Squamous Carcinoma of the Lung Presenting as Migraine-Type Headache: A Case Report

Eswaran Waran

Department of Palliative Medicine, Box Hill Hospital, Box Hill, Vic., Australia

Key Words

Lung cancer · Orthostatic hypotension · Headache · Migraine · Paraneoplastic effects

Abstract

Introduction: Orthostatic hypotension has long been recognised as a paraneoplastic effect of lung cancer. Lung cancer presenting with orthostatic hypotension and migraine-type headaches has not been previously described in the literature. **Case Report:** A 62-year-old Caucasian male presented with headaches, typical of his migraine, after a 30-year migraine-free period. An examination revealed a significant postural drop in BP with reflex tachycardia and no other features of dysautonomia. Investigations showed a metastatic squamous cell lung cancer. Pharmacological treatment of orthostatic hypotension resolved the migraine-type headaches. **Discussion:** Orthostatic hypotension is associated with lung cancer. Prompt pharmacological treatment in patients not responding to non-pharmacological therapy can provide relief from disabling symptoms of orthostatic hypotension. In this patient, this included symptoms consistent with migraine-type headaches.

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Introduction

Paraneoplastic effects of tumours are remote effects that are not related to the direct invasion, obstruction or metastasis. Lung cancer is the most common cancer associated with paraneoplastic neurologic syndromes [1]. Orthostatic hypotension (OH) has long been recognised as a paraneoplastic effect of bronchial carcinoma [2]. Migraine is an episodic disorder, the crux of which is a severe headache generally associated with nausea and/or light and sound sensitivity. The case described below is that of a man presenting with a recurrence of his typical migraine-type headaches associated with OH and squamous cell lung

carcinoma. Lung cancer presenting with OH and migraine-type headaches has not been previously described in the literature.

Case Report

A 62-year-old Caucasian male presented for inpatient assessment of a soft tissue mass in the right superior sulcus of his lung (see [fig. 1](#)). He had presented to his local medical officer some weeks previously with headaches typical of his migraine as well as with right peri-orbital throbbing, nausea and photophobia. He had not had his migraine-type headaches for more than 3 decades. The character and associated nausea with light sensitivity were identical to those from the distant past. The current headaches only differed by being triggered and relieved by postural changes. He was headache free when supine but suffered from headache within minutes of standing. Symptoms were relieved on adopting the recumbent position. In the weeks prior to admission, he had also suffered from a loss of appetite, loss of weight, right posterior chest wall pain and postural light-headedness. The patient did not report any other symptoms of dysautonomia.

His relevant past medical history included a stable ischaemic heart disease, mechanical aortic valve replacement (life-long anticoagulation), atrial fibrillation, type 2 diabetes mellitus and being an ex-smoker with a 40-pack-year history. His medications on admission included metformin 500 mg b.d., atorvastatin 80 mg nocte, gliclazide 60 mg mane, nebivolol 2.5 mg nocte, sitagliptin 100 mg mane, thyroxine 125 µg daily and venlafaxine 75 mg mane. There had been no recent changes to this regimen. An examination revealed a significant postural drop in BP (60 mm Hg systolic and 25 mm Hg diastolic) with an appropriate increase in heart rate (20 bpm) within 2 min of standing. The patient had no evidence of dehydration or intravascular volume depletion. No features of Horner's syndrome were detected. There were no other neurological, cardiovascular or endocrine findings of concern.

CT-guided biopsy of the lung mass was undertaken, which provided a diagnosis of poorly differentiated squamous cell cancer, likely of lung origin. Staging CT and a bone scan likely revealed metastatic disease in the left 5th rib and left iliac bones. There was no evidence of metastatic disease at other sites including the brain and adrenal glands. Basic haematology and biochemistry were unremarkable (including thyroid function and serum cortisol). Multiple urine analyses were unremarkable. He had an HbA_{1c} of 9.6. His electrocardiogram was unremarkable and in sinus rhythm. An echocardiogram revealed normal left ventricular systolic function with mild left ventricular hypertrophy.

The patient was commenced on regular paracetamol, oxycodone and pregabalin for his headache and chest wall pain. This was titrated up with good relief of his chest wall pain but not the headache. Palliative chemotherapy was commenced with carboplatin and gemcitabine. He continued to experience consistently significant postural symptoms including migraine-type headache. Significant postural BP drops continued to occur (drop in systolic BP between 30 and 60 mm Hg). Non-pharmacological options including increase in salt and fluid intake, wearing of compression stockings and cessation of nebivolol did not provide relief. Endocrinology, neurology and cardiology teams were consulted; the patient was diagnosed with likely paraneoplastic aetiology for his postural hypotension. A combination of high-dose fludrocortisone (800 µg daily) and midodrine (2.5 mg t.d.s.) achieved objective (systolic BP falls consistently less than 20 mm Hg) and symptomatic relief of postural hypotension and the headaches. The patient was subsequently discharged home. At outpatient review 3 weeks later (second cycle of chemotherapy) the patient remained free of the mi-

graine-type headaches or postural light-headedness. There was no significant postural drop in BP.

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Discussion

OH is defined as a persistent, consistent, orthostatic fall in systolic BP of ≥ 20 mm Hg or diastolic pressure of ≥ 10 mm Hg within 3 min of standing up [3]. A study examining causation of OH found that 27% of patients had primary autonomic failure, 35% had secondary autonomic failure, and 38% had hypotension without evidence of generalised autonomic degeneration [4]. The absence of the compensatory heart rate increase with posturally-induced hypotension is typical of autonomic failure-induced OH [5]. The patient described in this study consistently had reflex tachycardia on standing associated with his hypotension, a feature not consistent with autonomic failure. He also lacked other symptoms or signs of generalised autonomic failure. Conditions such as diabetic autonomic neuropathy are associated with widespread effects on the autonomic nervous system even in the early stages [6], and a lack of reflex tachycardia on standing [5].

OH has long been associated with bronchial carcinoma. In 1963, Siemsen and Meister [2] described a case of autonomic failure and OH associated with lung cancer. Park et al. [7] demonstrated an improvement in heart rate response to posture and resolution of OH after treatment of primary lung cancer with radiotherapy. Paraneoplastic effects of tumours are remote effects that are not related to the direct invasion obstruction, or metastasis. Graus et al. [8] have provided rigorous diagnostic criteria for paraneoplastic neurological syndromes. Small cell lung cancer is the histological type (amongst lung cancers) most often associated with paraneoplastic neurological disorders including OH [1]. The OH associated with small cell lung cancer histology is that of autonomic and often pan-autonomic failure [9]. Pelosof and Gerber [9] describe various onconeural antibodies associated with neuronal damage in these instances.

The case described here is of a patient with non-small cell histology and OH without evidence of autonomic failure. Neal et al. [10] described a similar case of OH (with reflex tachycardia) as the isolated feature of a paraneoplastic neuropathy. Their case likewise had no additional features of autonomic failure. Their patient, however, had small cell lung cancer and elevated levels of anti-CRMP-5 antibodies, an onconeural antibody associated with small cell cancer. The well-characterised onconeural antibodies associated with paraneoplastic neurological syndromes are not associated with non-small cell lung cancers [8]. In the definition of paraneoplastic neurological syndromes as set out by Graus et al. [8] this case would fall under the category of a possible paraneoplastic syndrome (non-classical syndrome, no defined paraneoplastic antibodies and cancer present within 2 years of diagnosis). Gosney et al. [11] postulated a role for vasodilatory peptides to explain paraneoplastic OH not accompanied by other features of autonomic dysfunction, but they could not find any correlation between the peptides studied and OH.

To the authors knowledge, there are no previously published case reports that have described headaches (of any nature, including migraine type) induced by OH in association with or as the presenting symptom of lung cancer. Migraine is an episodic disorder, the crux of which is a severe headache generally associated with nausea and/or light and sound sensitivity. The International Headache Society (IHS) requires a headache of a minimal duration of 4 h for a diagnosis of migraine [12]. What the patient described fulfilled all IHS criteria for

a diagnosis of migraine without aura, with the exception of the duration criterion. The headache described here would best fit the IHS diagnosis of probable migraine (attacks fulfilling all but one of the criteria for a diagnosis of migraine without aura). Given the patient description of the identical characteristics to his previously diagnosed migraine, the headache is not better accounted for by another IHS diagnosis.

Syncope, orthostatic intolerance and OH have long been reported as part of the migraine syndrome [13]. However, only recently have researches suggested the possibility of OH triggering migraine. Curfman et al. [14] have suggested the existence of syncopal migraine (i.e., migraine headache immediately preceding or following syncopal episodes). A significantly higher proportion of their syncopal migraine subjects reported headache with tilt table testing than the migraine-without-syncope group. They suggest orthostatic change and migraine bear an undescribed patho-physiologic relationship. A large majority of their syncopal migraine patients responded to anti-migraine therapy (topiramate, valproate, pregabalin). These authors conclude with the suggestion that anti-migraine therapy may play a role in such patients with treatment-refractory OH, a conclusion supported by Gupta, who presented a case where metoclopramide relieved recurrent OH and migraine [15].

In this case, treatment targeted towards OH led to a resolution of the patient's headache symptoms. With further anti-cancer treatment, fludrocortisone and midodrine doses could be reduced and possibly ceased with careful monitoring of symptoms. Failure of improvement of OH may suggest a progressive underlying disease. However, another explanation in that instance could be permanent neuronal damage from as yet uncharacterised onconeural antibodies associated with non-small cell lung cancer. In such an instance, anti-migraine therapy may be an option for this patient, given the adverse effect profile of long-term high-dose fludrocortisone and midodrine.

Conclusion

To the best of the author's knowledge, this is the first report describing a case of lung cancer presenting with OH and migraine-type headaches. OH is associated with lung cancer. Prompt pharmacological treatment in patients not responding to non-pharmacological therapy can provide relief from disabling symptoms of OH, which, in this patient, included severe headaches.

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Disclosure Statement

The author declares that he has no competing interests.

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Fig. 1. Contrast CT scan of the chest. Right apical tumour, with mediastinal extension.