Addison's disease as a presentation of metastatic malignant melanoma

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ABSTRACT

Melanoma accounts for 5% of all skin cancers. The risk of metastasis is related to the thickness of the tumour, and can affect local, regional and distant sites. Adrenal metastasis from melanoma of the head and neck is uncommon and often asymptomatic. Addison's disease as a presentation of metastatic melanoma is extremely rare and we are unaware of previous reports in the world literature. We report a case of a patient with metastatic melanoma presenting with signs and symptoms of Addison's disease.

KEYWORDS

Melanoma – Addison's disease – Metastasis

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Case history

A 71-year-old man presented with anorexia, vomiting, tiredness, unexplained weight loss of 2 stone in 6 months, dizziness, hypotension and a past history of melanoma of the skin of the nose. He had areas of café au lait type pigmentation on the trunk and legs. Biochemistry revealed low sodium of 111mmol/l and serum lactate dehydrogenase (LDH) of 162iu/l (normal ranges: 132–146mmol/l and 92–265iu/l respectively). A tetracosactrin test showed no increase in the cortisol levels after corticotropin stimulation, excluding central pathology and indicating the possibility of adrenal insufficiency, suggesting metastasis. Whole body computed tomography (CT) revealed bilateral necrotic suprarenal masses (Fig 1), a suspicious 13mm nodule in the right lung, a subcarinal, a para-aortic and a paratracheal lymph node. An ultrasonography guided biopsy of the adrenal mass found metastatic melanoma cells.

A good biochemical recovery was noted following steroid therapy and the patient subsequently had three cycles of dacarbazine chemotherapy. He died six months after development of the adrenal metastases.

The initial pathology analysis showed a superficial spreading melanoma (Clark's level 4) in a vertical growth phase with a Breslow's depth of 4mm, extensive surface ulceration and a mitotic count of 32 per 10 high power fields. There was no evidence of distant or regional metastasis on imaging, and the lesion was completely excised with clearance of 7mm and 5mm at the peripheral and deep margins respectively.

Discussion

Melanoma has a 90% overall mortality rate and distant metastasis is common in stage IV disease.¹ Primary melanoma rarely arises from the adrenal gland. However, the presence of secondary metastatic deposits is not uncommon.^{2,3} Although adrenal insufficiency secondary to other metastatic disease is recognised, Addison's disease as a presentation of metastatic melanoma has not been reported previously.

Adrenal metastases are more common in the elderly (mean age 62 years) and are often associated with other metastatic lesions.⁴ The most common metastasis is from the lungs, stomach, oesophagus and liver. Bilateral adrenal metastasis has been reported in 50% of cases.⁴

Addison's disease is hypoadrenalism and can be primary or secondary. Symptoms include tiredness, weakness, anorexia, weight loss, nausea, vague abdominal pain, postural dizziness and musculoskeletal pains. Hyperpigmentation of skin and mucous membranes is a characteristic feature, along with postural hypotension. A tetracosactrin test is used to differentiate between hypopituitarism and adrenal pathology. Our patient presented with typical symptoms of Addison's disease and there was no overt clinical evidence of metastatic lesions.

Patients with adrenal metastasis are often asymptomatic. For those in whom symptoms are present, pain is the most common.⁵ Symptomatic adrenal disease is reported in 4% of cases and adrenal insufficiency is reported in 1%.⁴ The mean diameter of adrenal metastases has been reported as

Figure 1 Coronal (A) and axial (B) computed tomography showing bilateral adrenal gland metastases

2cm.⁴ Our patient presented with metastases measuring 9.6cm on the left and 7.4cm on the right.

The most important prognostic factors for metastatic disease include tumour thickness, mitotic rate and ulceration.^{1,6} The prognosis is poor for patients with adrenal metastases; the median survival is 4–8 months and the 5-year survival rate is <10%.⁵ Patients with isolated adrenal metastasis have an increased survival of 18.7 months versus 6.6 months in patients with synchronous metastases ($p < 0.0001$).² The outcome for our patient was in keeping with that reported in the literature.

LDH is a recognised marker of tumour burden and metastatic disease. In adrenal metastasis patients, Mittendorf *et al* reported decreased survival for those who had elevated LDH levels.² The median survival for patients with a LDH of >618iu/l was 4.6 months versus 11.5 months for those with normal LDH. Several treatment modalities have been advocated for adrenal metastasis, including chemotherapy, immunotherapy and surgery. Chemotherapy and immunochemotherapy are indicated for inoperable tumours and stage IV metastatic disease; dacarbazine, interferon and interleukin-2 have been used with varying success.^{1,2} Bilateral adrenalectomy (either laparoscopic or open) is advocated in carefully selected patients, with a two-year survival rate of 39% being reported for the minimally invasive approach.⁵ The median overall survival after adrenalectomy was 16 months from the time of diagnosis versus 5 months for non-surgical patients.²

Conclusions

Symptomatic adrenal insufficiency from metastatic adrenal disease is uncommon and a high index of suspicion should be entertained in elderly patients with symptoms suggestive of Addison's disease. Timely imaging and biopsy can be diagnostic. Although adrenal metastases carry a poor prognosis, surgical resection of the glands can increase survival.

References

1. Garbe C, Peris K, Hauschild A *et al*. Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline. *Eur J Cancer* 2010; **46**: 270–283.
2. Mittendorf EA, Lim SJ, Schacherer CW *et al*. Melanoma adrenal metastasis: natural history and surgical management. *Am J Surg* 2008; **195**: 363–368.
3. Collinson FJ, Lam TK, Bruijn WM *et al*. Long-term survival and occasional regression of distant melanoma metastases after adrenal metastasectomy. *Ann Surg Oncol* 2008; **15**: 1,741–1,749.
4. Lam KY, Lo CY. Metastatic tumours of the adrenal glands: a 30-year experience in a teaching hospital. *Clin Endocrinol* 2002; **56**: 95–101.
5. Branum GD, Epstein RE, Leight GS, Seigler HF. The role of resection in the management of melanoma metastatic to the adrenal gland. *Surgery* 1991; **109**: 127–131.
6. Balch CM, Gershenwald JE, Soong SJ *et al*. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol* 2009; **27**: 6,199–6,206.