Metastasizing “benign” pleomorphic salivary adenoma: A dramatic case-report and literature review

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Article history:
Paper received 4 September 2013
Accepted 3 January 2014

Keywords:
Metastasizing pleomorphic salivary adenoma
Parotid gland tumours
Multiple pleomorphic adenomas

ARTICLE INFO

1. Introduction

Pleomorphic salivary adenomas (PSAs) are the most common neoplasm affecting the salivary glands (Jukić et al., 2012). 90% occur in the parotid. The remainder is found in the submandibular, sublingual, or accessory salivary glands of oral cavity and parapharyngeal space (Cassoni et al., 2013). Surgical excision is the treatment of choice (Zernial et al., 2007) with a low rate of neurological complications (Torretta et al., 2012). Its appearance in childhood is rare and there are no large series available in this age group for comparison with its presentation in adults (Garcia-Perla et al., 2002). PSAs comprise both epithelial and mesenchymal structures and are considered biologically benign (Gnepp, 1991). Occasionally, the epithelial component, in isolation or in conjunction with the stroma, undergoes malignant transformation, giving rise to carcinoma ex pleomorphic adenoma or carcinosarcoma, respectively. These are both aggressive malignant tumours. Very occasionally however, metastatic lesions are identified in patients with a history of PSA, which, on detailed pathological evaluation, are found to exhibit all the histological hallmarks of the preceding benign lesions. This enigmatic entity has been termed the metastasizing pleomorphic adenoma (MPA) (Barnes et al., 2005). Diagnosis of benign metastasizing pleomorphic adenoma of the salivary gland is extremely rare and still under debate.

We present the first case-report in literature of multiple metachronous nasal cavity, scalp and encephalic metastases of a pleomorphic adenoma of the parotid gland in a young girl.

2. Case report

A 10-year-old child was evaluated in January 2008 for a relapse of a pleomorphic adenoma of the left parotid gland (Fig. 1). One year before she had had surgical enucleation of a pleomorphic adenoma localized in the superficial lobe of her parotid gland. In 2008 we performed a parotidectomy with facial nerve preservation. Histologic evaluation revealed a typical morphologic aspect of benign pleomorphic adenoma (Fig. 2).

One year later she was evaluated for left nasal obstruction that had increased over the previous months and hyposmia. Rhinoscopy revealed a small nodule close to the inferior left nasal meatus. No other abnormalities in the nasopharynx, oral cavity, or larynx were described. The neck was clinically negative. Facial nerve function was intact (House–Brackmann scale grade I).

The nodule was removed using an endoscopic approach. Histological examination revealed to be a pleomorphic adenoma and confirmed that the nasal tumour and the recurrent parotid pleomorphic adenoma of our patient had identical morphology (Fig. 3).
One year later the patient, during the routine MRI (Fig. 4) and clinical evaluation, was diagnosed to have a new nodule in the floor of left nasal cavity (Fig. 5) and two scalp nodules.

Endoscopic removal of the nasal nodule (Fig. 6) and surgical removal of the scalp localizations were performed. Histological definitive examination showed the typical biphasic appearance resulting from intimate admixture of epithelium and stroma for all nodules removed (Fig. 7).

A total body TC-PET with FDG was performed in order to exclude other visceral localizations.

Six months later the patient had a head MRI for radiologic follow-up and it showed multiple intracranial nodules (Fig. 8).

3. Discussion

More attention should be devoted to diagnosing metastasis of benign pleomorphic adenoma of the salivary glands. An exhaustive review of the literature disclosed going back to 1942 found 60 cases (Perrin, 1942). Most of the described cases are still controversial. Chen (1978), critically reviewed the literature and concluded that diagnosis could be confirmed in only eight cases, including the case he himself reported (Chen, 1978). In 1998, El-Naggar maintained...
that none of the reported cases were free of doubt on the grounds that atypical histologic features were present in the primary tumours and metastases (El-Naggar et al., 1988). In the opinion of El-Naggar, the cases described by Gerughty (Gerughty et al., 1969) (lack of clinicopathologic information), Youngs and Scheuer (Youngs and Scheuer, 1973) (hepatic carcinoma), Giltman (Giltman et al., 1977) (strong probability of intraoperative seeding), and Wajed (Wajed et al., 1978) (malignant neoplasm) also had to be excluded.

The mechanism underlying the metastatic behaviour of salivary pleomorphic adenoma is still not clear. Because most reported cases occurred after surgical treatment of primary or recurrent lesions of the salivary gland, it has been hypothesized that surgical manipulation may determine tumour-cell dislodgement and vascular implantation with subsequent haematogenous spread. Wermuth (Wermuth et al., 1988) also advanced the hypothesis that metastasis to the lung of pleomorphic adenomas from minor salivary glands of the oral cavity might be due to seeding of aspirated tumour cells. However, a lymphatic metastatic route has also been described (Collins et al., 1989).

Primary metastasizing pleomorphic adenoma localizations included the parotid gland, submandibular gland, minor salivary glands of the palate (Klijianienko et al., 1997), and the nasal septum (Freeman et al., 1990). A review of the literature revealed that most cases had at least one recurrence of primary pleomorphic adenoma before development of metastatic foci. Multiple recurrences before metastasizing proved to be the norm. There was often a long interval between diagnosis of primary pleomorphic adenoma and metastases. Indeed, the metastases were diagnosed from 3 to 52 years after occurrence of the primary lesion (Wenig et al., 1992).

In our case, the first metastasis was discovered 3 years after a primary pleomorphic adenoma of the parotid gland and 1 year after its local recurrence.

The clinical behaviour of these rare lesions does not seem to justify inclusion in a benign category. Assessment of the mortality rate of the cases reported in the literature showed that approximately 20% died as a result of metastatic pleomorphic adenoma (Klijianienko et al., 1997). Nevertheless, the histologic analyses of the reported cases failed to recognize specific parameters (mitotic rate, infiltrative growth, vascular, or lymphatic invasion) of malignancy. Clinical rather than pathologic evidence supports the hypothesis that metastasizing pleomorphic adenomas are an unrecognized malignancy. Biologic behaviour (mortality rate, development of metastatic lesions with a delay of many years after the primary tumour) seems to justify inclusion of metastasizing salivary pleomorphic adenoma in the group of low-grade malignant salivary tumours (Klijianienko et al., 1997).

Surgical excision seems to be the treatment of choice for metastases diagnosed in accessible sites. The value of radiotherapy in the treatment of metastases and in avoiding the development of new metastatic lesions seems to be limited. The limited number of reported cases of metastasizing salivary pleomorphic adenoma makes it difficult to establish a specific follow-up protocol.

Nevertheless, long-term follow-up is mandatory after treatment of a metastatic lesion considering the demonstrated delay in presentation of subsequent metastases. Accordingly, although both MRI and CT can be used to define the margins and extent of the primary tumour, MRI is undoubtedly better in detecting development of any new metastatic lesions. Follow-up is best performed by MRI thanks to its superiority in distinguishing neoplastic tissue from fibrosis in postoperative and postradiation patterns. Considering the biologic behaviour of these tumours, we consider it...
appropriate to start with a 6-month postsurgical MRI examination to allow for small part oedema resolution, followed by MRI examinations at 1-year intervals.

4. Conclusion

To the best of our knowledge, this is the first reported case of parotid pleomorphic adenoma metastasizing to the nasal cavity, scalp and encephalic tissue. It is of paramount, and indeed obvious, importance to prospective reviewers that published reports are produced meticulously, including all clinically, radiographically, and histologically relevant data.

Funding

No funding sources supported this study.

Conflicts of interests

None.

References


Fig. 8. Encephalic MRI showing multiple parietal and occipital nodules.