Aggressive Malignant Mesothelioma In A Patient Without Previous Asbestos Exposure

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Citation

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Abstract

We describe an 80-year-old male with a history of idiopathic lung fibrosis who was feeling generally unwell over a few weeks. Tissue biopsy from a rapidly growing ulcerated skin lesion on the abdomen showed a malignant epithelioid tumour positive for epithelial, mesothelial and embryonal tumour markers. The patient deteriorated rapidly and passed away. A post mortem examination was carried out and revealed thickened right pleura with multiple intra and extra-thoracic metastatic deposits. Histology of the pleural thickening and the multiple deposits were identical to that seen in the skin. The diagnosis of malignant epithelioid mesothelioma with rhabdoid features was made on histology. This is a rare case of malignant metastatic mesothelioma with ectopic hCG production and rhabdoid morphology in a patient without previous asbestos exposure.

INTRODUCTION

Malignant mesothelioma is an uncommon, pleural tumour which accounted for 2% of all cancer deaths in the UK in 2014 (1). Approximately seven new cases are reported every day in the UK and the incidence is increasing (1). A majority of pleural mesotheliomas are related to asbestos exposure with a long latency period (2). Malignant mesotheliomas uncommonly give rise to clinically detected metastases with a small number of distant subcutaneous metastasis cases reported (3). Only a handful of malignant mesothelioma cases showing rhabdoid morphology have been reported (4). Malignant mesothelioma with ectopic hCG (human chorionic gonadotropin) production is rare though described in literature (5, 6). We report a case of metastatic malignant mesothelioma presenting with a skin lesion in a patient without previous exposure to asbestos. We also report malignant mesothelioma associated with ectopic production of hCG and rhabdoid morphology, both of which are rare features and have not been reported together before.

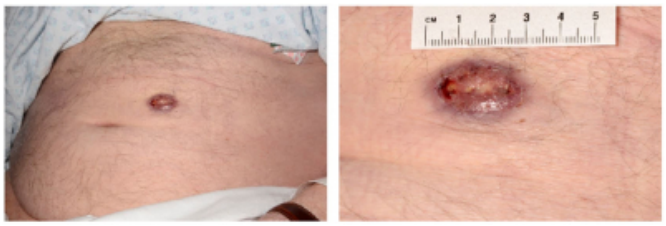
CASE REPORT

An 80-year-old retired banker with multiple medical comorbidities including idiopathic lung fibrosis was admitted to hospital for feeling generally unwell in the last few weeks. He was a non-smoker and had no previous history of exposure to asbestos. He was under the care of the respiratory physicians for his lung condition and had been on an anti-fibrotic agent, Pirfenidone for the last two years. He remained clinically stable whilst on this agent. He was last seen in the respiratory clinic one month prior to feeling unwell when he was recruited for a pharmacokinetics drug trial. This trial lasted for one week where he was on both Pirfenidone and Nintedanib. Both drugs were stopped when his blood test results showed an increase in inflammatory markers. He was briefly admitted for pneumonia and then discharged. Three days after his discharge, he became progressively poorly and was readmitted.

During this admission, he was found to have massive right pleural effusion and a chest drain was inserted. The pleural fluid was sent for cytology and the result was reported as blood only. An ulcerated skin lesion (figure 1) was identified on his abdomen which the patient noticed only a few weeks ago.

Figure 1

Ulcerated skin lesion on the abdomen



The skin lesion was biopsied by the dermatologist for suspicion of cutaneous metastasis. The histology of the skin lesion is shown in figure 2.

The tumour on immunohistochemistry was positive for AE1/AE3, CK7, CK5/6, MNF116, EMA, vimentin, calretinin, thrombomodulin, WT1, PLAP and hCG. The tumour showed positivity in epithelial, mesothelial and embryonal tumour markers as shown in figure 3.

Figure 2

Left figure shows a low power (x10) view of the skin biopsy showing dermal infiltration by a malignant epithelioid tumour. Right figure shows the high-power view (x40) of the malignant epithelioid tumour cells with rhabdoid morphology (eccentric and vesicular nuclei, prominent nucleoli and eosinophilic intracytoplasmic inclusions).

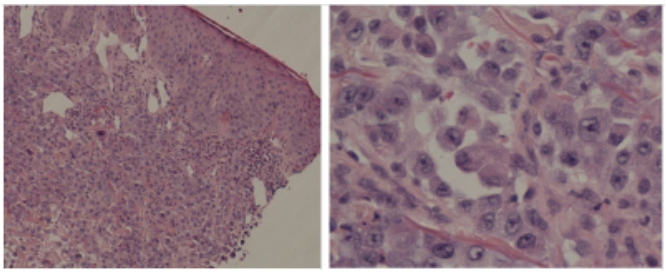
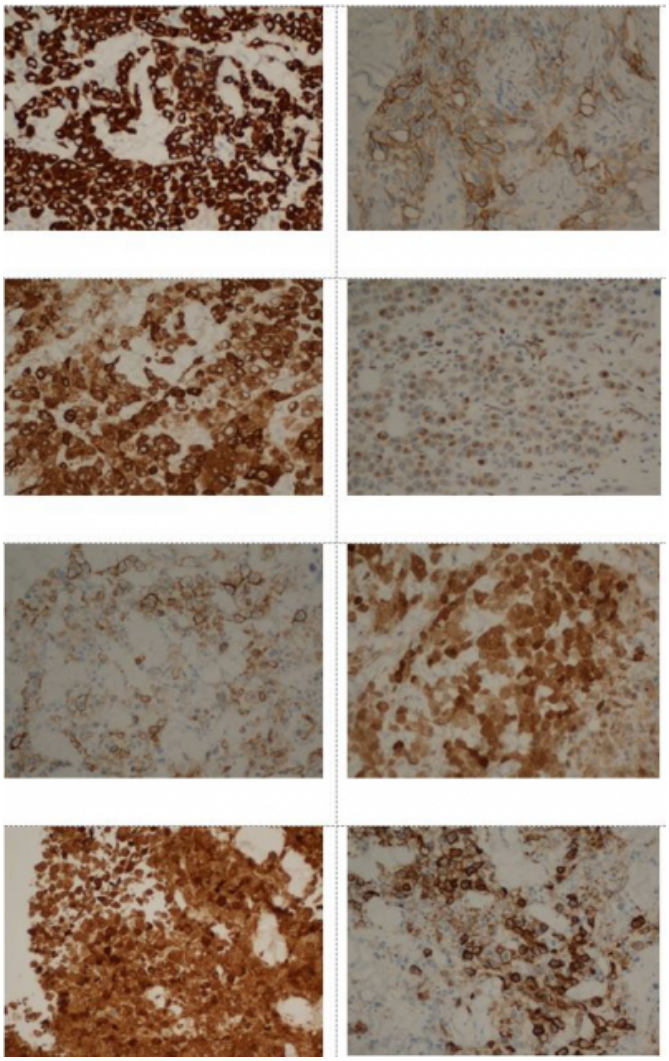


Figure 3

Immunohistochemistry showing tumour cells positive for (from top left to bottom right): CK7, BerEp4, EMA, WT1, Thrombomodulin, Calretinin, hCG and PLAP



CT scan revealed multiple lesions in the lungs, kidneys, adrenal glands and abdominal wall, likely to be metastatic deposits. Diffuse right pleural thickening was also noted. However, the primary tumour could not be definitely determined. Unfortunately, the patient deteriorated clinically and required respiratory support in the intensive care unit. He passed away seven days after being admitted.

A post mortem examination was carried out. We identified thickened lower right parietal pleura which extended to the surface of the diaphragm. Multiple firm white lesions were also seen in the organs aforementioned. Both lungs showed changes in keeping with pneumonia. However, no pleural plaques were present.

Tissue samples were taken during post mortem for histology from the right pleural thickening and multiple metastatic

deposits. The slides were also reviewed by thoracic pathologists at the Royal Brompton Hospital in London. The histology showed infiltration by a tumour identical to that seen in the skin biopsy specimen. It was concluded that the appearances are most in keeping with malignant epithelioid mesothelioma. No asbestos bodies were found on either thick unstained or Perl's stained sections.

The cause of death for the patient was determined as pneumonia secondary to metastatic mesothelioma.

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DISCUSSION

In the UK, 52% of mesothelioma deaths are in people above 75 years old (1). Approximately 20% of patients with mesothelioma have no history of asbestos exposure (7). Malignant mesothelioma can give rise to haematogenous metastases in various organs. The reported metastatic sites include lung, liver, adrenals, kidneys, heart, brain, pancreas, bone, soft tissue, skin and lymph nodes (8). Only a small number of cases have reported distant subcutaneous metastases (3). With the increase in incidence, metastatic deposit from mesothelioma should be considered as part of the differential diagnosis in an elderly patient who develops a new malignant skin lesion.

In addition, there was no literature or evidence to suggest the link between Pirfenidone or Nintedanib and mesothelioma. The patient's last CT scan was prior to starting his anti-fibrotic agent three years ago and this showed extensive sub-pleural reticular shadowing and dense areas of fibrosis at the bases with honeycombing. It was reported as appearances consistent with advanced interstitial pulmonary fibrosis. A year later, a chest x ray was performed which showed basal reticulation which may be due to fibrosis. No suspicious lesions were reported. This was his last chest x ray before he fell ill two years later. Whilst it is apparent that the patient passed away within a month of feeling unwell, it would be difficult to ascertain definitely when he developed mesothelioma.

Mesotheliomas exhibiting rhabdoid features are rare and only a handful of cases have been reported. It is important for pathologists to be aware that mesotheliomas can exhibit rhabdoid features as it can be confused with other tumours showing similar morphology. The other tumours include rhabdomyosarcoma, synovial sarcoma and lung carcinomas with rhabdoid features involving the pleura (4). Immunohistochemical studies will be useful in differentiating mesothelioma from these tumours. Rhabdoid mesothelioma is an aggressive subtype evidenced by the short mean survival time of 3.8 months (in 5 out of 6 patients) reported in a small study of 10 patients (4). More studies with larger numbers are required to fully understand the prognostic significance of rhabdoid features in mesotheliomas.

Human chorionic gonadotropin (hCG) is a hormone expressed in the human placenta. The uses of hCG as a laboratory test for diagnosing pregnancy, screening for trophoblastic disease and germ cell tumours are known. Pleural mesotheliomas with ectopic hCG production are vanishingly rare in that there are only a few articles that have described this (5). In one study, two patients with pleural mesothelioma demonstrated raised serum β-hCG levels and giant trophoblast-like cells in the tumour stained positive for hCG. The authors suggested that this finding occurred as a result trophoblastic differentiation (6). An article published recently described the first case of peritoneal mesothelioma

in whom serum -hCG levels increased with disease progression and the peritoneal mesothelioma stained positive for hCG (9). Whilst there are reports in certain types of carcinoma where hCG positive tumour cells appear to reflect poor differentiation, hCG positivity in mesothelioma is still poorly understood (10). Therefore, it is clear that more studies are required to determine the relation between hCG positivity and mesothelioma.

CONCLUSION

This was an interesting and unusual case of malignant mesothelioma which presented in a patient without previous exposure of asbestos. The patient presented with a dramatic decline in health and an ulcerated subcutaneous lesion. This was diagnosed histologically as malignant epithelioid mesothelioma with rhabdoid morphology showing ectopic production of hCG. These features are rarely seen in mesothelioma but it is important to be able to recognize them as there may be prognostic implications, especially mesothelioma with rhabdoid features.

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