CASE REPORT

Metastasising pleomorphic salivary gland adenoma presenting as synchronous pulmonary and hepatic metastases

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SUMMARY

Pleomorphic salivary adenomas (PAs) are the commonest benign tumours of glandular origin in the head and neck. Occasionally PAs undergo malignant transformation to carcinoma-ex-PA and can metastasise. More rarely they metastasise without malignant transformation of the primary tumour. We present a case of a benign pleomorphic salivary gland adenoma, presenting 7 years later with multiple liver metastases and a synchronous pulmonary metastasis. Histological analysis of the lung and liver lesions confirmed a diagnosis of metastasising pleomorphic adenoma (MPA). The lung lesion was fully excised, but the multifocal nature of the liver lesions rendered them inoperable. The patient is being managed conservatively and to date has no local recurrence of the primary salivary gland tumour or any further metastases. To the best of our knowledge this is the first case of MPA with simultaneous metastasis to both lungs and liver, and also the first to describe multiple liver metastases.

BACKGROUND

The diagnosis of metastasising pleomorphic adenoma (MPA) of salivary gland origin is challenging and remains under debate. Controversy exists due to the discrepancy between the histologically benign and biologically malignant behaviour. We present a novel case of MPA with multiple metastases to the liver and a synchronous pulmonary metastasis, diagnosed 7 years after the primary salivary gland tumour. Because of the benign diagnosis of the primary tumour it was initially not thought to be linked to the metastases. Only after histological analysis of the lung and liver lesions and comparison with the original salivary gland tumour could the diagnosis of MPA be made. A history of histologically benign pleomorphic adenomas (PAs) in primary and secondary sites is considered diagnostic. There have been occasional previous cases of MPA metastasising to the liver or to the lungs. This, however, is the first case of simultaneous metastasis to lungs and liver, and also the first to describe multiple liver metastases. Despite the benign appearance of MPA, its biological behaviour and its prognosis is one of a low-grade malignancy and should be treated promptly wherever possible.

CASE PRESENTATION

A 57-year-old man presented with a 6-month history of upper abdominal swelling and discomfort. His medical history included a superficial

parotidectomy for a benign PA of the parotid gland 7 years previously.

INVESTIGATIONS

A CT scan showed a 21×17 cm simple cyst and a 9×7 cm multiloculated cyst within the liver. Subsequent blood tests, including liver function tests and hydatid disease serology, were normal so the patient was conservatively managed by outpatient follow-up.

An MRI scan 8 months later showed that both original liver lesions had increased in size and a further solid liver lesion (1.6 cm) and a lung nodule (1.7 cm) were seen. A fludeoxyglucose (FDG)-positron emission tomography (FDG-PET-CT) scan showed limited tracer uptake by all three liver lesions suggesting benign pathology, and low-grade FDG activity in the lung lesion suggesting malignancy.

TREATMENT

In 2005 the left parotid gland was removed surgically and a PA was diagnosed. Following this the patient re-presented in 2011 with abdominal fullness. Imaging revealed liver and lung nodules. These were monitored and in 2012 a pulmonary wedge resection of the lung nodule was undertaken by video-assisted thoracic surgery in a tertiary cardiothoracic centre and histopathological analysis revealed a well-circumscribed lesion of variable appearance. At the tumour periphery, adjacent to background lung tissue, the architecture was cellular with closely packed, medium-sized, round cells with scanty cytoplasm, and foci of nest formation (figure 1A). More centrally there was a prominent myxoid component and areas of fibrosis (figure 1B). Immunohistochemistry showed strong positivity with CAM 5.2, MNF, AE1/3 (figure 1C) and S-100 (figure 1D). The histological and immunohistochemical profile was consistent with a PA.

Five months later liver biopsies were obtained from a diagnostic laparotomy, as the size and location of the metastatic deposits prevented curative surgery. These biopsies showed islands of epithelial cells, myoepithelial cells and ductal structures within a myxochondroid stroma (figure 1E, F). These features were similar to those of the lung lesion and again consistent with PA.

Despite extensive sampling, none of the liver lesions showed any histological features of malignancy, such as anaplasia, necrosis, increased mitosis or invasive growth pattern. The lung lesion was similar but showed more prominent mitotic activity.

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Figure 1 H&E-stained sections from the lung nodule showing (A) peripheral cellular appearance of the tumour; adjacent normal lung tissue is shown (L). (B) Central myxoid appearance of the tumour. (C) Immunohistochemistry showing positive staining for the peripheral area of lung tumour with AE1/AE3 and S-100. (D) H&E-stained sections from a liver biopsy showing nested appearance of the tumour (E and F). Adjacent normal liver tissue (L) is also shown in (F).

OUTCOME AND FOLLOW-UP

Following expert histopathology review at a tertiary centre, and correlation with the previous history and histology, both the lung nodule and the multiple liver lesions were confirmed to be PAs, and the diagnosis of MPA was made.

The lung nodule was completely excised and there has been no recurrence or further lung metastases. The patient is being managed conservatively with regular multidisciplinary follow-up to monitor disease progression, particularly of the unresectable liver metastases which had already increased in size and number over the 8-month imaging interval. The patient has been monitored over the past 16 months and to date there is no evidence of further metastases or local recurrence of the primary salivary gland tumour.

DISCUSSION

PAs are a common benign tumour of the salivary gland and have rarely been found in other tissues such as lungs and breast.^{1 2} PAs occasionally undergo frank malignant transformation into a carcinoma ex-PA, or a carcinosarcoma, both capable of metastasis. The WHO classify these as malignant epithelial tumours, defined as a PA from which an epithelial malignancy arises.³ In rare cases, PA can metastasise without histological malignant transformation. Distant metastases from these supposedly benign tumours have been reported in various tissues,⁴ including occasional cases involving lungs,⁵ or liver.^{6 7} Most recently Tarsitano *et al*⁸ reported a case of MPA in a young girl, with scalp and intracranial metastasis 3 years after the initial parotidectomy.

There has been debate over the existence, nomenclature and diagnostic criteria of these tumours. Controversy regarding their classification exists due to the discrepancy between the histologically benign and biologically malignant behaviour.⁹ A history of histologically benign PAs in primary and secondary sites, however, is considered diagnostic.³ MPA has metastasising behaviour resembling other salivary gland malignancies and a high mortality rate.³ The mechanism of metastatic spread of MPA is unclear but has been hypothesised to result from blood-stream permeation following surgical disruption of the primary

tumour. There have also been reports of lymph node metastases suggesting that lymphatic spread is possible.¹⁰

Our case demonstrated multiple distant metastases to the liver and lungs. This is in keeping with the hypothesis of haematogenous iatrogenic implantation of tumour following excision of the primary lesion, and its classification as an MPA. However, primary non-salivary gland PAs have also been described in other sites including lungs,¹ hence there is a remote possibility of simultaneous lung and/or liver primary tumour.

There have been occasional previous cases of MPA metastasising to the liver^{6 7} and lungs.⁵ This, however, is the first case of simultaneous metastasis to lungs and liver and also the first to describe multiple liver metastases. Despite the benign appearance of MPA, its biological behaviour and its prognosis is one of a low-grade malignancy and should be treated promptly wherever possible.

Learning points

- ▶ Metastasising pleomorphic adenomas are benign tumours that metastasise without malignant transformation of the primary tumour.
- ▶ A history of histologically benign pleomorphic adenomas in primary and secondary sites is considered diagnostic.
- ▶ This is the first case of simultaneous metastasis to lungs and liver, and also the first to describe multiple liver metastases.
- ▶ Despite its benign appearance, its biological behaviour and prognosis is one of a low-grade malignancy and should be treated appropriately.

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Contributors AJM, MM, AA-F and DB wrote the manuscript. AJM and DB took the photographs. AJM obtained patient consent. RP and AK were involved in the diagnosis and clinical management of the patient and edited the manuscript.

Competing interests None.

Patient consent Obtained.

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