Defining the Role of Hemithorax Irradiation for Thymomas Is Difficult

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Sugie et al. evaluated postoperative mediastinal radiotherapy (MRT) for invasive thymoma with low-dose entire hemithorax radiotherapy (EHRT) for pleural dissemination. This was done to clarify the role of EHRT.

Following removal of disseminated lesions, EHRT was given to 12 patients with pleural dissemination using doses of 11.2 to 16 Gy in 7 to 10 fractions (mean dose: 14.1 Gy). This was given in addition to MRT which included 30 to 64 Gy (mean: 44 Gy) depending on the extent of the disease. They treated 52 patients with MRT alone and eight with EHRT + MRT. Of these eight patients, seven had stage IVa disease and one had stage II disease with tumor spillage at the time of resection. They also gave EHRT to another four of these patients who later developed pleural dissemination. Twenty-four of the 60 (40%) patients also received chemotherapy.

Survival was associated with the Masaoka stage ($p = 0.048$) and extent of resection ($p = 0.0046$), but not the extent of radiotherapy (RT). The pleural control rate for stage IVa patients was relatively high (71% at 3 years) in patients undergoing EHRT + MRT compared with 49% in those receiving MRT alone, although this difference was not significant ($p = 0.38$). Overall survival and local control rates did not differ significantly based on extent of RT. Severe (grade $\geq 3$) RT related toxicity occurred in 1 (2%) of the 52 patients who received MRT compared with 1 (8.3%) of the 12 patients who received EHRT + MRT.

The authors conclude that new radiation techniques like intensity modulated radiotherapy (IMRT) would improve the outcome by increasing the dose and reducing the possibility of radiation pneumonitis. IMRT has been used widely in the United States since the year 2000. The basic concept is to tightly conform the RT to a target by the converting a single radiation field of a uniform intensity to a field composed of many tiny subfields, each with its own intensity. Thus, the intensity of radiation varies across the field. Many radiation beams (often $\geq 7$) all coming from different angles of attack are added together to deliver the dose. IMRT allows one to create dose plans that tightly wrap radiation around targets. IMRT has allowed radiation oncologists to administer greater doses of RT more safely than three-dimensional RT. IMRT is dependent on a high level of computer technology only recently available. However, even if one could administer a greater dose more safely to the periphery of the thoracic cavity with IMRT, it may not completely address thymoma cells floating in the pleural fluid. To spare lung from radiation using IMRT, one would need to spare the pleural space within the lung fissures. It is quite possible these portions of the pleural space would act as a sanctuary for thymoma cells disseminated in the pleural space. However, despite this concern, more research is warranted using IMRT to see whether it can be more successfully used for thymomas than other RT systems. Sugie et al. recommended EHRT + MRT for patients with nonextensive pleural dissemination and good postoperative pulmonary function using a multidisciplinary approach. Based on their data, one can question the value of this approach because EHRT was not shown to significantly improve survival nor decrease toxicity.
However, this is not the entire story of EHRT use for thymomas. M. Uematsu et al. evaluated prophylactic EHRT in addition to MRT following a complete resection of stages II and III invasive thymoma. Forty-three patients had a complete surgical resection and then received EHRT + MRT or MRT alone. In most cases, EHRT was 15 Gy/15 fractions over 3 weeks (without inhomogeneity corrections). In both the EHRT + MRT and MRT group, the total radiation doses to the mediastinum were similar with a median of 40 Gy. Only one of the 23(4%) patients with EHRT+MRT relapsed compared with eight of the 20(40%) with MRT. The pleura was the most common site of failure. At 5 years, the relapse-free rate was 100% for those receiving EHRT+MRT compared with 66% with MRT ($p = 0.03$). The overall survival rate was 96% for those with EHRT + MRT compared with 74% for those with MRT ($p = $ not significant). The only significant treatment-related complication was radiation pneumonitis requiring treatment in one (5%) of the 20 patients who received MRT and three (13%) of 23 who received EHRT + MRT. They concluded that except for elderly patients (who they felt were predisposed to toxicity), “EHRT + MRT following a macroscopically complete resection appeared to be safe and feasible, and reduced intrathoracic relapses.”

Yoshida et al. evaluated 11 thymoma patients with thoracic dissemination and less than complete resection. RT was administered postoperatively in all patients. RT doses ranged from 10 to 17 Gy to the entire hemithorax of the disseminated site and from 30 to 55 Gy to the primary tumor bed. Chemotherapy of various types was administered prior to RT in 7 cases. The 5- and 10-year survival rates were 80 and 64%, respectively. Six of the 11 patients were free from recurrence with a median follow-up of 60 months. EHRT was suggested as postoperative or definitive treatment for most patients with pleural spread of thymoma.

Thus, it is difficult with the available data to be show that EHRT + MRT significantly improve the survival of patients who have had complete resection compared with MRT alone based on the studies of Sugie et al. and Uematsu et al. However, for patients who have had less than a complete resection, EHRT + RT appear to salvage a large fraction of patients with pleural dissemination. Based on the large French Experience of Cowen et al., four factors were associated with poorer survival: mediastinal compression on presentation ($p < 0.001$), absence of chemotherapy ($p < 0.001$), biopsy alone ($p = 0.003$), and young age ($p = 0.013$). Thus, an overall treatment plan should integrate resection (which should be as complete as possible) with RT for given invasive thymomas going beyond the capsule, and chemotherapy used for those with advanced disease (stage III-IVa disease and mediastinal compression on presentation). Chemotherapy and/or RT can also be used preoperatively to potentially improve resectability.

REFERENCES