INTRODUCTION

Assessment of the lymph nodal status is of utmost importance in the work up of a patient with breast cancer and is considered the most valuable prognostic factor. The regional lymph nodes in the axilla are always critically evaluated in assigning the clinical stage and taking therapeutic decisions. The supraclavicular lymph nodes (SCLN) are in direct extension of the lymphatic drainage of the apex of the axilla. Therefore, their involvement in patients of breast cancer has importance in determining prognosis and in imparting treatment.

Isolated metastasis to ipsilateral SCLN without any other distant spread was previously staged as N3 (stage IIIB) subcategory. However in 1988, in the American Joint Committee on Cancer (AJCC) revised staging system, this group of patients were moved to stage IV category and given ‘M1’ status since it was believed that their prognosis is poor as their biological behaviour is like that of patients with other
distant metastasis.

Conventionally metastatic breast cancer is considered incurable and the goals of management are to palliate symptoms, improve quality of life and prolong life. At present, all non-metastatic breast cancer patients (stage I-III) are treated with curative intent whereas those with stage IV disease receives therapy with a palliative intent. However, a significant number of patients with breast cancer presents with SCLN metastatic disease and in view of the changes in the staging system, physicians are often not clear regarding the intent of therapy in patients with isolated ipsilateral SCLN (IISCLN) metastatic disease without any other distant spread. Patients with supraclavicular nodal spread are surgically incurable, however with combination of chemotherapy and radiotherapy to supraclavicular fossa the disease can be controlled in a significant number of patients. In our institution, as a policy, patients with IISCLN metastasis were treated like those with locally advanced breast cancer (LABC) with an intent to cure by combined-modality approach using chemotherapy, surgery and radiotherapy. We present our experience of the management of this subset of patients treated with curative intent in terms of local control, disease-free survival (DFS) and overall survival (OS).

**Material and Methods**

A retrospective analysis of breast cancer database of the Surgical Oncology unit of Institute Rotary Cancer Hospital (IRCH), All India Institute of Medical Science (AIIMS), New Delhi was performed. Between January, 1993 to December, 2000 a total of 670 patients were operated including 16 patients (2.4%) with FNAC proven IISCLN metastasis without evidence of any other distant spread. The records of all these patients were analysed for treatment details, recurrence pattern, DFS and OS. A subgroup analysis of LABC (stage III) that included 299 (45%) patients was also performed separately and compared with IISCLN group of patients. Historical data of metastatic breast cancer patients survival was used for comparison.

**Treatment protocol:** The patients were initially evaluated in the Breast Cancer Clinic with clinical history and physical examination. They were investigated, to exclude any other distant metastasis, with a complete haemogram, liver function test, chest X-ray, nuclear bone scan and ultrasonography of the liver. Thereafter, all patients with LABC (stage III) and stage IV with IISCLN spread were treated with a combined multimodality approach with six cycles of anthracycline based chemotherapy, surgery, locoregional radiotherapy (LRRT) with or without hormonal therapy. Neo-adjuvant chemotherapy was given initially and the clinical response was assessed after each cycle with physical examination of the primary tumour and the axilla. The response of SCLN was also determined. The patients who responded were given the full course of neo-adjuvant chemotherapy followed by surgery whereas those who did not respond were taken up for surgery after 2 or 3 cycles. The surgical procedure consisted of modified radical mastectomy or radical mastectomy. Thereafter, all the patients received adjuvant postoperative radiotherapy (LRRT) 50 GY in 25 fractions over five weeks, to the chest wall, axilla and supraclavicular fossa. Hormonal therapy with tamoxifen 20 mg daily was given to all patients who were estrogen receptor positive.

After the completion of treatment, regular follow-up was undertaken at three months interval in the first two years, once every six months in the next three years and yearly thereafter. At each visit assessment was done with a clinical history, physical examination, liver function test and chest X-ray. Any abnormality in these were further evaluated with ultrasonography, bone scan or computed tomography as indicated. Mammography of the contralateral breast was done yearly. A record of local, regional and systemic metastasis was maintained.

**Results**

The incidence of IISCLN disease in this study was 2.4% (16 patients) who had a mean age of 46.5 (range 30-60) years. The primary tumour was mostly large with a mean size of 7.75 (range 3-12) cm and had an advanced T stage with 12 (75%) patients having T4b while four (25%) had T3 lesions. The axillary nodal status was advanced (N2) in eight (50%) patients while N1 and N0 status was seen in six (38%) and two (12%) patients respectively. All the patients had FNAC proven metastasis to ipsilateral SCLN without any other distant spread.

All the patients completed full course (6 cycles) of chemotherapy. The most commonly used regimen was cyclophosphamide, epirubicin and fluorouracil (CEF) in eight patients (50%) and rest consisted a combination of epirubicin and other agents. Complete clinical response of supraclavicular nodes to neo-adjuvant chemotherapy was observed in all the patients. The overall response of primary tumour to chemotherapy was 75% in IISCLN group and 76% in LABC group. Pathological complete response was 13% in IISCLN group and 11% in LABC group.

The surgical procedures included modified radical mastectomy (MRM) in 14 patients (88%) and radical mastectomy (RM) in two (12%). RM was required for large tumours with pectoralis major muscle infiltration. All patients completed planned locoregional radiotherapy after surgery. The estrogen receptor positivity rate in the IISCLN group was 44% (seven patients) while the progesterone receptor positivity rate was 31% (five patients) and they were put on tamoxifen for five years. At a median follow-up of 36 (range 9-72) months the recurrence patterns observed in the IISCLN and LABC groups are shown in Table 1. Comparative disease-free survival and overall survival between the two groups are shown in Fig. 1.

**Discussion**

Rapid advances have been made in the management of breast cancer in recent years. Despite this, the presence of distant metastatic disease is thought to have ominous implications and is considered incurable. The presence of...
IISCLN metastasis constitutes a subgroup of patients who are included in the stage IV category of the AJCC classification system\(^2,3\) as it was believed that their prognosis is dismal and similar to that of patients having metastasis to other distant sites. However, until 1988 they were included in the N3 (stage IIIB) subcategory\(^1\) before being ascertained the M1 status. Currently, there is no clear consensus on the treatment policy to be adopted in patients with IISCLN metastatic disease.

It has been seen that the median survival of patients with metastatic breast cancer is 2 to 3 years and even with therapy the median prolongation of survival is a matter of months.\(^5\) Zlotecki \textit{et al} observed that the median survival in metastatic breast cancer ranges from 4 to 15 months in most series with a two year survival rate of only 15 to 20%.\(^6\) Hence the outlook of these patients is very grim and once distant metastatic disease is detected death is considered imminent. On the other hand, the outcome in LABC is comparatively better especially when multimodality approach is adopted using anthracycline based chemotherapy, surgery and radiotherapy. Amongst the larger series, Hortobagyi \textit{et al}\(^7\) could attain 5-year OS and DFS of 56% and 33% while in the Milan trial the 5-year OS and DFS were 49.4% and 25% respectively\(^8\) using combined modality treatment including anthracycline based chemotherapy.

The presence of IISCLN metastasis is being considered a grave sign, an indicator of distant metastatic disease with a poor survival. Halstead\(^9\) reported survival of more than five years in only 5% patients with histologically proven involvement of supraclavicular lymph nodes during pre-chemotherapy era. Kiricuta \textit{et al}\(^10\) observed a 2- and 5-year

\begin{table}[h]
\centering
\caption{Comparison of recurrences patterns between IISCLN metastasis and LABC groups.}
\begin{tabular}{|l|c|c|}
\hline
 & IISCLN & LABC \\
\hline
Total No. & 16 & 299 \\
Recurrence & & \\
Total & 5 (31%) & 77 (26%) \\
Systemic & 4 (25%) & 75 (25%) \\
Loco-regional & 2 (12%) & 21 (7%) \\
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\end{tabular}
\end{table}

IISCLN - Isolated ipsilateral supraclavicular lymph node; LABC - Locally advanced breast cancer

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Comparison of survival between IISCLN metastasis and LABC groups. IISCLN - Isolated ipsilateral supraclavicular lymph node; LABC - Locally advanced breast cancer; OS - Overall survival; DFS - Disease-free survival.}
\end{figure}
survival of 52% and 34% respectively in this group of patients which was similar to that seen in LABC patients in post-chemotherapy era. Supraclavicular disease is surgically incurable but with a combination of chemotherapy and radiotherapy the disease can be controlled in a significant number of patients. At the University of Texas MD Anderson Cancer Centre, this subgroup of patients have been categorised as “Regional stage IV LABC” and are being treated with combined modality approach like that in other LABCs. Hortobagyi et al reported a five year disease-free survival of 29% and overall survival of 42% with this approach in patients with IISCLN metastasis. Subsequently Brito et al have analysed the outcome of combined modality approach in subset of patients with IISCLN involvement and reported an overall survival of 41% and disease-free survival of 34% at five years. This survival was not significantly different from that of patients with stage IIIB disease while it was superior to that of patients having metastasis to other of patients having metastasis to other distant sites.

In our institution, the patients with IISCLN metastasis without any other distant disease are being treated with combined multidisciplinary approach with an intent to cure. The relapse rates and survival IISCLN group patients were comparable to that of LABC patients. The outcome in patients with IISCLN metastasis appears better than what have been described in literature in patients with spread to other distant sites. Based on the recent literature and results of the current study we recommend a multimodality treatment approach with curative intent in patients with IISCLN spread. We also feel that the staging of this group patients in the metastatic or stage IV category may be inappropriate and there is a need to revise the TNM staging system.

**CONCLUSION**

Breast cancer patients can present with IISCLN metastatic disease in about 2.4% cases. This subgroup of patients have a less aggressive biological behaviour compared to that of patients having metastasis to other distant sites. Advent of multiagent chemotherapy and radiotherapy to supraclavicular fossa has altered the outcome of disease significantly in these patients. Hence, these patients should be included in the locally advanced group instead of metastatic group and treated aggressively using multimodality approach for prolonged survival.

**REFERENCES**