

PATTERN OF LYMPHATIC SPREAD IN MEDULLARY THYROID CARCINOMA

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ABSTRACT

Background: Medullary cancer arises from C- cells and accounts for 5-10 % of thyroid cancers. Most common site of metastasis is central compartment of neck and then ipsilateral neck nodes. Involvement of contralateral neck nodes shows poor prognosis. The only curative treatment in medullary cancer is surgery. The objective of this study was to see the pattern of lymphatic spread in medullary carcinoma.

Materials & Methods: It was a retrospective review from 1995 to 2010. The patients who were treated initially outside were excluded.

Results: Total number of the patients were 40; 25(62.5%) males and 15(37.5%) females. Mean age was 46.2 years. In all patients, diagnosis was made on FNAC. Patients were divided in three groups on the basis of primary tumor size. In group A (16 patients), tumor size was less than 2 cm, in group B (13 patients), tumor size was 2-4cm and in group C (11 patients), tumor size was more than 4cm. On final histopathology reports, in Group A, 6(37.5%) patients had positive central neck nodes. In group B, central neck nodes were positive in 8(61.5%) patients and 3(23%) patients also had ipsilateral positive nodes. All patients in Group C shown metastasis in central nodes (100%), while 5(45.45%) patients had positive ipsilateral nodes and 3(27.27%) patients had contralateral positive nodes.

Conclusion: Chances of metastasis increase with tumor size and the most common site is the central neck compartment.

KEY WORDS: Medullary carcinoma, Thyroid, Lymphatic metastasis.

INTRODUCTION

Medullary thyroid carcinoma (MTC) arises from the calcitonin producing parafollicular cells of thyroid gland. The tumor was described for the first time by Hazard and colleagues in 1959.¹ They made a differentiation between poorly differentiated thyroid carcinoma and MTC. In 1961, Sipple described the association between MTC and multiple endocrine neoplasia (MEN2) type 2 syndromes.² MTC accounts 5-10% of thyroid cancers presently. Most of them are sporadic but around 20% are due to mutation in (ret) proto-oncogene. Hereditary MTC can be found in isolation (familial MTC) or as a part of MEN syndrome type 2 (2A or 2B).

Nodal metastasis is a feature of MTC, which significantly worsens the prognosis.^{3,4} Lymph node involvement is found in 10-30% of tumor less than 1cm and it is more frequent in tumors larger than 1cm. Surgery is the only curative treatment for MTC and should remove all the neoplastic foci present in the neck. Total thyroidectomy with central neck dissection is the treatment of choice for all MTC patients but the indications of lateral neck dissection is still controversial. Some⁵ advocate the need

of modified radical neck dissection initially even in the absence of any suspicious lymph node. This aggressive approach may result in high morbidities even in good centers but can eliminate the disease completely and result in better prognosis. In our study, we evaluated the pattern of lymph node metastases which may be helpful in standardizing the extent of surgery in MTC patients.

MATERIAL AND METHODS

It was a descriptive study of the patient records from 1995 to 2010. All the patients who were treated at Aga Khan University Hospital Karachi were included and the patients who were treated initially outside were excluded from the study.

The data was analyzed on SPSS version 16. Percentage and mean was used to analyze the results of study.

RESULTS

Total number of the patients were 40; 25 (62.5%) males and 15 (37.5%) females. Mean age was 46.2 years.

In all patients, diagnosis was made on FNAC. Calcitonin was also raised in all the patients. Ultrasonography was done in all patients to assess the size of primary thyroid tumor and to see any cervical lymphadenopathy. No patient was found to have MEN2 syndrome.

Patients were divided in three groups on the basis of primary tumor size. In group A, tumor size was less than 2cm, in group B tumor size was 2-4cm and in group C tumor size was more than 4cm. 16 patients came into Group A, 13 in Group B and 11 in Group C. Pre-operatively, no neck nodes were assessed in group A, 4 patients had neck nodes on ipsilateral side in group B and in group C, 6 patients had ipsilateral nodes and 5 patients had bilateral nodes.

All the patients of group A underwent total thyroidectomy and central neck dissection. In Group B, 9 patients underwent total thyroidectomy and central neck dissection while remaining 4 patients underwent total thyroidectomy, central and ipsilateral neck dissection also. In group C, 6 patients had ipsilateral neck dissection while 5 patients underwent bilateral neck dissection along with total thyroidectomy and central neck dissection.

On final histopathology reports, in Group A, 6 (37.5%) patients had positive central neck nodes. In group B, central neck nodes were positive in 8 (61.5%) patients and 3 (23%) patients also had ipsilateral positive nodes. All patients in Group C shown metastasis in central nodes (100%), while 5 (45.45%) patients had positive ipsilateral nodes and 3 (27.27%) patients had contralateral positive nodes.

Overall pattern of metastasis among 40 patients has shown that central compartment is the most commonly involved site (62.5%), followed by ipsilateral metastasis (20%) and contra-lateral involvement is seen only in 7.5% patients. More over, tumor size remained the major factor regarding neck metastasis.

DISCUSSION

There is a scarcity of published data about the pattern of lymph node metastasis in MTC. In few series, low number of patients does not allow the detailed analysis while other series failed to make a clear distinction between primary and reoperative tumors.⁶ The present literature shows that most common site of metastasis in MTC is central and ipsilateral compartment. More over, ipsilateral compartment is involved more frequently than the contralateral compartment.⁷ Therefore, when there is extensive cervical nodal metastasis then lymphatic tumor cells tend to spread to me-

diastinal and hilar⁸ nodes. In this study also, it has been shown that central and ipsilateral compartment are frequently involved by the tumor while contralateral site is the less frequently involved site.

There are many factors which predict the prognosis and cure rate in MTC. These are age, sex, tumor size, tumor capsule, multicentricity and nodal metastasis.⁹ Tumor size is the major factor which predicts the lymph node metastasis and outcome of the disease.¹⁰

In our study, the tumor greater than 4cm had 100% lymph node metastasis to the central nodes, 45.45% to the ipsilateral side and 27.27% to the contralateral side. These results may help to consider the neck dissection in tumors larger than 4 cm. Surgery is the only curative treatment modality in MTC. The role of chemotherapy and radiotherapy has not been established so far. Therefore, due to limited therapeutic options, it becomes very crucial that at first time adequate surgical procedure must be offered. It is very clear that total thyroidectomy and central neck dissection should be done in all patients of MTC. Controversy is present regarding ipsilateral and contralateral neck dissection. Some advocate that lymphatic spread is very frequent in MTC; therefore, central and bilateral neck dissection should be performed in all the patients with MTC.¹¹ But in other studies, it has been shown that ipsilateral or bilateral neck dissection should only be done when there are evidence of diseases metastasis because biochemical cure is reached only in few cases regardless of any surgical procedure.¹²

At our center, ipsilateral and contralateral neck dissection was only performed when there was evidence of metastatic neck disease. As shown in this study, central compartment is the most common site for metastasis, so it should be cleared meticulously from hyoid bone above to the innominate vessels below in all the MTC. Long term survival of MTC patients is 60-90% without metastatic disease while patients with metastatic disease has 5 years survival rate of approximately 50%.¹³⁻¹⁵

Lymph node metastasis is one of the major prognostic factors in MTC. Therefore, we should be familiar with the pattern of lymphatic spread and on these basis, extent of surgery can be decided which may be helpful in curing the patients. The results of our study are compatible to the international studies, however due to limited number of patients and retrospective review; clear cut recommendation can not be made. In this regard, larger prospective studies are needed to reach on concrete conclusion for better outcomes in medullary thyroid carcinoma patients.

CONCLUSION

Critical to the treatment of medullary thyroid carcinoma is complete surgical resection as there is no other option available till now. Central compartment is the commonest site involved by the tumor metastasis, followed by ipsilateral and contralateral compartments. Metastasis becomes more evident with increasing tumor size. However, more research is needed to identify the causes and other therapies able to cure the disease.

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