Does Primary Pulmonary Choriocarcinoma Really Exist?

To the Editor:

We read with interest the article by Tsai et al (March 2002), but several points make us doubtful about the diagnosis of primary pulmonary choriocarcinoma, as follows:

1. There is no comment concerning the technique (physical examination? ultrasonography? CT scan? MRI? other?) adopted to exclude for certain that the patient had no testicular lesion. Moreover, it is well known that the “burnt-out” phenomenon occurs in germinal tumors in general, and in choriocarcinoma in particular. Choriocarcinoma is likely to metastasize greatly prior to detection of the primary lesion, leaving only zones of scarring and hemosiderin-laden macrophages in the testis.

2. Chest radiographs and CT scanning displayed bilateral pulmonary involvement by ground-glass opacities and nodules, showing many clinicoradiologic similarities with the previously report by McGowan et al, who described a testicular choriocarcinoma with pulmonary metastases presenting as ARDS. These authors correctly underlined that only at autopsic examination, “the right testicle was essentially replaced by choriocarcinoma but was the same size as the uninvolved left one.”

3. We have investigated two solitary pulmonary nodules in adult men (one of whom presented with gynecomastia) showing a dimorphic neoplasms characterized by polygonal mononuclear cells closely admixed with multinucleated syncytiotrophoblast-like cells in a hemorrhagic and necrotic background, thus sharing many morphologic features with a choriocarcinoma. Both tumors displayed a nuclear immunoreactivity for thyroid transcription factor (TTF)-1, the best immunohistochemical marker of pulmonary origin. Although a weak cytoplasmic immunostaining for 

4. Finally, it is well documented that many nontrophoblastic malignancies may produce and/or express ectopic placental hormones, including primary conventional lung carcinomas. Granted the diagnosis of pulmonary choriocarcinoma is debatable and far from being clarified, the authors recommended the use of a urine pregnancy test as a rapid diagnostic method of primary pulmonary choriocarcinoma. We retain that a more detailed and rigorous clinicopathologic analysis should be preferred before one can establish such a diagnosis.

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REFERENCES

3 McGowan MP, Pratter MR, Nash G. Primary testicular choriocarcinoma with pulmonary metastases presenting as ARDS. Chest 1990; 97:1258–1259

Observation-Only Management of Inoperable Lung Cancer

Do Not Do That: A Loud and Clear Radiographic Point of View!

To the Editor:

We have read with interest the recent article in CHEST by McGarry et al (April 2002) on three different treatment options in 128 patients with early stage non-small cell lung cancer (NSCLC). Although the authors acknowledge the limitations of their retrospective study, which showed no advantage for radiation therapy (RT) over observation only, we believe that additional aspects need to be brought to the attention of the readership of the journal, so as to leave no doubts regarding treatment choice in this patient population. These aspects are as follows:

1. More information about differences between the treatment groups regarding various pretreatment characteristics should have been disclosed, principally regarding patients’ refusal to surgery (14 refusals in the observation-only group vs no refusal in RT group; reason for radiotherapy referral not specified in 7 patients in the RT group). This may have seriously imbalanced prognosis, since it was shown that patients’ refusals inversely correlate with the incidence of intercurrent deaths, which, on the other side, directly correlate with increasing age and pre-existing comorbid-
ity.\textsuperscript{5,6} Also, it is not clear whether patients were staged as having early NSCLC both initially and immediately before RT administration. If they were treated with RT because of symptom progression (majority of RT group), then they may have not been at an early stage before RT administration at all, but rather placed into a locally advanced group, which additionally undermines the effectiveness of RT.

2. While McGarry et al\textsuperscript{2} offer actuarial analysis using survival as an end-point, this patient population is notorious for having excessive cancer-unrelated deaths. It is mandatory, therefore, to have other end-points, such as cause-specific survival, to correct for these events. Indeed, when 5-year cause-specific survival/disease-specific survival rates in the RT series were reported,\textsuperscript{5-7} they were usually twice as high as rates of overall survival in the same studies, the difference being approximately 10\% vs 20\%. Also, no causes of death were offered in surgical patients who were younger and had smaller tumors and better lung function than RT patients. To extend this, perhaps patterns of failure and/or other end-points, such as local recurrence-free survival or distant metastasis-free survival, may have helped to gain better insight into possible differences in the treatment outcome.

3. Other issues may well have been quality-of-life and/or economic issues, because it is not unrealistic to expect that observation-only patients should have had more symptoms (best supportive care) treatments, which are often prolonged and more expensive than RT alone. Additionally, information on postoperative treatment morbidity/mortality in this largely geriatric population is lacking, as well as RT-related toxicity, particularly with different RT regimens used and observed inconsistencies even within palliative RT.

It seems, therefore, that the somewhat inferior results obtained with RT, and particularly with high-dose RT, may be explained at least in part by an RT population that clearly has poor prognoses, as evidenced by low-RT doses frequently used, and most likely has higher stages of the disease. Thus, any reliable comparison to both observation-only and surgical group is almost impossible.

Finally, the authors state that local field RT is a standard RT approach in this disease. This is not so. First, there is not a single prospective randomized study evaluating the issue of optimal RT held in this patient population. Second, the studies achieving the best results are actually those using some elective nodal RT, that is, inclusion of uninvolved ipsilateral hilum and/or ipsilateral mediastinum,\textsuperscript{2-4} which can be seen as the radiotherapeutic equivalent of lobectomy.

Numerous studies have clearly documented the effectiveness of RT alone in this disease, with median survival times of >30 months and a 5-year survival rate of >30\%,\textsuperscript{2-7} going up to 40\% in T1N0 patients.\textsuperscript{8} This should assure referring physicians that we can offer our patients a “best treatment approach” which, we believe, in technically operable but medically inoperable early stage NSCLC, is RT alone. We are opponents, not advocates, of “therapeutic nihilism” in treating this disease and in this patient population. As we have observed the increase in patient numbers in recent years, discovery of successful treatment options must become one of our top priorities in the near future.

\textbf{References}


To the Editor:

Thank you very much for allowing me to comment. I would like to take the opportunity to clarify some points raised in this review.

1. With respect to the various pretreatment characteristics between the groups, all patients at the Richard L. Roudebush VA Medical Center are assessed in both pulmonary medicine and surgery departments prior to a treatment decision. It often seems the case that these decisions occurred prior to patient presentation at the multidisciplinary chest conference attended by all the other services involved in the delivery of care. Patients who refused surgical treatment were not usually seen by the radiation therapy service to discuss this option.

All patients were staged according to the American Journal of Critical Care staging criteria by the multidisciplinary chest conference at the time of diagnosis and were entered as such into the institutional tumor data base. Dr. Jeremic raises an important point. Indeed, many of the patients classified as early stage lung cancer did not reach our service until their cancers had progressed to the point of requiring palliation; therefore, our estimation of mortality due to lung cancer for those who received no treatment early in their disease is an underestimate of the total misery resulting from observation.

2. Cause of death was obtained from the tumor registry that recorded the International Classification of Diseases, Ninth Revision code from death certificates. The detailed records of these patients, including patterns of failure, would be exceedingly hard to obtain. Indeed, a prospective study would likely provide better and more comprehensive information on patterns of failure and cause-specific survival, but it is unlikely that any such study will ever be attempted. The main point we can derive from our work is that many of these patients died of their cancers, many required palliation by radiotherapy resulting from progression of their early stage cancers and, in my opinion, observation or “best supportive care” is not the best strategy for management of these patients when radiotherapy can be delivered safely and effectively.

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