

Carcinoma-induced diffuse pulmonary haemorrhage

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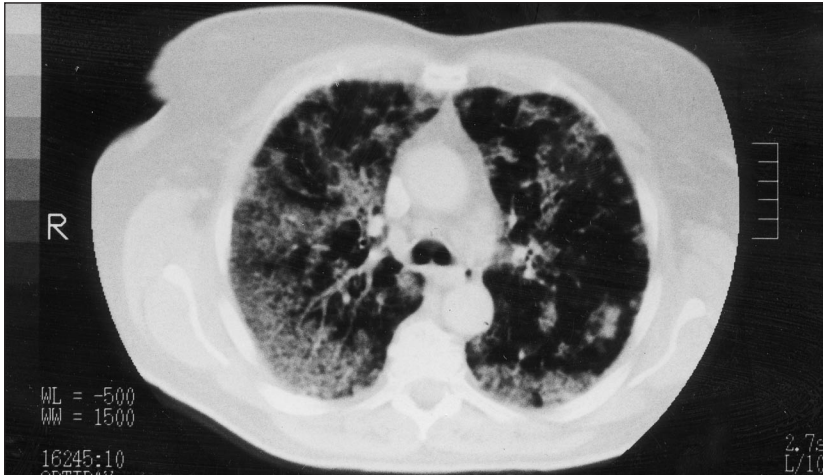


Figure 1. Computed tomography of the thorax revealing bilateral ground glass opacities and multiple widespread pulmonary nodules.

CASE REPORT

A 71-year-old woman was hospitalized with increasing dyspnoea and pleuritic chest pain, following a 1-month history of recurrent haemoptysis, malaise, fever and night sweats. She had a past history of osteoporosis, had had an ovarian carcinoma removed 6 months previously and had been a heavy smoker for most of her life. The ovarian carcinoma was a poorly differentiated grade 1a adenocarcinoma, which had been an incidental finding following removal of a large ovarian cyst.

On admission, she was pale, apyrexial, her heart rate was 100 beats per minute, her blood pressure was 120/68 mmHg and her respiratory rate was 28 breaths per minute. Physical examination revealed decreased air entry and bilateral coarse crackles. Initial oxygen saturations were 75% breathing room air. There was neither a rash nor haematuria. Blood tests showed anaemia, haemoglobin 7.4g/dl, white blood cell count 12.4×10^9 /litre, platelets 251×10^9 /litre, erythrocyte sedimentation rate 25 mm/h. Urea and electrolytes, liver function tests, calcium and clotting studies were all normal. Chest radiograph showed bilateral widespread shadowing with possible small nodules. Subsequent computed tomography of the thorax revealed bilateral ground glass opacities and confirmed multiple widespread pulmonary nodules (Figure 1).

She was initially treated with a combination of amoxicillin, erythromycin and prednisolone, but suffered continual haemoptysis and progressively worsening hypoxia. There were no stigmata of vasculitis, and no anti-neutrophil cytoplasmic antibodies were detected.

Eight days after admission, she was bronchoscoped and found to have diffuse pulmonary haemorrhage with blood trickling from all bronchopulmonary segments of both lungs. Transbronchial biopsies showed intra-alveolar haemorrhage, with no evidence of tumour. Bronchial washings showed no organisms or malignant cells. She was treated for possible vasculitis with high-dose steroids (prednisolone 60 mg), intravenous cyclophosphamide, intravenous methylprednisolone and oral tranexamic acid. She was also transfused with four units of blood. Her condition continued to deteriorate, with increasing tachypnoea, tachycardia and hypoxia. She was transferred to the intensive care unit, where she was ventilated and underwent plasma exchange therapy, without success. She died on the 14th day of admission.

Post-mortem histological examination revealed extensive bilateral intra-alveolar haemorrhage with scattered deposits of metastatic anaplastic tumour. The tumour had invaded some blood vessels and had also spread along alveolar septa. There was no evidence of vasculitis. No primary cancer source was found.

INTRODUCTION

Diffuse pulmonary haemorrhage is an uncommon disorder usually associated with the vasculitides, collagen vascular diseases or anti-basement membrane antibody disease (Schwarz and Brown, 2000). Malignancy is not well recognized as a cause of widespread alveolar haemorrhage, and this paper describes a case caused by metastatic carcinoma in which the diagnosis was only finally confirmed at post-mortem examination.

DISCUSSION

This patient was unusual in that cancer very rarely presents as diffuse pulmonary haemorrhage. As severe haemorrhage is uncommon with pneumonia, she was treated with prednisolone in case she had vasculitis. Widespread metastatic lung disease was considered a possibility, and the subsequent computed tomography scan was compatible with this diagnosis. When the transbronchial biopsies failed to confirm this suspicion, treatment for vasculitis was intensified with the addition of intravenous cyclophosphamide and methylprednisolone. Cancer was finally confirmed at post-mortem examination.

Diffuse alveolar haemorrhage has been most frequently associated with the vasculitides (e.g. drug-induced, Henoch-Schönlein purpura, Wegener's syndrome), collagen vascular disease (e.g. systemic lupus erythematosus, scleroderma) and anti-basement membrane antibody disease (e.g. Goodpasture's syndrome) (Schwarz and Brown, 2000).

In malignant disease, pulmonary haemorrhage is normally localized. In a large series of cases of lung cancer, Miller and McGregor (1980) described haemoptysis to be present in 19% – this

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was not related to cell type. Massive terminal haemoptysis occurred in 3% but was localized and most frequently associated with cavitated squamous cell carcinoma (Miller and McGregor, 1980).

Diffuse pulmonary haemorrhage has rarely been reported with malignancy. Supervia et al (1995) described alveolar haemorrhage secondary to vascular permeation in a patient with metastatic renal cell carcinoma, but this was not associated with haemoptysis. Epithelioid haemangioendothelioma is an uncommon bronchoalveolar intravascular tumour that can rarely cause haemoptysis.

In one case, as with this patient, bronchoscopy revealed blood oozing from all bronchopulmonary segments (Briens et al, 1997). Post-mortem lung histology showed numerous vascular neoplastic

growths. Nara et al (1996) reported diffuse alveolar haemorrhage resulting from metastases from ovarian angiosarcoma. Histology showed tumour emboli invading and destroying vascular walls.

Similarly, there is a report of disseminated cardiac haemangiosarcoma causing extensive bilateral nodular pulmonary infiltrate, severe haemoptysis and death from respiratory failure (Edwards et al, 1977). Lung metastases are common, but diffuse haemorrhage from them is not. Perhaps in this case, and those few previously described, the tumour had a particular predilection to invade and destroy the lung vasculature.

CONCLUSION

Diffuse pulmonary haemorrhage is rare. Where there are no features of

vasculitis nor connective tissue disease, and in the presence of multiple nodular radiographic shadows, metastatic tumour should be remembered as a possible cause. **HM**

Briens E, Caulet-Maugendre S, Desrues B et al (1997) Alveolar haemorrhage revealing epithelioid haemangioendothelioma. *Respir Med* **91**: 111–14

Edwards RL, Chalk SM, McEvoy JD, Donald KJ (1977) Pulmonary haemorrhage in disseminated cardiac haemangiosarcoma. *Br J Dis Chest* **71**: 127–31

Miller RR, McGregor DH (1980) Haemorrhage from carcinoma of the lung. *Cancer* **46**: 200–5

Nara M, Sasaki T, Shimura S et al (1996) Diffuse alveolar haemorrhage caused by lung metastasis of ovarian angiosarcoma. *Intern Med* **35**: 653–6

Schwarz MI, Brown KK (2000) Small vessel vasculitis of the lung. *Thorax* **55**: 502–10

Supervia A, Curull V, Corominas JM, Campodarve I, Sanjuas C (1995) Pulmonary metastases from renal cell carcinoma simulating alveolar haemorrhage. *Respir Med* **89**: 67–8

IN THE PUBLIC'S VIEW...

Dying for a tan

To show that when public fear is acute enough there is nothing better than spending lots of money, £7 million is to be spent researching the health risks of mobile phones. Scientifically, it's a waste of money. Even as public relations, it's probably a waste of money because the public is not inclined to listen to or understand scientific evidence. A stark example was Jon Snow trying to trip up Professor Liam Donaldson about measles, mumps and rubella (MMR) vaccine on Channel 4 news (7 February). Whether MMR is safer than three single vaccines does not depend on short, snappy soundbites and combative wordplay. It depends on careful consideration and lengthy, thoughtful explanation which a typical 2-minute news slot cannot provide. In the circumstances, Donaldson did well and avoided being bullied by Snow into saying that parents were irresponsible if they rejected MMR. But he is fighting a public 84% of whom (according to a Channel 4 poll) believe parents should have the choice.

For mobile phones, why should public money be spent trying to convince the largely unconvinced, especially

as you can see drivers on every street, turning corners and negotiating difficult junctions while talking into these infernal devices? They apparently do not care about endangering the lives of others, so why spend £7 million checking whether they are putting their own lives at risk?

Perhaps the money should be spent because it is children who may be most at risk. That's what they said about electricity power lines. Interestingly, the same scientists and lawyers who were so vocal and media-obsessed about power lines are the ones who are now uttering the dire warnings about mobiles. They've had to change horses; there was no evidence to back their earlier bets. Power lines are not pretty, but they are not a health risk unless they fall on your head. The money spent – largely in pursuit of a scare caused by poor epidemiology and vested interests – was a scandal.

For both power lines and mobiles, there is no obvious plausible carcinogenic mechanism, and the epidemiological evidence was never strong. This has not stopped the media splashing dire warnings on front pages. But where are the warnings about sunbeds?

Here are devices that, by a well understood mechanism, would be expected to cause cancer. There is sound epidemiological evidence. At intervals, the media publish stories, but – as with the latest research (*Guardian*, 6 February) – always as matter-of-fact news stories. Missing are the maverick scientists fighting an uncaring establishment and the heart-wrenching human interest stories: 'My child got leukaemia from a sub-station'.

Internet discussion groups are full of these. A father whose son is dying of leukaemia posts: 'I live next to overhead powerlines and a train line that uses overhead powerlines. Despite this, everybody, including the consultant at the hospital, says this has nothing to do with this. I think they are lying.' The irony of using the Internet to voice this fear does not escape everyone. 'As a society of educated and informed human beings,' posts Angela from California, 'we really are a bunch of hypocrites. For example, everyone who is worried about the effects of electromagnetic radiation should get off their computers.' **HM**

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