

● **p23**
UPDATE
informs you of changes in clinical practice. This week: understanding CUP

● **p26**
SYSTEMS OF LIFE
offers information on anatomy. This week: an overview of the lymphatic organs

● **p28**
GUIDED LEARNING
includes online CPD. This week: fluid resuscitation in burns

● **p30**
DEVELOPMENT
shows how nurses are developing practice. This week: managing pleural effusions

● **p32**
RESEARCH
presents research papers. This week: supporting self-care in the community

UPDATE

SUPPORTING PATIENTS WITH CANCER OF UNKNOWN PRIMARY

As NICE begins developing the first clinical guideline on cancer originating from an unknown primary, John Symons details what is known about this phenomenon

Cancer of unknown primary (CUP) is a challenging diagnosis for healthcare professionals as well as for patients. It often falls to nurses to explain this poorly understood diagnosis to patients and their families. To do this effectively, it is important to know what is understood about CUP.

Problems of classification and the lack of consensus on terminology and treatment mean that there is no definitive figure for CUP incidence in the UK.

Estimates range between 3–10% of all cancer diagnoses. However, Pavlidis (2007) stated that CUP represents one of the 10 most frequently presenting cancers and the fourth most common cause of death from cancer.

DEFINITION AND DIAGNOSIS

CUP is an umbrella term for a heterogeneous group of clinical presentations associated with hidden or occult cancers. This heterogeneity exacerbates the problems of classification. The phenomenon is referred to using a range of terminology such as carcinoma of unknown primary, occult primary malignancy and tumour of unknown origin.

The National Comprehensive Cancer Network (NCCN, 2008) states that: 'Occult primary tumours or cancers of unknown primary are defined as histologically proven metastatic malignant tumours whose primary site cannot be identified during pretreatment evaluation.'

In a confusing arena that lacks consensus, it may be helpful in practical terms to distinguish between diagnoses that are of an 'uncertain' primary – where the primary tumour's lineage is eventually determined through specialised pathology – and those that are truly 'unknown' – where the primary is never conclusively identified. Some patients with CUP may be treated for a 'known' primary for pragmatic reasons even though this is not diagnosed with certainty. For reasons why the primary site may be hidden, see box p24.

A patient with cancer presenting with a metastatic lesion is likely to undergo a biopsy so pathologists can try to determine the origin of the cancer. When tumour cells spread or metastasise, the secondary or metastatic tumour cells are those of the original tumour, whether it can be found or not. Every secondary tumour will have a

primary and certain secondaries tend to originate from certain primaries. This is significant because effective cancer treatments seek to target the original, ancestral cells.

Depending on their condition, patients with CUP face further tests to try to identify the primary tumour. If it cannot be found, treatment will be primarily palliative. Life-expectancy statistics in the literature vary considerably depending on the type of CUP and the effectiveness of chemotherapeutic agents. Baron-Hay and Tattersall (2001) recorded a median of 4–11 months with a 6% five-year survival rate.

CATEGORISATION AND TREATMENT

Options for treatment will be based on the metastatic pattern and the evidence that can be determined from histopathological analysis.

Greco and Hainsworth (2004) reported that the primary site of cancer becomes obvious in only 15–20% of patients with CUP during their lifetime with 70–80% having the primary site detected at postmortem.

CUP occurs equally in men and women and tends to be more common in older

REFERENCES

Baron-Hay, S.E., Tattersall, M.H.N.

(2001) Cancer of unknown primary site. In: Souhami, R.L. et al (eds). *Oxford Textbook of Oncology*. Oxford: Oxford University Press.

Dennis, J. et al (2005) Markers of adenocarcinoma characteristic of the site of origin: development of a diagnostic algorithm. *Clinical Cancer Research*; 11: 10, 3766–3772.

Greco, F. A., Hainsworth, J.D. (2004) Cancer of unknown primary site. In: Devita, V.T. et al (ed). *Cancer: Principles and Practice of Oncology* (7th ed). Philadelphia, PA: Lippincott Williams & Wilkins.

National Comprehensive Cancer Network (2008) *Clinical Practice Guidelines in Oncology Occult Primary*. www.nccn.org

Pavlidis, N. (2007) Forty years experience of treating cancer of unknown primary. *Acta Oncologica*; 46: 5, 592–601.



For more clinical information subscribers can log on to nursingtimes.net and click on to NT Clinical and Archive

people than younger (NCCN, 2008). Treatment will depend on the patient's resilience. In 'chasing the primary' the oncologist may attempt one or more therapeutic regimens for CUP. Empiric chemotherapy is based on the oncologist's experience and what the location of the secondary tumours and the tissue sample may suggest.

CUP BIOLOGY AND THE FUTURE

Little is known of the biological features of CUP and it is well recognised that, in relation to CUP, better diagnostic markers are needed to enable the assignment of metastases to likely sites of origin from pathological samples (Dennis et al, 2005).

It is generally accepted that CUP is a clinical presentation of metastases in patients in whom the primary tumour cannot be detected. As a result, the oncologist's attention is focused on diagnostic evaluation to find the origin of the tumour and then

treat it accordingly. This puts the main focus on imaging tools and, perhaps more significantly for the future, genetic profiling techniques. The latter is in early stages of development but it can be used to investigate CUP tumours. However, this technique is not funded presently by either the NHS or independent healthcare providers in the UK. Genetic profiling seeks to identify genetic patterns or the 'fingerprints' of the cancer to detect the specific tumour lineages of the malignant cells involved.

The development of epidermal growth factor receptor (EGFR) inhibitors may prove valuable in the treatment of CUP – as they have for other metastatic late-stage diseases.

HELPING PATIENTS

Any cancer diagnosis is frightening for both patients and their family and friends. Not knowing where cancer has originated accentuates fear and anxiety.

CUP is a diagnosis of exclusion in two senses. First, because it refers to a condition that cannot be established from examination or testing; and second, because patients and their families can feel isolated and excluded by the lack of information available to them. It is in this latter area, particularly immediately after diagnosis, that a well-informed nurse can offer comfort and support to patients and their loved ones.

Most patients will never have heard of CUP and will seek answers to their questions as the diagnosis sinks in. It can seem incomprehensible to them that in this scientific age, with all the sophisticated diagnostic imaging techniques available, a primary tumour is invisible and that there are no clearly defined treatment paths for their cancer.

Knowledge can help dispel the fear of this diagnosis, and a social network that offers patients emotional support, information and

practical assistance has been shown to prolong and enhance life.

While general support is available from cancer charities, such as Macmillan Cancer Support and Maggie's Centres, the following charities offer specific information on CUP and can provide targeted support to patients with this condition:

- Cancerbackup (www.cancerbackup.org.uk);
- CancerHelp UK – the patient website of Cancer Research UK (www.cancerhelp.org.uk);
- The Cancer of Unknown Primary (CUP) Foundation – Jo's friends (www.cupfoundjo.org).

It must be recognised that not all patients will want to receive additional information, although their carers may. Patients' reactions will vary but can include fighting spirit, denial, hopelessness and acceptance. The positive message that can be given is that many of those with a CUP diagnosis will have their primary cancer found and receive effective treatment; and all can experience remission and palliative care appropriate to their particular needs and condition.

CONCLUSION

CUP, where the primary consistently defies discovery, covers a wide range of clinical presentations and histological appearances. For patients and their loved ones there is no adequate way of describing a CUP diagnosis. The patient is told: yes, you have cancer but so far it can't be determined what sort of cancer.

CUP is a little-known and little-understood phenomenon that will remain a diagnosis of exclusion in the absence of evidence. ■

- John Symons is director of the CUP Foundation – Jo's friends (www.cupfoundjo.org).

WHY IS THE PRIMARY SITE HIDDEN?

- **Size:** the primary may be too small to be picked up by present day scans. A malignant tumour is not usually considered significant until it is 2mm.
- **Fallen on stony ground:** the primary may have been successfully

attacked by the body's immune system as it tries to obtain a hold and migrated through the body to an easier place to thrive and confuse the immune system.

- **Sloughed-off:** the primary might have been

pushed out of the body, for example if it was loosely attached to part of the digestive system.

- **Obscured:** the secondaries, if growing close to the primary, may obscure the primary from imaging techniques.