symptoms, enlarged lymph nodes, or a previous history of lymphoma) [30]. CT scan may add information regarding the malignant nature of the disease, with signs such as irregular borders and extra-parotid extension. Currently, there are still no pathognomonic findings indicative of lymphoma on CT scan. The procedure of choice for the diagnosis of lymphoma in the parotid gland should be core biopsy.

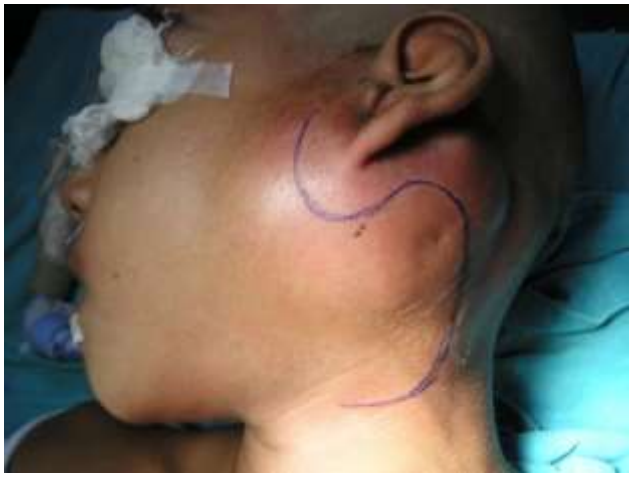

Fig-1: Parotid Swelling- primary complaint

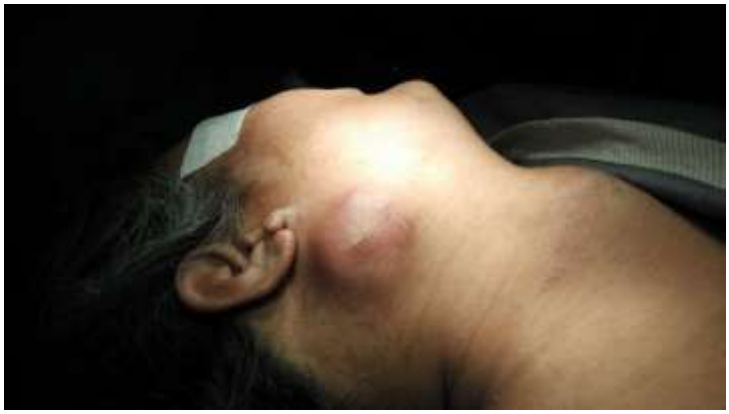

Fig-2:External presentation

The mean age at diagnosis is around 50-60 years with male preponderance, reason being unclear. In our study male to female ratio was 1:1, with mean age of 40. None of the cases reported any underlying autoimmune disorder, but one was found to be HIV reactive. Most primary parotid lymphomas are B marginal zone. In our study, 2 of the cases belonged to marginal cell, 1 was follicular variant and remaining 1 was diagnosed as CML which was further confirmed on IHC and bone marrow analysis.

Survival rate for the parotid lymphoma is better than other extranodal lymphomas, however many of the studies vary considerably in survival rate. Multiple factors seem to affect the survival including age, grade and the histology of lymphoma, tumour size and associated co-morbidities[33-34]. Of the all the factors tumour size is found to be most consistently related to survival.

The main modality of treatment for parotid lymphomas is Radiotherapy +/- Chemotherapy [35-37]. Patients with stage I/II low grade can benefit from RT alone. However in our study chemotherapy was used in all the cases as a useful adjunctive. Localised low beam RT was given on parotid bed. The complications of chemotherapy were managed symptomatically. The role of surgical intervention was as a diagnostic tool. The inference that can be drawn is that superficial parotidectomy is recommended for all undiagnosed lump and inconclusive FNAB cases without any B symptoms.

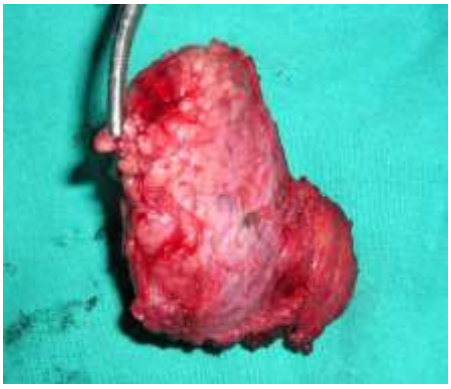

Fig-3: Specimen

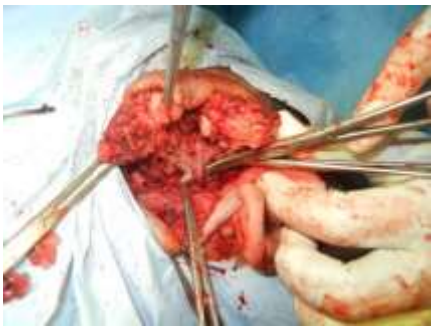

Fig-4: Intra-op facial nerve

CONCLUSION

Presence of parotid swelling is a common presentation in surgical practice and the patients having parotid lymphomas are clinically indistinguishable from other lesions. Difficulty in clinical as well as imaging including FNAB to diagnose the pathology has lead us to conclude that superficial parotidectomy is essential to reach a definitive diagnosis and, staging is required for post-operative RT and CT.

The treatment protocols followed i.e. radiotherapy + chemotherapy followed in our series showed good response with better outcome, with positive outlook to both patient and physician

REFERENCES

1. Rosenberg SA, Diamond HD, Jaslowitz B, Craver LF;Lymphosarcoma: A review of 1269 cases. Medicine,1961; 40:31-84.
2. Doll R, Muir C, Waterhouse J; Cancer in Five Continents, Vol. 11. New York: UICC and Springer, 1970, 90.
3. Lennox B, Clarke JA, Drake F, Ewen SWB; Incidence of salivary gland tumours in Scotland Accuracy of national records.Br Med J.,1978; 1:687-689.
4. Cancer Statistics and Survival; Office of Population and Censuses Survey. Her Majesties Stationery Office, London, 1980.
5. Tullio A, Marchetti C, Sesenna E, Brusati R, Cocchi R, Eusebi V; Treatment of carcinoma of the parotid gland: the results of a multicenter study. J Oral MaxillofacSurg., 2001;59:263-70.
6. Cooper JS, Porter K, Mallin K, Hoffman HT, Weber RS, Ang KK, Gay EG, Langer CJ; National Cancer Database report on cancer of the head and neck: 10-Year update. Head & neck, 2009; 31(6):748-58.
7. Urquhart A, Berg R; Hodgkin's and non-Hodgkin's lymphoma of the head and neck. Laryngoscope, 2001;111:1565-9.
8. Sarris AH, Papadimitrakopoulou V, Dimopoulos MA, Smith T, Pugh W, Ha CS, McLaughlin P, Callender D, Cox J, Cabanillas F; Primary parotid lymphoma: the effect of International Prognostic Index on outcome. Leukemia& lymphoma, 1997; 26(1-2):49-56.
9. Gleeson MJ, Bennett MH, Cawson RA; Lymphomas of salivary glands.Cancer, 1986;58(3):699-704.
10. Harris NL; Lymphoid proliferations of the salivary glands.Am J ClinPathol., 1999;111(Suppl. 1):S94-S103.
11. Freeman C, Berg JW, Cutler SJ; Occurrence and prognosis of extranodal lymphomas.Cancer,1972; 29:252-260.

12. Schmid U, Helbron D, Lennert K; Primary malignant lymphomas localised in salivary glands. Histopathology,1982; 6:673-687.
13. Desai PB, Meher-Homji DR, Paymaster JC; Malignant lymphomas: A clinical study of 800 Indian patients. Cancer,1964; 18:25-33
14. Freeman C, Berg JW, Cutler SJ; Occurrence and prognosis of extranodal lymphomas.Cancer1972; 29:252-260.
15. Balm AM, Delaere P, Hilgers FJ, Somers R, Heerde PV; Primary lymphoma of mucosa associated lymphoid tissue (MALT) in the parotid gland. Clinical Otolaryngology & Allied Sciences, 1993; 18(6):528-32.
16. Gleeson MJ, Bennett MH, Cawson RA; Lymphomas of the salivary glands. Cancer, 1986; 58:699-704.
17. Hyman GA, Wolff M; Malignant lymphomas of the salivary glands. Review of the literature and report of 33 new cases, including four cases associated with the lymphoepithelial lesion. Am J ClinPathol., 1976; 65:421-438.
18. Mehle ME, Wood BG, Tucker HM, Lavertu P, Tubbs R, Kraus DH; Lymphoma of the parotid gland. The Laryngoscope, 1993; 103(1):17-21.
19. Schusterman MA, Granick MS, Erickson ER, Newton ED, Hanna DC, Bragdon RW; Lymphoma presenting as a salivary gland mass. Head & neck surgery, 1988; 10(6):411-5.
20. Mehle ME, Wood BG, Tucker HM, Lavertu P, Tubbs R, Kraus DH; Lymphoma of the parotid gland. The Laryngoscope, 1993; 103(1):17-21.
21. Zucca E, Roggero E, Bertoni F, Cavalli F; Primary extranodal non-Hodgkin's lymphomas. Part 1: Gastrointestinal, cutaneous and genitourinary lymphomas. Skin, 1997; 19:20.
22. Yencha MW; Primary parotid gland Hodgkin's lymphoma.Ann OtolRhinolLaryngol., 2002; 111(4): 338-42.
23. Von Stritzky M, Wereldsma JCJ, Pegels JG; Parotid mass as first symptom of a malignant lymphoma.J SurgOncol., 1998; 67(1): 25-7.
24. Barnes L, Myers EN, Prokopakis EP; Primary malignant lymphoma of the parotid gland.Arch Otolaryngol Head Neck Surg., 1998; 124(5): 573-7.
25. Biasi D, Caramaschi P, Ambrosetti A, Carletto A, Mocella S, Randon M, Bambara LM; Mucosa-associated lymphoid tissue lymphoma of the salivary glands occurring in patients affected by Sjögren's syndrome: report of 6 cases. Acta haematological, 2001; 105(2):83-8.
26. Hyman GA, Wolff M; Malignant lymphomas of the salivary glands: review ofthe literature and report of 33 new cases, including four cases associated withthelymphoepithelial lesion. Am J ClinPathol., 1976; 65(4): 421-38.
27. Feind CR; The head and neck. In: Haagensen CD, Feind CR, Herter FP, eds. The lymphatics in Cancer. Philadelphia: WB Saunders, 1972; 60-230.
28. Gross M, Ben-Yaacov A, Rund D, Elidan J; Role of open incisional biopsy in parotid tumors. ActaOtolaryngol.,2004; 124(6): 758-60.
29. Heller KS, Dubner S, Chess Q, Attie JN; Value of fine needle aspiration biopsy of salivary gland masses in clinical decision-making. The American journal of surgery, 1992; 164(6):667-70.
30. Hughes JH, Volk EE, Wilbur DC; Cytopathology Resource Committee, College ofAmerican Pathologists. Pitfalls in salivary gland fine-needle aspiration cytology: lessons from the College of American Pathologists Interlaboratory Comparison Program in Nongynecologic Cytology. Arch Pathol Lab Med.,2005; 129(1): 26-31.
31. Shine NP, O'Leary G, Blake SP; Parotid lymphomas – clinical and computedtomographic imaging features. S Afr J Surg., 2006; 44(2): 60, 62-4.
32. Dispenza F, Cicero G, Mortellaro G, Marchese D, Kulamarva G, Dispenza C; Primary Non-Hodgkins lymphoma of the parotid gland. Brazilian journal of otorhinolaryngology, 2011; 77(5):639-44.
33. Goldwein JW, Coia LR, Hanks GE; Prognostic factors in patients with early stage non-Hodgkins lymphomas of the head and neck treated with definitive irradiation. Int J RadiatOncolBiol Phys., 1990;20(1):45-51
34. Jagannath S, Velasquez WS, Tucker SL, Fuller LM, McLaughlin PW, Manning JT, North LB, Cabanillas FC; Tumor burden assessment and its implication for a prognostic model in advanced diffuse large-cell lymphoma. Journal of Clinical Oncology, 1986; 4(6):859-65.
35. Wilder RB, Jones D, Tucker SL, Fuller LM, Ha CS, McLaughlin P, Hess MA, Cabanillas F, Cox JD; Long-term results with radiotherapy for stage I–II follicular lymphomas. International Journal of Radiation Oncology* Biology* Physics, 2001; 51(5):1219-27.
36. Mac Manus MP, Hoppe RT;Is radiotherapy curative for stage I and II low-grade follicular lymphoma? Results of a long-term follow-up study of patients treated at Stanford University. J ClinOncol., 1996;14(4):1282-90.
37. Portlock CS, Rosenberg SA; No initial therapy for stage III and IV non-Hodgkins lymphomas of favorable histologic types. Ann Intern Med., 1979;90(1):10-3.