

Sinonasal neoplasms again

Sinonasal neoplasms are uncommon neoplasms, accounting for only 1% of all malignancies and only 3% to 5% of all head and neck malignancies. In 2010, *Rhinology* published the European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base ⁽¹⁾. This issue of *Rhinology* again contains interesting new data on tumours in the nose and sinuses and raised my interest in potential role of external (occupational) factors that may influence the pathophysiology of sinonasal disease.

The first paper I would like to emphasize is the paper of Jangard and colleagues on the increased prevalence of primary sinonasal malignant melanoma in Sweden ⁽²⁾.

Primary sinonasal tract mucosal malignant melanomas are extremely rare, accounting for between 0.3% and 2% of all malignant melanomas and about 4% of head and neck melanomas. The incidence of cutaneous melanoma is increasing over time. This trend is usually attributed to increased sun exposure, however, it is also possible that improved detection has played a role. There are only very limited data on the incidence of nasal mucosal melanoma. Very recently, a USA paper showed a significant increase in nasal mucosal melanoma from 1987 to 2009 with an annual change of 2.4% ⁽³⁾. Now that observation is confirmed by the data of Jangard et al. showing an average annual age-standardized incidence per million population for females to increase from 0.54 1960-1964 to 1.08 during 1995 - 2000. The corresponding figures for males were 0.25 and 0.67, respectively. Of course this increase cannot be attributed to increased UV exposure. When going to the literature several etiological agents for sinonasal melanoma have been proposed, including tobacco exposure, occupational exposure to formaldehyde and infection with the human papilloma virus (HPV), none of which are thought to be important risk factors for the development of cutaneous melanoma. Recently, Hasegawa showed that HPV infection is involved in the pathogenesis of inverted papilloma, and that high viral load and integration of HPV have an important role in malignant lesion in association with inverted papilloma ⁽⁴⁾. Most of these factors have also been described for other sinonasal tumours and suggests a common factor ⁽¹⁾. However, a clear factor that can explain the increase of these tumours has not been identified.

Also in this issue of the journal, Bonzini et al. describes the prevalence of occupational hazards in patients with different

types of epithelial sinonasal cancers ⁽⁵⁾. They conclude that in their case-series of sinonasal cancer, a very high frequency of previous occupational exposure to carcinogens was detected, suggesting that occupational hazards may be associated to the aetiopathogenesis, primarily for adenocarcinoma, but also for other histotypes. They indicate that besides leather or wood, other chemical agents such as solvents, formaldehyde, PAHs, metal fumes must be recognized as occupational risk factors. Also in inflammatory disease not only smoking ⁽⁶⁾ but also occupational hazards have been described in the pathogenesis and persistence of chronic rhinosinusitis ^(7,8). The high concentration of inhaled substances that are filtered by the nasal mucosa might have a significant impact on nasal mucosal disease leading to inflammatory diseases even sometimes to tumours in this area. However, at the moment data are insufficient to point to prevention of these diseases. For now, we can only aim at early detection and treatment.

Surgical treatment of sinonasal tumours can usually be done endoscopically ⁽¹⁾. Even in melanoma, endoscopic resection is the method of choice. Lund et al. compared (endoscopic) resection with or without radiotherapy. They showed a five-year overall survival of 28% and disease-free survival was 23.7%. Endoscopically resected cases showed a significant overall survival advantage up to 5 years. Radiotherapy did not improve local control or survival ⁽⁹⁾. Also, at the present time, no significant improvement in survival can be obtained by systemic and local adjuvant treatment in primary sinonasal mucosa melanomas ⁽¹⁰⁾. However, recent data point to new target for non-surgical treatments showing primary sinonasal mucosal melanomas to be characterized by changes in the PI3K/Akt pathways and show RAS-MAPK and c-KIT pathways mutations. The occurrence of these abnormalities did not represent a prognostic factor in terms of patient survival but might lead to the development of tailored therapies targeting these mutations or inhibiting PI3K/Akt-mTOR pathway for primary sinonasal mucosal melanomas ⁽¹⁰⁻¹²⁾. In this issue of the journal, we have been warned of an increasing prevalence of sinonasal melanoma.

Having evolved from mutilating surgical excision to more refined endoscopic surgery with the same outcome but less morbidity, we can now focus on new molecular and gene therapy to improve the outcome of this devastating disease.

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