Resection and heated pleural chemoperfusion in patients with thymic epithelial malignant disease and pleural spread: A single-institution experience

Alon Yellin, MD,[a] David A. Simansky, MD,[a] Ronny Ben-Avi, MD,[a] Marina Perelman, MD,[b] Nona Zeitlin, MD,[a] Yael Refaely, MD,[a] and Alon Ben-Nun, MD[a]

Objective: Our objective was to evaluate whether resection and heated pleural chemoperfusion (HPCP) is an effective treatment for de novo stage IVa thymoma (DNT) and thymic carcinoma (TC) and for thymoma with pleural relapse (TPR).

Methods: A retrospective study was conducted of patients undergoing resection and HPCP in 1 center. HPCP with cisplatinum ± doxorubicin (adriamycin) was performed for 60 minutes using a standard roller pump and a modified heat exchanger to a maximal intrapleural temperature of 43°C. Follow-up included at least 1 annual computed tomographic scan until death or March 2012.

Results: Thirty-five patients, 17 DNT, 14 TPR, and 4 TC, completed 42 intended treatments and were followed up for 4 to 202 months (median, 62 months). Seven patients had repeated HPCP at an interval of 2 to 12 years. There was no systemic toxicity. Ninety-day mortality was 2.5%. Major and minor morbidity occurred in 12% each. Five-, 10-, and 15-year overall survivals for DNT, TPR, and TC were 81%, 73%, 58% (DNT), 67%, 56%, 28% (TPR), and 0%, 0%, 0% (TC). Five- and 10-year progression-free survival was 61%, 43% for DNT and 48%, 18% for TPR. Presently, 11 of 17 DNT patients are alive (6, no evidence of disease), and 8 of 14 TPR are alive (6, no evidence of disease). Median survival for thymoma was 157 months. Overall survival was unrelated to any preoperative or intraoperative variable. Progression-free survival was improved in R0 compared with R1-2 resection ($P < .001$). Local control achieved in 21 (57%) of 37 procedures in thymoma patients was related only to completeness of resection ($P = .015$).

Conclusions: (1) Lung-sparing resection and HPCP is feasible and safe. (2) In thymoma with pleural spread it offers excellent survival despite moderate pleural control. (3) Preliminary results with stage IVa TC are disappointing. (J Thorac Cardiovasc Surg 2013;145:83-9)

Thymic epithelial tumors (TET) are relatively uncommon neoplasms, the majority of which are discovered in early operable stages. About 7% of thymomas present at de novo stage IVa thymoma (DNT) and are associated with 5- and 10-year survivals of 59% and 36%, respectively.[1] Thymic carcinoma (TC) is a rare tumor, presenting usually at advanced stages and associated with a poor prognosis. Although the relapse rates for stage I-III thymoma are relatively low,[1] more than 50% of these occur in the pleural space (thymoma with pleural relapse, TPR) and thereafter have an unfavorable fate.[2,3]

The literature pertaining to TET with pleural spread, whether de novo or recurrent, is limited. The condition has been treated with chemotherapy alone[4] but, more often, in a multimodality manner that almost always includes surgery.[5,6] The surgical arm varies from debulking[7,8] to radical and, occasionally, as extensive as pleuropneumonectomy[9,10] or extrapleural pneumonectomy.[11,12] Owing to the small cohorts of TET with pleural spread and the versatility of treatment options, the preferred approach for this condition has not been established.

Dissatisfied with the reported results and our own experience and learning from experience with pleural chemotherapy in mesothelioma and malignant effusions,[13-15] we embarked as early as 1995 on a new management protocol consisting of surgical resection plus heated pleural chemoperfusion (HPCP). Preliminary reports with a small group of patients were reported in 2001.[16,17] The current study aims to analyze the operative results and the long-term outcome of a relatively large cohort in an attempt to verify whether it could be recommended as an acceptable treatment for TET with pleural spread.

PATIENTS AND METHODS

Included in this study are all patients with TET and pleural spread who underwent surgery plus HPCP since 1995. They were either referred

From the Departments of Thoracic Surgery[a] and Pathology,[b] Sheba Medical Center, Tel Hashomer, Israel.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Read at the 92nd Annual Meeting of The American Association for Thoracic Surgery, San Francisco, California, April 28-May 2, 2012.

Received for publication March 26, 2012; revisions received Sept 13, 2012; accepted for publication Oct 2, 2012; available ahead of print Oct 29, 2012.

Address for reprints: Alon Yellin, MD, Department of Thoracic Surgery, Sheba Medical Center, Tel Hashomer, Israel 52621 (E-mail: ayellin@sheba.health.gov.il).

0022-5223/$36.00

Copyright © 2013 by The American Association for Thoracic Surgery

http://dx.doi.org/10.1016/j.jtcvs.2012.10.013

Abbreviations and Acronyms
DNT = de novo stage IVa thymoma
HPCP = heated pleural chemoperfusion
TC = thymic carcinoma
TET = thymic epithelial tumor
TPR = thymoma with pleural relapse

selectively by other institutions or taken from our own pool, in which case all patients with pleural spread were discussed in a multidisciplinary meeting. Patients (n = 2) with major chest wall involvement were considered unsuitable for this treatment. Data were acquired from a prospective database and, when necessary, admission charts were pulled and reviewed. Follow-up information was gathered from outpatient records, telephone conversations, and the national demographic registry. The study was approved by the institutional ethics committee and the off-label use of the chemotherapeutic agents by the institutional pharmacologic board.

Follow-up was scheduled at 6-month intervals and computed tomographic scans were performed at a minimum of 1 annually. Other studies like positron emission tomography–computed tomography, magnetic resonance imaging, octreotide scans, and biopsy were ordered on an individual basis.

Histologic material was revised by an experienced thoracic pathologist (M.P.) using hematoxylin and eosin stain and classified according to the 2004 World Health Organization. ''Mixed thymomas'' were designating by the predominant cell type, which comprised more than 50% of the submitted sections.

The number of pleural implants (from 2 to infinite) and the total implant volume (1-350 mL^3) were recorded for every procedure.

Preoperative and Postoperative Treatments

All of the TC patients and 13 of the 31 thymoma patients received chemotherapy at some point before HPCP, with a response rate of 88%. We have not used chemotherapy intentionally in a neoadjuvant setting. Full details as to the exact agents and doses are lacking, inasmuch as those were administered in many institutions. Radiation therapy was used in 8 TPR patients after their initial operation.

Adjuvant chemotherapy was administered to patients with TC or to thymoma patients with pleural R2 resection. Adjuvant radiotherapy was used in DNT patients with R1-R2 resection of their mediastinal component. In other patients, these modalities were reserved for the management of local or systemic relapses on an individual need to treat basis.

Surgical Approach

Surgery was aimed toward complete resection of any mediastinal involvement and gross resection of all pleural disease. Partial pleurectomy was performed mainly on the chest wall pleura. Diaphragmatic implants were removed along with partial muscle thickness when required. Visceral pleural implants were removed locally or by wedge excision. Pneumonectomy was avoided as far as possible. In this report R1 and R2 resection were grouped together as incomplete resection.

Chemoperfusion

Perfusion was performed in a routine manner described by us previously.[13] In essence, it was done in the supine position after final closure of the incision, using 2 28F chest tubes connected to a standard roller pump and a heat exchanger, which was modified in 1999 to allow an output of 45°C. The amount of perfusate varied from 1500 to 3500 mL. The perfusion was initiated without the chemotherapeutic agents. When the temperature stabilized, 100 mg/m^2 of cisplatinum and since 2002 also a 50 to 60 mg total dose of doxorubicin were added. Perfusion was carried out for 60 minutes at a flow of 1000 to 2500 mL/min. Pleural temperature was considered as the mean of the input and output temperatures as determined by earlier studies with an intrapleural temperature probe. Flow rates were adjusted as required to maintain the set temperature and hemodynamic stability. Renal protection was accomplished with adequate preperfusion hydration and maintaining a urine output of more than 80 mL/h.

On 2 occasions, HPCP was delayed for a few days owing a very lengthy operation associated with hemodynamic instability.

Statistical Analysis

Survival analysis was performed by the Kaplan-Meier method and was calculated from the date of the first HPCP using SPSS software (SPSS, Inc, Chicago, Ill). We used the term disease-free progression rather than disease-free survival because it is doubtful whether R0 resection can indeed be achieved in stage IVa TET unless extrapleural pneumonectomy is performed. For morbidity and mortality figures the denominator used was the number of operations. To examine combined effects of various factors on overall and progression-free survival and on local control, we used nonparametric tests, that is, χ^2 and Mann-Whitney.

RESULTS

Forty patients were considered for surgery and HPCP. Five were rejected: 2 owing to TC histology (after midterm analysis of the early experience), 2 because of major chest wall involvement, and 1 intraoperatively owing to complete macroscopic and microscopic pleural response. The remaining 35 patients were divided into 3 groups: TC (n = 4), DNT (n = 17), and TPR (n = 14). The demographic and clinical parameters are summarized in Table 1. The majority of thymoma patients had B2 histology and 15 (48.4%) had myasthenia gravis at diagnosis.

Reoperation was performed in 11 patients with disease progression, of whom 4 did not continue to HPCP owing to liver metastases (n = 1), minute space (n = 1), single implant (n = 1), and hemodynamic instability (n = 1). The data pertaining to these 7 patients (redo HPCP) were added to Table 2, which summarizes the surgical and perfusion results. As a group, they were obviously older (mean age, 55 years) than the 35 ''original cohort.''

Mortality and Morbidity

The 90-day mortality was 2.5% (1 patient) owing to empyema complicating a redo operation 14 years after the initial HPCP. Another patient died 11.5 months after pneumonectomy, superior vena cava resection and reconstruction, and partial resection of both atria from a bronchopleural fistula. Nonfatal complications occurred after 11 procedures: DNT, 3; TPR, 4; TC, 2; and redo, 2 (27%), including grade III/IV nausea (n = 3), prolonged air leak (n = 2), bleeding requiring reexploration (n = 1), and pneumonia (n = 1), all occurring in the early postoperative period. Delayed morbidity consisted of myasthenic crisis (n = 2), chronic respiratory failure (n = 1), and purulent pericarditis with sepsis (n = 1). The later was the sole patient who had supraventricular tachycardia.

Download English Version:

https://daneshyari.com/en/article/5991277

Download Persian Version:

https://daneshyari.com/article/5991277

Daneshyari.com