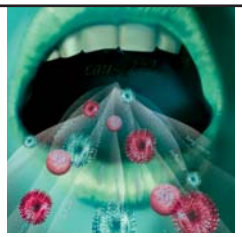
Lung cancer



BACKGROUND Lung cancer is a preventable disease that has a poor prognosis in most patients. It has a high association with tobacco smoking. Diagnosis involves looking for new symptoms and signs, or changes in existing ones, with a heightened index of suspicion in patients who have ever smoked.

OBJECTIVE This article outlines the role of the general practitioner in the diagnosis, treatment and palliative care of the patient with lung cancer.

DISCUSSION The risk of developing lung cancer increases with increasing cigarette smoking and decreases when smoking is ceased. The development or change in a 'usual' cough should alert the GP to a diagnosis of lung cancer. Any referral to a respiratory specialist must be preceded by informing the patient of the nature of the possible disease, and ensuring that the patient has a realistic understanding of the limited chance of cure. Palliation is required by most patients with the GP playing an important role. Promotion of smoking cessation is the only real strategy available to doctors to reduce morbidity from this disease.

Of all the lung conditions that general practitioners manage, the one patients fear most is lung cancer. While it is not the most common serious lung condition, an inexorable path toward death for most patients gives it a worthy reputation as a very serious and unremitting illness.

Lung cancer is the leading cause of cancer death in Australia. Most patients with lung cancer die from it. The 5 year survival is approximately 10%. Cigarette smoking is the major aetiological factor; occupational exposures add marginally to the risk. The lifetime risk of the disease in smokers is approximately 15%.[1] While the incidence in men is decreasing, it is increasing in women. The risk of developing lung cancer increases with increasing cigarette consumption and decreases in those who stop smoking; the earlier smoking is stopped, the lower the risk of developing lung cancer.[1]

The most practical pathological classification of lung cancer is:

- small cell lung cancer (SCLC) – which accounts for approximately 20% of all lung cancers, and
- nonsmall cell (NSCLC), which accounts for 80%.

The NSCLC group includes squamous cell cancer, which accounts for 30% of all lung cancers, adenocarcinoma (30%) and large cell cancer (10%). Nonsmall cell lung cancer and SCLC behave very differently in their presentation, metastatic spread, prognosis, and response to treatment.[2] Nonsmall cell lung cancer grows more slowly, spreads later and hence, has a better prognosis; unfortunately, it responds poorly to chemotherapy. By contrast, SCLC is invariably disseminated at the time of diagnosis, has a median survival if untreated of 2–3 months, and a response rate to chemotherapy of approximately 75%.

Finally, metastatic lung cancer arising from a primary tumour elsewhere may present as a localised lung lesion and hence may be confused with a primary lung tumour.

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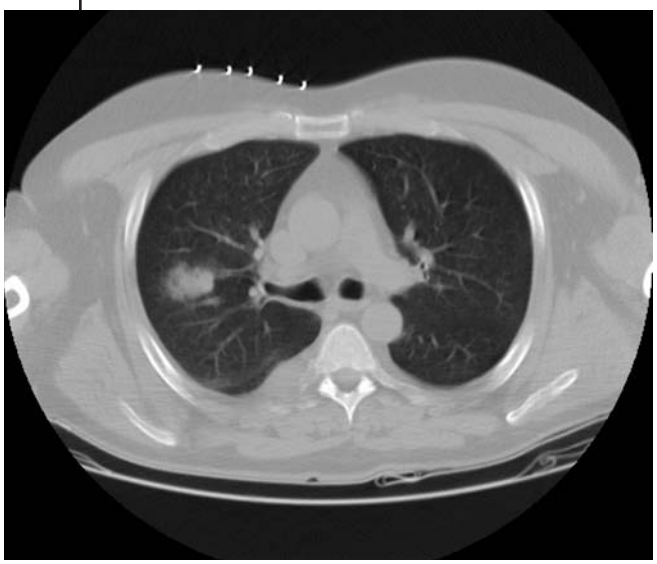

Figure 1. CT of isolated lung tumour in left lung. Note erosion of left posterior rib

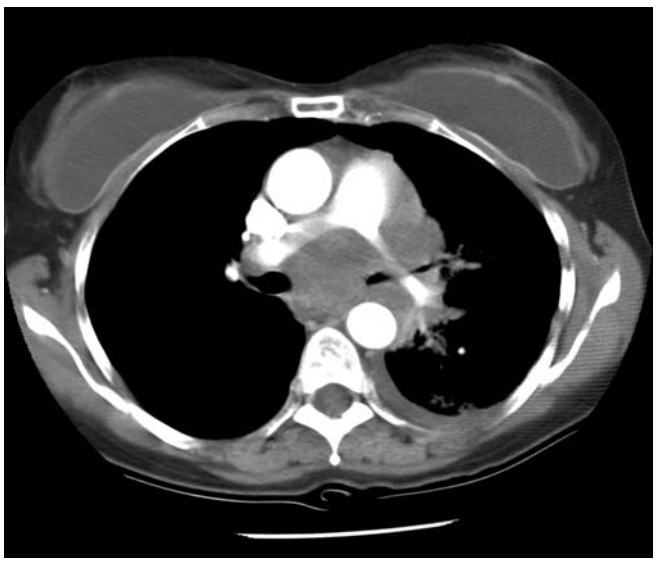

Figure 2. Small cell invasion of mediastinum at level of tracheal bifurcation. Compression of right main brenchus and right pulmonary artery

Diagnostic features

Persistent cough

The key diagnostic feature for primary lung cancer is the development of a persistent cough.[3] A change in the nature of a patient's usual cough is equally important. The cough may or not be productive of sputum and the presence of blood stained sputum significantly increases the likelihood of cancer. Patients with more advanced disease can also suffer from significant breathlessness on exertion, usually due to central airway obstruction or a pleural effusion. When an airway becomes totally obstructed, infection with constitutional symptoms and perhaps pleuritic pain may occur. Weight loss occasionally occurs early but is more common in the later stages of the disease.

Examination and investigation

While on examination a primary lung cancer may be quite asymptomatic, from time to time it will be possible to hear a monophonic wheeze arising from the single area of obstruction. If there is significant obstruction of the respiratory tract, atelectasis will lead to deviation of the trachea in the direction of the collapsed segment of the lung. The patient may exhibit signs of lymphatic spread and the neck, supraclavicular and axillary regions should be examined for enlarged lymph nodes. Abdominal examination should be undertaken seeking hepatomegaly (although this is not a sensitive sign of liver metastases). The finding of an elevated serum alkaline phosphatase is more sensitive and should be performed, as should a serum calcium which, if elevated, may indicate bony secondaries or ectopic production of a parathyroid-like hormone.

Chest X-ray

Unexpected chest X-ray abnormality can be a first presentation of lung cancer. Bronchogenic cancers tend to be found centrally in association with the main bronchi and therefore tend not to appear on X-ray. Evidence of distal collapse may be seen. Some tumours appear as isolated single nodules in the periphery of the lung field and can look like an isolated secondary malignancy (*Figure 1*). Widening of the mediastinum can occur with lymph node spread, and is more commonly seen in SCLC. Secondary malignancies can either be single (so-called cannon ball shadows, or 'spots' on the lung), or multiple. Secondary malignancy can also invade the lymphatics of the lung and can produce an X-ray appearance similar to pneumonitis, the so-called 'lymphangitis carcinomatosis'.

Diagnosis – the GP's role

The actual diagnosis of lung cancer can be very difficult, or quite straightforward. Any persistent or worsening lung symptoms or signs in an adult over the age of 40 years, particularly with a history of smoking, demands a consideration of lung cancer and a plan to actively exclude the diagnosis. This may involve taking a chest X-ray at the outset. A negative chest X-ray does not necessarily exclude lung cancer, particularly where the tumour is in a central airway or is small. Sputum cytol-

ogy and serum biochemistry should be arranged. Where the diagnosis of lung cancer is likely, a chest CT with contrast is indicated to check for hilar and mediastinal lymphadenopathy (*Figure 2*). Further investigation by a respiratory physician is highly recommended.

Should a firm diagnosis of lung cancer be made, or if referral is to exclude the diagnosis of cancer, it is essential that the patient is made aware of the actual or potential presence of the disease. The management of this issue requires much sensitivity, but in most situations it is highly desirable to raise the issue. Patients who are not prepared for the diagnosis may react with anger, denial, and agitation or withdrawal when it is confirmed. Preparation by the GP can make a substantial difference to the acceptance of the diagnosis and appropriate treatment.

Treatment options and prognosis – the GP's role

Many patients with lung cancer have comorbid conditions related to smoking and age. Curative surgery is an infrequent option, as patients' general condition or impaired lung function often rule out pneumonectomy or lobectomy. Hence, it is essential that patients are referred to a specialist with a realistic expectation of what may be offered. In particular, cure will probably not be the aim of treatment. It may be more appropriate to aim for amelioration of symptoms, some prolongation of life, or reaching particular life events such as births, weddings or Christmas.

Similarly, it is important to empower the patient to be an active participant in formulating treatment plans. Aggressive treatment may not always be their best option. Using a 'burden-benefit' approach can make this process less traumatic. The aim is to determine whether 'on balance' the benefits of continuing (or starting or stopping) treatment outweigh the burdens consequent on each of these three options.[4] The GP can undertake or assist with this task when the time arises.

Treatment

Treatment depends on cell type, anatomical stage and performance status. The latter is often influenced by age and the presence of comorbidities related to smoking. More than half of lung cancers occur in patients over the age of 65 years. This is not a barrier to any modality of treatment, but general ill health may be.

Radiotherapy/chemotherapy

In patients with SCLC where there is limited disease (ie. localised to one side of the chest with or without mediastinal node involvement), chemotherapy with radiotherapy may be offered.[5] Because the brain is a common site of subsequent metastases in patients who have had a good response to initial treatment, prophylactic cranial radiation is often offered.

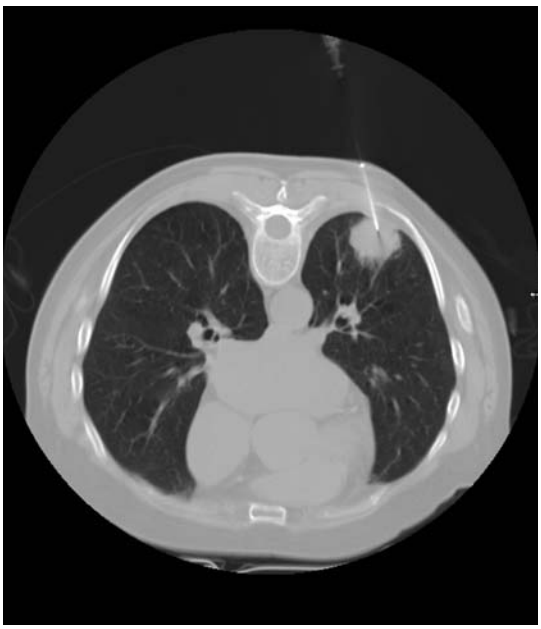

Figure 3. Peripheral lung tumour invading chest wall. Biopsy needle in place

In patients with extensive disease (where the tumour has spread to the other side of the chest or outside the chest), chemotherapy is often offered. Radiotherapy is reserved for symptom control where chemotherapy has failed.

There are now many chemotherapeutic drugs that are effective against SCLC. Most often, a combination of agents is used. A common combination is cisplatin or carboplatin with etoposide. Most regimens are administered over 1–3 days every 3 weeks or so. In patients with limited disease, the response rate is approximately 80%; in half of these the response will be complete. In those with extensive disease the respective rates are 70% and 30%. Unfortunately, even in those with a complete response recurrence occurs in most within 1–2 years.[5]

Drug toxicity is common with neutropaenia, nausea, vomiting, diarrhoea, hair loss and deteriorating renal function being some of the more frequent side effects. All patients should be made aware of the possibility of neutropaenic sepsis so they will present early with symptoms such as fever and rigors.

Radiotherapy is reserved for those patients who have significant symptoms due to localised disease

that can be included in a single radiation field. Pleural effusions should be drained and pleurodesis attempted. This is often achieved by the introduction of talc introduced as a powder or a slurry.

In patients with advanced NSCLC, treatment is directed at controlling symptoms and possibly slowing the progress of the tumour.[7] Chemotherapy with regimens containing cisplatin or carboplatin has been shown to improve survival at 12 months and should be offered to those with good performance status. It is questionable that such treatment should be continued in those who do not tolerate their initial cycles.

Surgery

Surgery has little to offer most patients with SCLC. In a small minority where the disease has been detected at an early stage and is clearly localised, surgery may be appropriate and offer the patient their best chance of a cure.

Patients with localised NSCLC (stages 1 and 2), have the best chance of a good outcome with surgery.[6] Where the disease has not spread to lymph nodes or invaded the chest wall or diaphragm (stage 1), surgery offers a 70% chance of 5 year survival. In those where the tumour has spread to hilar lymph nodes or involved the chest wall or diaphragm (stage 2), surgery offers a 30–40% chance of 5 year survival.[6] Surgery has a limited role in patients where the tumour has spread to mediastinal glands and beyond.

Palliation

With such poor cure rates, palliation is required by most patients with the GP playing an important role. The core principles underlying the treatment of the palliative care patient – care for the patient and the carers, looking at the whole situation and being prepared to participate in a team approach – apply to lung cancer as to all cancers. Palliative care does not stop with the death of the patient. Follow up of the bereaved carer looking for signs of abnormal grief reactions is essential.[8]

The most common problems experienced related to the primary cancer are dyspnoea, cough, haemoptysis and chest wall pain.

Dyspnoea

Dyspnoea is the sensation of breathlessness, and is not related to hypoxia. The symptom may be a manifestation of anxiety. This can be alleviated by anti-anxiety agents (eg. diazepam) or low dose opioids. For patients already receiving opioids for pain, an increase of approximately 25% of the existing daily dose may help. For opioid naïve patients, commencing with a small daily dose (eg. morphine 5 mg four times per day) and titrating up every 2–3 days should achieve control in most cases. Always start a laxative when commencing regular opioids. Orally administered opioids work better than nebulised opioids.[9]

Oxygen may reduce the sensation of breathlessness and improve the pO2, but it is notoriously hard to cease once started. Cessation may be appropriate if the dyspnoea is the result of a reversible complication of the cancer such as pleural effusion.

Cough

A dry cough is helped by centrally acting cough suppressants, particularly opioids. Copious sputum production may be helped by physical measures such as physiotherapy, including postural changes and percussion. Medications such as hyoscine and glycopyrrolate can be useful. Bisolvon probably does help. Tenacious sputum can be helped by nebulised saline.

Chest wall pain

Chest wall pain is almost always nociceptive in origin. It is due to chest wall or pleural infiltration by the cancer (*Figure 3*), torn muscles and even broken ribs from coughing. Simple physical support of the affected area when coughing or straining can be useful. Regular analgesia with simple analgesics, nonsteroidal anti-inflammatory drugs or opioids is helpful, depending on the severity of the pain.

Prevention and screening

The GP's only effective defence against lung cancer is prevention. Reinforcing the wise decision not to start smoking, and exhorting smokers to cease are the most effective strategies. It is imperative that GPs identify the smokers in their practice, in order to target appropriate advice.

To be effective it is imperative to have a high index of suspicion for smoking in the practice. Medical practitioners are not good at this, with up to half of smokers in their patient population not being identified as such.[10] Once identified, regular dispensing of brief smoking cessation advice (see *Resources*) is shown to lead to a 4–6% annual reduction in smoking, with a number needed to treat of 169.[11] Addition of nicotine replacement therapy[12] or the antidepressants imiprimine or bupirion are also effective in maintaining cessation in some individuals.[13]

X-ray screening for bronchogenic cancer in the

smoking population makes sense intuitively, but it is a strategy not supported by the literature.[14]

Conclusion

General practitioners have a key role in diagnosing lung cancer, preparing patients for the realities of treatment and prognosis, and in guiding the patient through the often painful process of deciding when and if to cease more aggressive treatment options.

Summary of important points

- The development of a persistent cough, or a change in the 'usual' cough of a patient is the key to diagnosis.
- Any persistent or worsening lung symptoms or signs in an adult over the age of 40 years should be investigated.
- Specialist referral is essential.
- Surgery is of little benefit to patients with small cell lung cancer.
- Palliative care is required by most patients with the GP playing an important role.
- The earlier smoking is stopped, the lower the risk of developing lung cancer.
- Promotion of smoking cessation is the only real strategy available to GPs to reduce the morbidity of lung cancer.

Resources

Quitline: telephone 131848

Litt J. How to provide effective smoking cessation advice. Aust Fam Physician 2002;31:1087–1094.

Conflict of interest: none declared.

References

1. Bilello KS, Murin S, Matthay RA. Epidemiology, aetiology, and prevention of lung cancer. Clin Chest Med 2002;23:1–25.
2. Travis WD, Colby TV, Corrin B, et al. Histological typing of lung and pleural tumours. Berlin, Germany: Springer, 1999.
3. Chute C, Greenberg ER, Baron J, et al. Presenting conditions of 1539 population based lung cancer patients by cell type and stage in New Hampshire and Vermont. Cancer 1985;56:2107–2111.
4. Mitchell G, Currow D. Chemotherapy and radiotherapy. When to call it quits. Aust Fam Physician 2002;31:129–133.
5. Komaki R. Combined treatment for limited small cell lung cancer. Semin Oncol 2003;30(Suppl 9):56–70.
6. Ginsberg RJ, Vokes EE, Rosenzweig K. Nonsmall cell lung cancer. In: DeVita VJ, Hellman S, Rosenberg SA, eds. Cancer: Principles and practice of oncology. 6th edn. Philadelphia: Lippincott, Williams and Wilkins, 2001.
7. Belani CP, Langer C. First line chemotherapy for NSCLC: an overview of relevant trials. Lung Cancer 2002;38(Suppl 4):13–19.
8. Writing Group. Therapeutic Guidelines: Palliative care. Melbourne: Therapeutic Guidelines, 2001.
9. Abernethy AP, Currow DC, Frith P, et al. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. BMJ 2003;327:523–528.
10. Frank E, Winkleby MA, Altman DG, Rockhill B, Fortmann SP. Predictors of physician's smoking cessation advice. JAMA 1991;266:3139–3144.
11. Huibers MJH, Beurskens AJHM, Bleijenberg G, van Schayck CP. The effectiveness of psychosocial interventions delivered by general practitioners. Cochrane Review. In: The Cochrane Library. Chichester, UK: John Wiley & Sons, 2004.
12. Silagy C, Lancaster T, Stead L, Mant DGF. Nicotine replacement therapy for smoking cessation. Cochrane Review. In: The Cochrane Library, Issue 1. Chichester, UK: John Wiley & Sons, 2004.
13. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Review. In: The Cochrane Library, Issue 1. Chichester, UK: John Wiley & Sons, 2004.
14. National Institute of Clinical Studies. Evidence practice gaps report. Melbourne: NICS, 2003.

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