

An 85-year-old woman with metastatic liver disease

Commentary by

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An elderly woman has metastatic liver disease but no obvious primary site.

In view of her age, what should be done to find a primary site?



Case scenario

I recently saw an 85-year-old woman who had been very fit all her life but now felt tired and anorexic. On examination, she had a very hard, craggy, enlarged liver. An upper abdominal ultrasound showed multiple deposits consistent with metastases. This finding was confirmed by a CT scan. No obvious primary site was found. The liver function tests were very abnormal, in line with metastatic liver disease. In view of the patient's age, what, if anything, should be done to find a primary site?

Commentary

This is a not uncommon clinical scenario faced by general practitioners, geriatricians and occasionally oncologists, and the immediate 'gut reaction' is to suggest that this lady should be left alone (that is, not investigated further) and treated with appropriate palliative medications. While this approach may ultimately be appropriate, it is important to discuss what the considerations should be in reaching this decision.

The diagnosis is likely to be an adenocarcinoma of unknown primary, which was the fifth most common malignant diagnosis by incidence in women in Australia in 1997 and the fourth most common cause of cancer death. Approximately 1800 patients per year are diagnosed with this condition, of whom approximately 1200 die. The average life expectancy for such patients may vary from a few weeks to one to two years, depending on the extent of liver abnormality and rapidity of disease progression

Assessing performance status and considering alternative diagnoses

Before anything else is determined, it is critical to establish the patient's performance status. This is an indication of the impact that the malignancy, or other sig-

nificant intercurrent illness, is having on the patient's day-to-day activities, and it has been shown to be the single most important prognostic factor for patients with malignancy. A number of scales have been developed to assess performance status, but the most simple are those based on the grade developed by the United States Eastern Clinical Oncology Group (ECOG; see the Table).

If this patient had an ECOG performance status of 3 or 4, further investigations would be inappropriate because the prognosis would be too poor.

Otherwise, the purpose of any further investigations in this patient would be to obtain a more treatable alternative diagnosis and to avoid or warn against potential complications from the (unknown) primary site. However, from the perspective of a treatable diagnosis, it should be appreciated that this is not the typical presentation of easily treatable conditions such as non-Hodgkin's lymphoma, hormone-positive breast cancer or ovarian cancer. None of these typically presents with hard, craggy hepatomegaly. Lymphoma is usually manifest by multiple sites of rubbery lymphadenopathy. While hepatic predominant lymphoma can occur, it is usually associated with a very poor prognosis. Similarly, hormone-responsive

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breast cancer is more usually associated with pulmonary, skin, nodal and bony metastases, and ovarian cancer is generally manifest by intraperitoneal disease. Only occasionally are subcapsular hepatic metastases identified with ovarian cancer, and rarely are these clinically detectable.

History taking

The most important part of the initial clinical interaction would be to take a careful history. This should be aimed at eliciting symptoms of a potential primary site and its complications. Statistically, the three most common cancers in women are breast, colorectal and lung cancer; thus the history should be somewhat biased towards eliciting symptoms suggestive of these conditions, especially as each commonly metastasises to the liver.

For instance, breast cancer might be suggested by a personal or family history and/or the awareness of an increasing breast mass. Colorectal cancer could be suggested by a history of unexplained anaemia, change in bowel habit or per rectal bleeding. Lung cancer might be

suggested by a long smoking history, increasing shortness of breath and cough, and haemoptysis. Symptoms suggestive of other malignancies that commonly metastasise to the liver, such as oesophageal, gastric or pancreatic cancers, should also be elicited.

Physical examination

Further physical examination should also be targeted at identifying signs suggestive of the more likely primary malignancies, and other possible sites of metastasis or complication. Thus the breasts should be examined for masses and skin changes, the abdomen for masses and evidence of acute or subacute bowel obstruction, and the chest for dullness and lymphadenopathy.

Which tests to perform

If specific symptoms or signs were present, further investigations might be indicated. For instance, if there were evidence of dysphagia or bowel obstruction, endoscopies might be indicated to permit palliative manoeuvres such as stenting aimed at overcoming an oesophageal

or colonic blockage.

There is no indication to put this patient through a wide range of invasive procedures in the absence of symptoms or signs, and only a small number of tests should be performed. These would include a full blood count, biochemistry including electrolytes (EUC), liver function tests, calcium and phosphate levels, and tumour markers including CEA, Ca 19.9 and Ca 125.

The blood count would be aimed at determining anaemia, which could be readily treated with transfusion. The extent of liver function derangement would be helpful in determining prognosis. It would also be important to find treatable abnormalities, such as hypercalcaemia. The tumour markers would assist in identifying a possible primary site. In this clinical scenario, if the markers were very elevated it might be sufficient to determine a diagnosis of malignancy and therefore avoid a diagnostic liver biopsy.

The purpose of a biopsy in this situation would be largely to satisfy any uncertainty of the patient or relatives as to the diagnosis and its attendant prognosis. It is highly unlikely that the biopsy would alter treatment or prognosis, and this should be spelt out to the patient and her relatives. However, it is frequently necessary to undertake a biopsy these days because of increasing community expectation that everything be done. If a biopsy were undertaken, immunohistochemistry should be performed to determine the presence of oestrogen and progesterone receptors, although these are likely to be negative in this patient.

Treatment

The treatment should consist mainly of simple analgesics, in combination with aperients if opiates are required. Low dose corticosteroids may assist with the management of hepatic capsular pain and lethargy. Early referral to palliative and community services would also be prudent.

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Table. ECOG performance status

ECOG grade	Patient's activity level
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light housework, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead