



Medicine for Managers

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Cancer of Unknown Primary

Over the years I have written about a number of types of cancer; breast, bowel, prostate, lung and so on. Cancer can develop in any of the body tissues and is the result of a breakdown in the orderly process of cell replacement. Abnormal cells survive and multiply in an uncontrolled manner to form tumours. They can grow locally or spread by invading other tissues.

Treatment of cancer depends in part on having a knowledge of the nature of the tissue from which the mutated cancer developed. Specific treatments are often more effective against specific types of cancer.

When cancer cells are examined microscopically they will have characteristics in common with the parent cells. In other words, cancerous breast cells will have some of the features of normal breast cells.

*In general, the more the appearance of the cancer cell is like the appearance of the originating tissue, the more likely it is to respond to treatment. Cells which have lost any similarity with the parent cells are called **anaplastic** and tend to respond less well to treatment.*

Sometimes a cancerous growth is discovered in the body but the location of the primary originating tumour is not known and cannot be found. When such a malignancy is identified but its primary

location cannot be found, it is described as a **cancer of unknown primary**. It may also be called an **occult tumour**.

In most cases, when a tumour is discovered and is not associated with the tissue in which it is found, it is called a **secondary tumour** or **metastasis**. This is important to know because the prognosis (forecasted survival) for a tumour which has spread from the primary site is less good than for a tumour localised to one site. The primary tumour may elude discovery for a variety of reasons:

- It is very small.
- It grows very slowly.
- The original tumour may have died or been destroyed after the metastasis had occurred. Such a situation might occur if, for example, the blood supply of the original tumour was compromised resulting in tumour death, or perhaps the body's immune system might have killed the primary tumour.
- The primary tumour may be removed or destroyed unknowingly during another procedure, such as, for example, a hysterectomy undertaken for a benign cause such as fibroids.

Like any tumour, a cancer of unknown primary may present in a variety of ways, depending on the symptoms it causes, which in turn may be influenced by the body tissue in which it is located. It may present as:

- Pain, bleeding or functional disturbances.
- A lump which may be painful or painless.
- A cough, hoarse voice or breathlessness.
- Disturbances of urination, including progressive obstruction.
- Bowel disturbances such as diarrhoea, constipation, inability to pass stool (obstruction) or abdominal pain.
- Unexplained weight loss.
- Persistent unexplained fever or night sweats.

Reaching a diagnosis for patients with presenting symptoms is undertaken using standard techniques of examination and investigation and, if a suspicious lesion of any sort is identified, it would be biopsied and assessed microscopically by a histopathologist.

The nature of the biopsy would depend on the location and size of the mass and might be done by:

- Incision (removal of part of the lesion).
- Excision (removal of the whole lesion).
- Needle biopsy, where a needle is inserted into the lesion and a core of tumour is removed.

The traditional approach of staining a specimen of the tissue and examining it under a microscope is now supplemented by a range of more advanced techniques including:

- Genetic evaluation to understand the nature and mutations of such tissue and which may predict how the tumour can be treated.
- Immunological assessment to look for tumour **antigens** which could be neutralised by body **antibodies** or by immunotherapy.
- Electron microscopy to review the cells at a subcellular level to identify specific cell changes.

These investigations may enable the clinicians to discover the nature of the parent tissue and give a further clue to the search for the primary tumour.

With the information gleaned from examination and biopsy, the clinician may be able to obtain a better idea of the location of the primary tumour.

Another clue may be the anatomical location of the metastasis.

- Tumours above the diaphragm tend to have come from above the diaphragm and the primary may be in the lung or breast
- Cancer from below the diaphragm is commonly from one of the organs in the abdomen, including the bowel, stomach, pancreas or liver.
- If the tumour is found in a lymph node, then the primary tumour may be in a tissue from which the lymph drains into the lymph node concerned.

If the diagnosis still remains elusive, the clinician may undertake more detailed scanning including;

- Dye enhanced CT scanning
- MRI scanning
- PET (Positron Emission Tomography) scanning using a radioactive glucose marker which makes malignant cells appear more distinct.
- Mammography

In addition, endoscopy may be employed, or the use of a Tumour Marker test may be used.

These tests rely on the fact that some tumours produce chemical markers which are at higher levels in the body.

They include:

- Prostate Specific Antigen (PSA)
- B-Human Chorionic Gonadotrophin (β -HCG)
- Cancer Antigen-125 (CA-125).

Despite all these examinations and investigations, the primary site of the tumour may remain elusive.

The cancer specialist (**oncologist**) will have to plan how to treat the tumour without knowing for sure whether there is one or more other tumours located elsewhere.

The specialist's judgement will be based on:

- Location
- Histology, particularly whether it is well-differentiated (which **may** indicate more specificity, slower growth and greater responsiveness to treatment) or poorly-differentiated (which **may** suggest more rapid growth and sometimes poor response to treatment).

Treatment of cancers of unknown primary utilises the some forms of treatment as all other cancers:

- Surgery
- Chemotherapy
- Radiotherapy
- Hormone therapy.

Depending on the nature and location of the cancer, one or more of the treatment modalities may be utilised.

For patients, there will be the same benefits, risks and complications as with any other form of cancer.

However, there may be an additional difficulty in offering a prognosis if there are other tumour deposits, undiagnosed elsewhere.

However, like all forms of cancer treatment, the management of disease is improving, new types of medical therapy are being introduced and new techniques of chemotherapy are achieving ever better results.

As a result of the increasingly sophisticated investigative techniques, the number of tumours, where the primary tumour remains unknown, are continuing to decline.

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