Editorial Commentary

Rare, rarer, rarest: lessons from the largest retrospective study to date on mediastinal sarcomas

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Physicians concerned with the diagnosis and management of patients with mediastinal tumors are used to the fact that they have to rely on hardly any secured data and little evidence-based knowledge for their decisions. But even by these standards, primary mediastinal sarcomas are extremely rare tumors that account for no more than 5% of mediastinal neoplasms. Less than 1% of soft tissue sarcomas are located in the mediastinum.

Therefore, a recent study published by Engelhardt *et al.*, in The *Annals of Thoracic Surgery* (1) is an unprecedented effort to gather and organize available information on mediastinal sarcomas. Taking advantage of the National Cancer Database (NCDB), one of the largest cancer registries worldwide, the authors were able to analyze retrospective data of 976 patients with mediastinal sarcomas. The limitations of such studies are well known and weigh heavily, since they have the potential to erroneously bias our conception and approach to a given disease. However, in the case of extremely rare cancers, such data are probably the best one can expect in a long time. Searches in cancer registries make it necessary to categorize and to simplify variables and are heavily dependent on the accuracy of the input, which may explain some surprising findings of the study, such as the fact that liposarcomas, a group that made up a substantial or even the predominant proportion in most previous studies (2), are not mentioned at all. This may in part be explained by the exclusion of thymic tumors from the dataset, where these tumors are frequently located. Similarly, the frequency of sarcoma subtypes is almost certainly skewed by the inclusion of cardiac sarcomas, which may explain why angiosarcomas were the most common histological subtype in this study. Setting such details aside, the authors have generated relevant and robust information, which will help define the major lines guiding the therapeutic approach to mediastinal sarcomas. Not surprisingly, five-year overall survival was poor (14.8%) for the entire cohort and only slightly better for younger patients with fewer comorbidities. In this largest study to date, the results clearly confirm previous findings from other studies that radical surgery with R0 margins is the only curative approach and is superior to all other treatment modalities (3-5). A combination of surgery followed by radiation resulted in the best overall survival, while the benefit of chemotherapy remained unclear (similar to the situation in other anatomic locations) (6-8). The impact of surgery is also highlighted by the fact that even debulking surgery (R1/R2) resulted in better five-year overall survival than non-surgical treatments (radiation and/or chemotherapy) (1).

It should be noted in brackets that the listed entities in this study (angiosarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumor, sarcoma not otherwise specified) all belong to the unfortunate group of tumors that have so far not benefited from precision medicine, in contrast to some other soft tissue sarcomas such as gastrointestinal stroma tumors (GIST) (9) or inflammatory myofibroblastic tumors (IMFT) (10), to name a few. In summary, while the mediastinum may be a

highly challenging anatomical compartment, mediastinal sarcomas seem to follow the general rules elsewhere in the body with respect to treatment. From the data presented by Engelhardt *et al*., it appears safe to conclude that radical surgery, in combination with radiotherapy, is currently the best hope for cure. This general statement should not ignore the possibility that specific single entities with targetable molecular alterations might well benefit from recent developments in precision medicine and immunotherapy.

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