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Original Research Article

Pulmonary resection for isolated pulmonary metastasis: patterns of disease

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ABSTRACT

Background: Pulmonary metastasectomy dates back to 1880s, sub lobar resections, lobectomy and pneumonectomy, described in the setting of metastatic sarcoma, renal cell cancer, testicular NSGCT. Extremity sarcoma is the most common primary site for metastasis to lung. Almost 20 % of patients with extremity sarcoma, give rise to isolated pulmonary metastasis at some point in the course of the disease. Though pulmonary metastasis commonly arises from primary tumors in extremities, they may arise from any histologic variant. Despite progresses in multimodality treatment, there are significant deaths, after metastasis from soft tissue malignancies. There is evidence that surgical resection is the treatment of choice for isolated pulmonary metastasis from extremity sarcoma. Chemotherapy has proved to be ineffective to increase survival in such cases. Keeping this in mind we report an analysis of 11 such cases in terms of patterns of disease, for Isolated pulmonary metastasis originating from various histologic variants.
Methods: This is a retrospective study from July 2006 to September 2016, carried out at NKP Salve Institute of Medical Sciences. During this period, total 13 patients were admitted with Isolated pulmonary metastasis. Out of 13 patients 2 patients were later on proved to have metastasis in the liver and so excluded from study. Of 11 patients, metastasis from soft tissue sarcoma of extremity were (5), cancer of uterine cervix (3), non seminomatous germ cell tumor of testis (3). All 11 patients were treated with pulmonary resectional surgery. Patterns of disease in terms of specific survival from various histological variants.
Results: The median survival for soft tissue sarcoma from the diagnosis of pulmonary metastasis for all 5 patients was 18 to 26 months. Reports suggest, with non-operative therapy for soft tissue sarcoma, the median survival was 11 months. After pulmonary mastectomy, three-year survival for these patients was around 23%. For world wide data suggest the prevalence of pulmonary metastasectomy was 3.6% in cancer cervix. In the present study, the mean disease-free duration for cancer cervix after pulmonary resection was more than 60 months. In the present study, all 3 patients are still alive even after 5 years with no recurring disease. Reports published in 2016 surgical clinics show 5-year survival in 80%. Patients with NSGCT showed persistent rising levels of (ß HCG, æ fetoprotein, LDH) and CT evidence of active pulmonary metastasis, with 4 or less nodules were subjected for surgery, with outcome of 2 patients had recurrent disease died at the end of 27th month. 1 patient is still alive after 11 years. Patients with complete resection of all metastatic disease was the important prognostic factor for survival.
Conclusions: Isolated pulmonary metastasis is not a very common disease in this part of the world. Complete surgical resection of metastasis is the single most important factor which determines outcome in these patients. Disease free interval (DFI), number of metastatic nodules, are important factors in surgical decision making. Long term survival is possible in selected patients, even when recurrent disease is resected.

Keywords: Cervical cancer, Extremity sarcoma, NSGCT, Pulmonary resection

INTRODUCTION

Lung welcomes metastasis from various organs, Extremity soft tissue sarcoma is one of the commonest site metastazing to lungs.[1] Incidence of Isolated Pulmonary Metastasis, is 20%.[2] Though lung is a site for metastasis from various histologic variants, like breast, kidney, bones, extremity sarcoma, testis and rarely from cancer cervix.[2,3] But the relation between histology and frequency of pulmonary metastasis is not very well understood.[4,5] Incidence of pulmonary metastasis from cancer cervix is around 3.6%.[6,7] The chemotherapy is not very effective in cervical cancer metastasis. Since the advent of cisplatin-based chemotherapy, non seminomatous germ cell tumors (NSGCT) have been considered as one of the most chemosensitive, and curable solid neoplasms. NSGCT has propensity to metastasize to lungs, after it's spread to retroperitoneal lymph nodes.[8,9] Though synchronous metastasis to retroperitoneum and chest is also well documented.[8,9] But the reported incidence is quite low, the reports justify the aggressive surgical approach for residual pulmonary disease after cis platinum based chemotherapy. With multimodality treatment results are not very encouraging. Overall survival for metastasis from soft tissue sarcoma was around 11 months.[3,10] Complete surgical resection of all metastasis has significant impact on survival.[9] The present study report 11 patients of isolated pulmonary metastasis from extremity sarcoma, Cancer cervix, NSGCT in terms of patterns of disease.[10]

METHODS

This is a retrospective study from July 2006 to September 2016, carried out at NKP Salve Institute of Medical Sciences, during this period, total 13 patients were admitted with Isolated pulmonary metastasis from different anatomic sites. All these patients were operated for primary cancers at our institute and Scrupulous follow up schedule was given to patients.

After initial surgery, review every 6 months for clinical examination, imaging and tumor markers. Every patient's data is obtained and entered into our database, which include detail history, primary disease and its anatomic site, stage. Initial primary operative procedure, histopathology report. Imaging and wherever applicable tumor markers.

Inclusion criteria

Primary disease must be well controlled. The disease-free interval (DFI) must be more than 12 months, pulmonary metastasis must be less than 3 or 4 nodules and must be isolated to one lobe of lung. Contralateral lung parenchyma must be normal. There is no direct or indirect evidence of any extra pulmonary metastatic disease, proved by imaging or tumor markers. Complete removal or control of primary lesions, sufficient pulmonary reserve after resection. patient tolerance of surgery. Surgical options were wedge resection, lobectomy or pneumonectomy. All these patients were operated by single surgeon, experienced in doing pulmonary resections since last 30 years.

Out of 13 patients, 11 patients were enrolled in our study as 2 patients with NSGCT had liver metastasis and so excluded from the study, remaining patients were considered for pulmonary resectional surgery, as they had CT evidence and consistently rising levels of tumor markers suggestive of active metastasis, after Platinum based chemotherapy. In NSGCT patients we preferred RPLND as the first procedure and if the Lymph nodes show viable disease then only we entered thorax to resect pulmonary nodules. As studies suggest that if RPLND has necrosis in Lymph nodes then chances of getting viable disease in pulmonary nodules is almost negligible.[16] We report patterns of disease in terms of specific survival from various histological variants.

RESULTS

In present study, 11 patients of isolated pulmonary metastasis were analyzed, the median age for patients with extremity sarcoma with pulmonary metastasis was between 32-39 years.

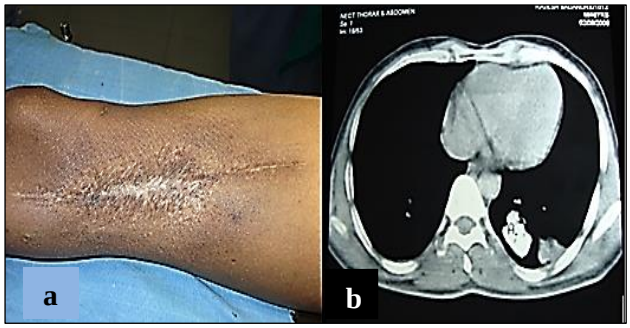

Figure 1: (a) Primary site of operation 5 years ago- Extremity sarcoma. (b) CT Scan of same patient.

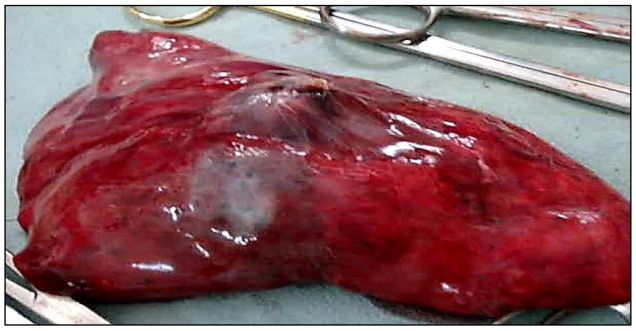

Figure 2: Left lobectomy with metastasis from extremity sarcoma.

All patients were male, commonest histopathological type was malignant fibrous histiocytoma, 3 patients (27.27%), 1 patient (9%) liposarcoma (high grade) and 1 patient (9%) synovial sarcoma. All 5 patients had 2-3

nodules in one lobe of lung periphery, with normal remaining lung parenchyma. All patients with extremity sarcoma included in this study had extended disease free interval, more than 12 months. 3 patients of malignant fibrous histiocytoma developed pulmonary metastasis 3 years after primary surgery.

Out of these 5 patients 4 had lobectomy and 1 had wedge resection. The average size of nodules was 3-5 cm and number of nodules were 3 and less.

Cancer of the uterine cervix is one of the most common cancers in females in India. 3 patients (27.27%) presented or developed isolated pulmonary metastasis during the course of the disease. The median age was 55 years, with a range of 36 to 60 years. All 3 patients were surgically treated at stage II disease, while follow up of all these patients, lung lesion was detected on CXR and CT scan, they were properly biopsied and primary lung cancer was ruled out. The mean EFD (duration from the diagnosis of initial cervical cancer to lung metastasis) was more than 24 months in two patients and more than 108 months, in one patient. All three patients had 3-4 pulmonary nodules of size between 3-6 cm in the periphery of the lung with involvement of only one lobe, remaining lung parenchyma appeared normal on radio imaging studies. Two of these patients underwent wedge resection, and in 1 patient left lower lobe lobectomy was done.

Platinum based chemotherapy has changed the outcome of NSGCT, now this is considered as curable solid neoplasm. Prevalence of pulmonary metastasis after Platinum based chemotherapy in NSGCT are almost 10% and metastasis in retroperitoneum is seen in 25% to 87 %. In this study, we treated 3 young patients of NSGCT with age group of 23 to 31 years, presented with isolated pulmonary metastasectomy. Diagnosis was made on CT scan of chest and persistently rising levels of tumor markers (ß HCG, æ fetoprotein, LDH) after chemotherapy. Adequate pulmonary function and reserve was assessed and pulmonary mastectomy was done with due anesthesia care. DFI was 16,18 and 26 months respectively. After wedge excision, the levels of (ß HCG, æ fetoprotein, LDH) came to normal in all these patients. In all our patients, the survival was more than 24 months after pulmonary metastectomy. Two patients had recurrence in the thorax and were not willing for surgery again, died at 27th month. One patient is still alive after 11 years where DFI was 26 months.

DISCUSSION

Pulmonary metastasectomy, in form of wedge resection, lobectomy and pneumonectomy, described in the setting of metastatic sarcoma, renal cell carcinoma, NSGCT and cervix cancer.[1] Our small study of 11 patients, is a single institutional study with pulmonary metastasis from three different histologic sites. Our data report that sarcoma arising from any anatomic site has a capacity to metastasize to lungs.[1,2] Another important aspect of this study was, all patients who had pulmonary metastasectomy, done in our institute were treated for the primary disease at our institute only. A study of 719 patients at Memorial Sloan Kettering Cancer Centre (MSKCC) either presented or developed lung metastasis only from sarcoma from different anatomic sites, and of various histologic grades. MSKCC analysis of the histology of primary lesions indicate that pulmonary metastasis arises most commonly in patients with malignant fibrous histiocytoma, synovial sarcoma, liposarcoma, leiomyosarcoma.[3] In the present study out of 5 patients of extremity sarcoma, high grade liposarcoma; 1 patient (9%), synovial sarcoma; 1 patient (9%), malignant fibrous histiocytoma; 3 patients (27.27%) had pulmonary metastasis. All these metastases appeared after 1 year of the surgery, all three patients of malignant fibrous histiocytoma had pulmonary metastasis after 3 years of primary surgery. A variety of prognostic factors have been reviewed in number of different series. The ability to resect metastatic disease completely is consistently the most significant factor in determining post metastasis survival.[3] Extended disease-free interval has been demonstrated as positive predictor of survival.[4,5] Number of metastasis in the lung has tremendous impact on outcome and survival.[6] Two large series indicated a prognostic significance associated with the number of nodules resected. Casson et al, documented that patients with three or less nodules on pre-operative chest CT had significantly longer survival than patients with 4 or more nodules.[4,5,7,8] In this study, the patients were selected with 4 or less pulmonary nodules for resection. Reports suggest that there is no impact of size of the nodule, Histological grade has no impact on outcome.[4,5,9]

Metastasis to lung from cervical cancer is rare presentation, cancer cervix spreads to the lung by hematogenous route, detected as pulmonary nodule or multiple metastasis, incidence is 3.6%.[9,10] In cases of solitary pulmonary nodule, it is to be differentiated from pulmonary metastasis, primary lung cancer, and carcinoid tumors.[10] The literature has led many investigators to focus on surgery upon a solitary pulmonary nodule and its outcome. However, multiple pulmonary metastases are frequent.[11] In this study, we included cervical cancer (Squamous cell carcinoma) patients who were diagnosed with lung metastases (solitary or multiple 3 or less than 4 nodules) after primary treatment. We had 3 patients with cervical cancer developed isolated pulmonary metastasis, 2 patients after 24 months of primary surgery, one patient after 108 months after primary surgery. One patient had nodule in right upper lobe and two patients presented with 2-3 nodules in left lower lobe of lung. In all three patients complete surgical resection of metastasis done, Post surgery platinum based chemotherapy was given to all three patients, considering the fact of multicentric disease. Many clinicians are treating pulmonary metastasis by using platinum based chemotherapy and response rate are reported to be 26% to 67.7%.[12-14] The response rates to Cytoxan and Adriamycin are reported to be 65% and 16-40%, respectively.[15,16] This confirms that

surgical treatment with complete resection of metastasis, is the best form of treatment. Fuller et al, report that longer EFD (> 36 months) is associated with good prognosis.[11,16] Extended disease-free interval is of paramount importance to have positive impact on the outcome. In the present study, patients were treated by surgery, followed by platinum-based combination chemotherapy, with a response rate of 100% as all three patients are alive and coming for follow up every year, and there is no evidence of any recurrence of pulmonary disease till date.

Since the advent of platinum based chemotherapy NSGCT is now the curable solid neoplasm, pulmonary metastasis persist after Platinum based chemotherapy in NSGCT, is an indication for surgical excision for histological diagnosis, to predict the prognosis and therapeutic benefit.[17] Studies show that surgical excision of pulmonary metastasis is required in about 10% patients.[17,18] while RPLND is more commonly performed procedure, 25% to 87% patients.[19] Post chemotherapy pulmonary metastasis are usually small and peripheral so they are amenable to surgical excision.[20,21] In our series we had 3 young patients, mean age of 23 to 31 years, with NSGCT, who were given Platinum based chemotherapy, but levels of tumor markers (beta HCG, alpha fetoproteins and LDH) were significantly high, and was suggestive of active disease in the lung. After wedge excision with negative margins, the levels came to normal in all these patients. In all our patients, the survival was more than 24 months after pulmonary mastectomy. Two patients had recurrence in the thorax and not willing for surgery, died within 27 months. One patient is still alive after 11 years. In 2011 (MSKCC) study suggest mean 5.6 years survival in 56% patients with pulmonary metastasis.[20,21] Those with Pulmonary and mediastinal metastasis, the mean survival of 5 years is less than 46.7%.[22] Reports from few studies show that residual masses contain viable tumor cells and teratoma in 12% to 15% and 34% to 42% of cases, respectively.[23] In the present study, histopathologically 69% had viable cancer and 31% patient had necrosis found in resected nodule from lung. Pulmonary mastectomy is widely accepted treatment with good long-term results.[23-24]

CONCLUSION

Extremity soft tissue sarcoma is one of the commonest primary site metastazing to lungs, but they may arise from any histologic variant. Isolated pulmonary metastasis from cancer of uterine cervix is rare, studies suggest, that role of chemotherapy, is limited. NSGCT has the higher incidence of metastasis to lungs than cervical cancer. RPLND should generally be performed before a thoracotomy is considered, because a purely benign histology at RPLND is highly predictive for necrosis in residual lung nodules. However, decision-making with regard to residual mass resection, remains complex. Complete surgical excision of pulmonary metastasis has a diagnostic as well as therapeutic benefits and offers excellent survival. Extended disease-free interval is the key factor in outcome. This study is limited by its retrospective design and small sample size. Further studies with a different design and good sample size is warranted.

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