AB010. Management of locally advanced thymic malignancies

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Abstract: Surgical resection has been the mainstay for the treatment of thymic malignancies, probably because most of these tumors are relatively indolent in nature. Even if complete resection could not be accomplished, volume reduction surgery such as tumor debulking together with adjuvant radiation to the residual lesion may still be associated with prolonged survival of the patients. Therefore, upfront surgery has long been a common practice in the management of thymic tumors. Even so, incomplete resection would without doubt lead to dismal prognosis, like in most solid tumors. In the Chinese Alliance for Research in Thymomas (ChART) database study, radical resection rate was only 72.6% in Masaoka stage III diseases as opposed to 99.7% in stage I and 95.4% in stage II tumors. It is thus not surprising that 10-year overall survival was merely 64.8% in stage III patients, while in stage I and II they were as high as 94.3% and 89.8%, respectively. And complete resection, together with Masaoka staging and WHO histology subtype, turned out to be the three main prognostic factors for thymic tumors. It is understandable to sort to adjuvant therapies in hope of improving the unsatisfactory outcomes after upfront surgery in stage III thymic tumors. Unfortunately the two ChART multi-center cohort studies on post-operative chemotherapy and radiotherapy failed show any benefit from adjuvant therapy in locally advanced diseases after surgery. Although adjuvant radiation is still recommended by current guidelines, it should be bear in mind that these suggestions are based on low-level evidences and that there has never been any strictly designed studies to prove its efficacy. A reasonable solution would be shifting from post-operative adjuvant treatment to neoadjuvant therapies before surgery, with the hope that effective induction could downstage the tumor and increase the chance of complete resection. According to the ChART retrospective database, although only a small percentage of patients (12.1% in stage III & IV tumors) received induction therapies, 25% of them had their tumors downstaged, leading to 93.8% survival rate in this subgroup. But up till now, standard induction approaches have not yet been established, probably due to the rarity of the disease. A previous retrospective study comparing different treatment modalities for inoperable thymic tumors at the Shanghai Chest Hospital has shown that concurrent chemoradiation had the highest response rate (87.5%) and thus the best 5-year survival (61.9%) comparing to sequential chemoradiation or radiation alone. Based on these results, a phase II trial on neoadjuvant chemoradiation (two cycles of cisplatin and paclitaxel chemotherapy together with 36–40 Gy IMRT) for potentially unresectable thymic tumors yield satisfactory results. Overall response rate was as high as 79%, with 58% of the lesions downstaged after induction. Complete resection was achieved in 85.7% cases, with a 33% complete response rate upon histological examination. A 65.8% survival rate was achieved in these patients with originally unresectable tumors. On the other hand, Masaoka stage III is a heterogeneous group of tumors ranging from readily resectable diseases (equals to IASLC/ITMIG T2–3, such as limited invasion into the pericardium or lung), to basically unresectable lesions (IASLC/ITMIG T4, invading into the heart or great vessels such as the pulmonary artery and aorta). While minimally invasive surgery has been increasingly used in the management of early stage thymic tumors, its role in locally advanced diseases has yet to be investigated. After the ChART has recently proved the oncological efficacy of minimally invasive thymectomy for IASLC/ITMIG stage I tumors through a multi-center cohort study, similar results was found in stage II and III tumors through a propensity score matching analysis in patients treated at the Shanghai Chest Hospital. Complete resection rate turned out to be similar in both minimally invasive and open surgery groups, with comparable survival and recurrence rates. This suggests that the benefit of minimally invasive surgery may still be expected in well selected group of patients with invasive tumors. So for locally advanced thymic malignancies, the IASLC/ITMIG staging system is more useful in differentiating those resectable or unresectable diseases and help selecting candidates for upfront surgery. And for those potentially unresectable tumors, effective induction (especially concurrent chemoradiation) may offer the best chance for tumor downstaging and hitherto improved outcome.

Keywords: Thymic tumor; multimodality therapy; surgery

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