



Thymoma Recurrences: Aiming for Optimal Treatment

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Editorial

Thymomas are usually considered as low-grade malignant tumors with slow-growing and indolent natural history. However, in up to 33% of cases, they behave aggressively, penetrating the capsule and extending into mediastinal fat, and adjacent organs such as pleura, pericardium, lung, chest wall and great vessels [1]. Surgical resection is presently considered the gold standard for the treatment of thymomas regardless of the histological type. The mainstay of thymoma treatment is to achieve complete macroscopic resection and microscopic clearance, by removing en bloc all the involved tissue. Many studies have demonstrated that complete resection of the thymomas has a significant effect on long-term outcome [1-5]. Although, even when complete resection is achieved, recurrence occurs in about 10% to 29% of patients [6-8]. A standardized uniform set of definitions for thymoma recurrence is lacking. The International Thymic Malignancy Interest Group (ITMIG) defined the term “recurrence” appropriate when after an R0 resection or a complete radiographic response have been previously achieved, and an adequate 5-10 years follow-up has been carried on [9]. Recurrences affect subsequent treatment and final outcome and there is still no general consensus on how to manage them [8,10,11]. Complete resection of recurrences should be attempted whenever possible to achieve a long term-survival and when complete resection is not feasible an iterative debulking may improve survival by reducing the size of these slow-growing tumors. Although extensive surgery has been also proposed by some Authors in case of thymoma recurrence [10], a uniform consent is not present in the literature [12]. In 1997, before the introduction of the WHO classification, Regnard reported a 10% recurrence rate in a series of 285 patients who had undergone complete thymoma resection. Most of the recurrences were intrathoracic and resectable; only two patients had concomitant extra thoracic metastases [13]. Even in our experience, 75% of the patients (9 out of 12) had intrathoracic recurrences and only three patients had concomitant extra thoracic metastases and all of them had undergone complete thymoma resection [11]. Analyzing our data, it raised that the 3 patients with concomitant extra thoracic metastases were also the only ones to have been undergone more than one surgery for recurrences, probably remarking a more aggressive behavior of the tumor. Histological subtyping has animated discussions during the last decade and it has recently been suggested that the cortical differentiation of the tumor is related to a higher degree of malignancy and consequently with a worse survival [1-4]. In their retrospective study, Ciccone et al [14] report that all the recurrences in their series occurred in cortical differentiated thymomas (B1, B2 and B3 subtype according to the WHO histological staging system), which may point to an adverse prognostic role of these histological subtypes. Besides, a histological change was noted between primary tumors and the recurrences in about 45% of the patients, mainly towards a higher malignancy, within the cortical differentiation subtypes. In our experience we also noticed that 10 out of the 12 patients with thymoma recurrence had a clinical progression to Masaoka stage III and IV regardless of the initial stage, and 2 patients, who were originally stage II and III, remained stable since the recurrence involved respectively the mediastinal fatty tissue in the first case and the lung parenchyma in the second one. Contrary to Ciccone’s data, none of our patients had a histological progression of the disease [11]. Still, there is as yet no well-defined approach to the management of their recurrences, due to the small number of patients in published series [15,16]. Ruffini et al [15] demonstrated that the best option for long-term survival was complete surgical resection of recurrences. When resection was necessarily incomplete, it was related to a poor prognosis even if followed by radiation. Haniuda et al. [17] suggest that an iterative debulking approach should be attempted if complete resection is not feasible, to reduce tumor size and improve survival, considering the slow growth of these tumors. However, local recurrences may also occur in early stage thymoma patients (mainly Masaoka stage I and II) who do not have adjuvant treatment after initial surgery. This reveals that recurrences are likely to occur where microscopic tumor residuals are left in place during surgery [18] and, as some Authors report, adjuvant therapy should also be given to stage I and II thymomas with cortical subtype differentiation, which usually have a poorer prognosis to decrease recurrence rate and to ensure a longer-term survival [14]. Currently,

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the literature shows that a multimodality approach, combining radiotherapy and/or chemotherapy with surgery, may be considered the best treatment for thymomas recurrences [7,11,19], also for early stage thymomas with cortical subtype differentiation, which usually have a poor prognosis [19]. For pleural recurrence the use of argon-beam coagulation has been reported and Maury et al. presented intra-thoracic chemo-hyperthermia in addition to surgical cytoreduction [19,20]. Optimal treatment of thymoma recurrence is not yet defined. Considering the slow progression of the disease, repeated surgery is justified. Intrathoracic chemo-hyperthermia could be considered an option that still needs further data to be supported for thymoma recurrence. Multimodal therapies that combine radiotherapy and chemotherapy with surgery, when feasible, are today widely accepted as a treatment for thymoma recurrences.

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