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LETTER TO THE EDITOR

Proper tumor classification and growth rate are key elements when considering indications and results of radiotherapy for head and neck paragangliomas

Dear Editor,

We read with great interest the article "Paraganglioma of the head and neck region, treated with radiation therapy, a Rare Cancer Network study" by Lassen-Ramshad et al.[1] Having one of the largest series of tympanojugular paragangliomas in literature, we would like to comment on a few issues raised in this article.

A major drawback of this study regards tumor characterization, as clinical implications and management greatly differ based on extension and localization. In reference to table 1, we found great heterogeneity in tumor characteristics and location: 30% are carotid body and 70% tympanojugular paragangliomas. Of the latter type, 16% are Fisch class A and B. These are tympanic and tympanomastoid tumors that can be treated surgically by expert otologists with standard approaches, like radical mastoidectomy or subtotal petrosectomy, with almost no complications, preserving inner ear function and offering the patient a complete cure.[2] In these cases, radiotherapy (RT) should not be indicated. Of note, 59% were Fisch class C and D. First of all, these are not separate classes but rather describe the involvement of different structures, namely the intrapetrous carotid artery (class C), and intracranial extension (class D). Class C tumors should be subclassified into C1-4 subcategories, as C1 and C2 tympanojugular paragangliomas can also be treated surgically with total excision via infratemporal fossa approach type A. This treatment has very low morbidity and preserves inner hearing and lower cranial nerve function.[3,4] Moreover, if the median tumor size reported for jugulotympanic lesions is 30 mm, it is reasonable to assert that at least 50% of all these tumors were small.

Similarly, carotid body tumors should be described according to the Shamblin classification. These can be managed by surgery alone, as stated in the article. In the hands of expert surgeons, it is possible to achieve complete removal with little intraoperative and postoperative risk, with or without preoperative carotid stenting and/or embolization.[5] It would have been interesting to know which factors influenced the choice of a radiotherapeutic treatment instead of a surgical approach.

Furthermore, an additional 21% were of unknown or not applicable classification, and tumor size is reported as unknown in 16 lesions. The article also does not report any volume, wait and scan data, or progression/growth rate before RT: how can local control be assessed in the absence of these parameters? Given the tendency for very slow progression of paragangliomas, with a median follow-up of 48 months, it is likely that the successful outcome of RT is overestimated. In a previously published series of class C and D TJP managed with wait and scan, we found no tumor growth or regression in 92% of the patients after 36 months of follow-up, in 83% after 60 months of follow-up, and in 45% after a follow-up longer than 60 months.[6]

The article states that 44% of the patients received RT after partial or radical resection. However, data on residual or recurrent disease are not clear; growth rate or, most importantly, malignancy are not reported. Only 4 of 82 lesions are reported as malignant, but it is not specified whether these cases are included in this series.

In table 1, it was reported that 21% of the lesions underwent radical surgical resection before RT. The term "radical resection" contradicts the need of subsequent RT, especially considering the benign nature of most paragangliomas. Why is adjuvant RT justified in these cases?

According to table 5, seven patients did not show macroscopic tumor present at the time of RT. These patients should be left out from the series, because of the impossibility to assess local control and successful result.

Furthermore, 37% were young individuals less than 40 years old; in this study, 80% of patients with a follow-up longer than 20 years showed disease progression. Given the current life expectancy and the general good health status of younger patients, why was RT the treatment of choice, considering the higher risks and morbidity of salvage surgery in case of disease progression? What should be the management for long-term relapse after RT in young patients?

RT can only offer tumor stability without complete cure, along with the possibility of developing secondary neoplasms or malignant transformation. Even though mostly reported as mild, acute and late toxicity rates are considerable (43% and 21%, respectively), with five severe cases. On the other hand, properly planned and executed surgery can achieve complete tumor removal regardless of extension and localization, with

low perioperative risks and morbidity, particularly in case of smaller masses.

All these elements have to be carefully considered in the decision-making process for younger patients, also keeping in mind the necessity of life-long surveillance scans and the psychological burden caused by living with the knowledge of having a residual tumor.

RT was considered in the past as a valid alternative because of the high morbidity associated with surgery, but in light of the technical advances made in the last two decades, the indications for surgery have expanded. Appropriate patient selection and description, and detailed tumor classification is key when evaluating the results from RT treatment.

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