

Patients' experiences of carcinoma of unknown primary site: dealing with uncertainty

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It is generally acknowledged that patients may find it particularly hard to accept a cancer diagnosis if the primary origin cannot be identified. However, there is very little research exploring this. **Aims:** This is an exploratory mixed-method, largely qualitative, pilot study to explore patients' understanding of carcinoma of unknown primary site, any concerns they may have and to assess their quality of life. **Methods:** Ten patients were recruited and nine completed semi-structured interviews and McGill quality of life questionnaires. Thematic analysis was used in conjunction with demographic data and quality of life scores. **Results:** Six main themes were identified. These were – poor understanding, struggling with uncertainty/contrasting with stoical acceptance, undergoing multiple investigations, inability to treat, healthcare professionals not having the answers and difficulty explaining to others. **Conclusion:** Many patients find the uncertainty difficult and would welcome more opportunity to ask questions and learn of others' experiences. *Palliative Medicine* (2008); xxx: 1–7

Key words: neoplasms; palliative care; quality of life; unknown primary

Introduction

Carcinomas of unknown primary site (CUP) are a heterogeneous group of tumours involving metastatic epithelial disease with no identifiable origin at the time of therapy.¹ It is a frequent diagnostic category, accounting for 2–6% of all invasive malignancies.² Median age at diagnosis is 71 in males and 73 in females.³

Treatment options are very limited for many of these patients (apart from a few favourable subgroups), and prognosis tends to be poor. Median survival ranges from four to 11 months, with one-year survival being 23% and five-year survival only 6%.³

It is generally acknowledged that patients may be extremely distressed and find it particularly hard to accept if the primary origin of the cancer cannot be identified.^{2,4,5} Hoskin and Makin describe it as a 'devastating and bewildering diagnosis for the patient and family'.⁴ The patient information charity CancerBACUP states 'it is all the harder to accept when doctors do not seem able to identify where the cancer is'.⁵ This is largely based on anecdotal evidence – there appears to be very little research exploring the impact of CUP on patients. Patients' needs and concerns must be explored if they are to be properly addressed.

In addition, there is minimal literature relating to the quality of life of patients with CUP.⁶ Rodary, *et al.* report

a study comparing patient preference for two different quality of life scores, in a group of patients with CUP but did not look at outcomes. There is, therefore, a need for rigorous, structured, qualitative research to explore these issues further.

Aims

- To explore patients' understanding of their cancer, how they describe it and rationalize the unknown nature of the primary.
- To identify any concerns, especially relating to the uncertainty of the diagnosis.
- To obtain quality of life data at the time of the interview, and to analyse this in conjunction with the themes emerging from the interviews.

Methods

An exploratory mixed-method, largely qualitative, design, with a thematic approach was used, since so little previous work has been done in this area. This enabled participants to describe their own perceptions and concerns so that theories are generated by patients, rather than by the researchers. Data was collected from semi-structured patient interviews and quality of life questionnaires, supplemented by observation, field notes and information from patient notes. Local Research Ethics Committee approval was granted.

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Setting and participants

Patients were recruited from two acute NHS trusts. Any patients with CUP aware of their diagnosis, able to provide written informed consent and well enough to talk to the researcher could be recruited. Potential participants were told about the study by healthcare professionals directly involved in their care. If interested, they were given an information sheet and subsequently approached by the researcher. Purposive sampling was used to incorporate a range of views.

Data collection

Patients were seen in their own home or in hospital (if an inpatient). Written informed consent was obtained.

Semi-structured interviews were used lasting an average of 30 minutes. The interviews were audiotaped and independently transcribed verbatim. Anonymized themes emerging from each interview were discussed in subsequent interviews to allow on-going validation of themes.

Patients completed the McGill quality of life (QOL) questionnaire immediately after their interview. This is an assessment tool that has been shown to be valid, acceptable and relevant to palliative care patients.^{7,8}

Demographic data was collected, by direct questioning and from patients' records, in order to put patients' views in context.

Data was collected between May 2006 and April 2007. Sampling of patients continued until no new themes were identified.

Analysis

Transcripts were reviewed as they were typed in conjunction with demographic data, field notes and quality of life questionnaires. Thematic analysis was used to develop categories and themes.

They were then re-categorized iteratively in the light of further emerging data.⁹

These themes were then compared with demographic and QOL data and scrutinized for any differences based on length of time from diagnosis, performance status and extent of disease.

One researcher performed the interviews and analysis. A coding framework was agreed with an independent researcher after analysis of the first transcript. A second independent researcher subsequently reviewed 20% of the transcripts, to ensure the thematic analysis was reproducible.

Results

Sixteen patients were identified. Five deteriorated rapidly before they could be seen and one declined. Ten patients

were therefore recruited. Their key characteristics are shown in Table 1. Nine patients had carcinoma of entirely unknown origin; they all had specialist palliative care involvement. One patient with adenocarcinoma of possible ovarian origin was recruited by purposive sampling to include a different experience. Eight interviews were conducted in patients' homes and two on hospital wards. Three patients had partners present at the interview. These partners discussed their views but this information was not included in the analysis.

One patient was found to be confused at the time of interview and her data could not, therefore, be included. Another patient spoke very quietly due to his Parkinson's disease and the audiotaped interview could not be fully transcribed. Themes from his interview and QOL data were incorporated into the analysis.

Thematic analysis identified six main categories related to having an unknown primary cancer. These were:

- Uncertainty contrasting with stoical acceptance
- Understanding of CUP/causality
- Undergoing multiple investigations
- Being unable to treat CUP
- Healthcare professionals not knowing the answers
- Difficulty explaining to others – not like other cancers.

The overarching theme of uncertainty influenced the five other categories.

In addition, coping strategies and concerns relating generally to the 'cancer experience' were identified.

Analysis of the themes in conjunction with demographic and QOL data revealed no relationship between more negative themes and length of time from diagnosis, extent of disease, physical symptoms or performance status.

Uncertainty contrasting with stoical acceptance

Many patients struggled with the uncertainty of the unknown nature of the primary. For most, this seemed to relate to the unpredictability of CUP – not knowing what might happen and a sense of it 'moving around' or 'suddenly reappearing.' Many patients described an ominous sense that it may be 'spreading,' 'lurking' or 'floating.'

I think that if that one there is a secondary and it can cause you that much jip, if there is a primary it could do you double the damage. I just don't understand how it can hide away somewhere ... it's the not knowing is the horrible thing ... the uncertainty of it all ... (if I knew) I would be more at ease.

(Patient 2)

Table 1 Patient characteristics

Patient	Age (median=60.5, mean=56.2)	Gender	Extent of disease	Treatment	Performance status ^a	Time since diagnosis	Global QOL score ^b
1	59	Male	Lymph nodes, bone, lung, spleen	Chemo ^c	1	4 months	5
2	70	Male	Bone	Local RT ^d	2	2 months	4
3	44	Female	Lymph nodes, peritoneum, pericardium	Chemo	4	9 months	6
4	78	Male	Pleural effusions, ascites, lymph nodes	None	1	2 months	8
5	62	Female	Bone, lung, lymph nodes	Chemo	4	2 months	N/A ^e
6	65	Male	Liver, peritoneum	None	3 ^f	3 months	3
7	23	Female	Lung, liver	Chemo	1	4 months	5
8	57	Male	Lung, bone	Chemo, local RT	1	1 month	6
9	40	Male	Lymph nodes	Chemo	1	15 months	10
10	64	Female	Possible ovarian primary, ascites	Chemo	1	3 months	5

^aEastern Cooperative Oncology Group performance status.

^bMcGill global quality of life score (maximum score=10).

^cChemotherapy.

^dLocal radiotherapy.

^eN/A, not available as found to be confused at time of interview.

^fPerformance status of 3 due to Parkinson's disease.

Others mentioned the need for a diagnostic label to provide greater understanding and sense of control, even if the cancer were still untreatable.

It's confusion because you don't know what to expect. I know there are loads and loads of cancers around and they know where most of them are, well why am I so different? Why are these unknown primaries? So ... I feel like screaming sometimes, literally screaming. (If they said where they are ... well, for me it would be peace of mind.

(Patient 3)

One participant contrasted the certainty of his diagnosis of leukaemia 20 years previously with the uncertainty of an unknown primary. He found the current unpredictability difficult with CUP, especially whether chemotherapy would be worthwhile or effective.

I've got no feeling where the actual cancer is and (my wife) quite often has a prod to see if she can find it. With the cancer I had before I knew exactly where it came from, but not knowing with this cancer makes me like unaware and I would like to know where it has come from.

(Patient 9)

A few patients said they accepted it was unknown and that they did not think about this, as there was 'no point.'

... if it is there it is there. I mean it doesn't make any difference to me now ... so trying to think about it is to me a bit of a waste of time.

(Patient 1)

Two patients with this attitude felt their ability to cope might be due to traumatic work experiences as a fireman and policeman. They and others also referred to their stoicism as their normal coping ability, trying to 'be positive' while acknowledging this can be difficult.

Even amongst those who were most stoical and unconcerned there was evidence of some ambivalence. This related more to the concerns of having any cancer rather than specifically CUP.

I feel fine, but I do know it's there, it's always at the back of your mind ... I certainly don't worry about it because there is nothing I can do about it and everything is in place if I need it ... well, that's not strictly true ... I am worried, I just don't show it out ...

(Patient 4)

The patient with a possible ovarian primary had made a conscious decision to believe it was ovarian cancer and that the targeted chemotherapy would be effective.

As far as I'm concerned it is in my ovaries ... because I'm being treated for ovarian cancer I'm not looking for anything else at the moment. It would be much more difficult if I didn't know where it was.

(Patient 10)

However, she admitted it still felt 'less clear cut' than when she was treated for breast cancer 17 years previously.

Understanding of CUP/causality

All patients with an entirely unknown primary discussed being told they had cancer but that the primary site could

not be found. Some said they did not fully understand this, only that they had cancer that could not be cured.

This kind of non-specific kind of ... they haven't found the primary tumour but it is spreading all over the place.

(Patient 1)

Many spoke of the sites where the cancer had spread. Several were concerned about the size of the cancer and how long it had been there.

I know I've got this alien under my arm ... but apart from that I don't where the rest are.

(Patient 3)

Several patients had questions for the researcher, asking how CUP can arise, how common it is and why the primary cannot be found.

Several patients had searched for possible causes, attributing it to smoking, past injuries, stress or else had found no possible cause. Some thought the cancer may have been present for a long time and may have 'manifested itself' at a later date. One patient described this as being like shingles.

Undergoing multiple investigations

All participants with an entirely unknown primary raised the theme of the number of investigations they had undergone to no avail, to search for the primary site.

... a whole series of tests, CT scans, MRI –you name it I had it ... and in the end they said well, we can't trace it.

(Patient 4)

They seem to have covered the whole of my body with tests and things.

(Patient 2)

Two patients described how they underwent multiple investigations and then were suddenly summoned to be told the bad news or treated with enormous urgency.

... then it was wam, bam and woof – you've got all these cancers and we don't know where they are coming from.

(Patient 3)

Being unable to treat

Another universal theme was the inability to effectively treat a cancer if the primary site is unknown. Many patients spoke of being able to target treatment much more effectively 'if you knew where it was.'

If they knew where it was they'd be doing something about it. I mean they have told me they cannot do anything about it at all, it's only palliative and I can accept that.

(Patient 2)

In addition, patients mentioned the difficulty in predicting response to treatment and whether undergoing treatment would be worthwhile. One patient described the need to ask for a second opinion to achieve 'closure.'

Two patients referred to the difficulties of having 'untried and untested treatment', and felt that the treatment they were receiving was not conventional chemotherapy.

She said ... they have not done that mixture before, so the side effects might cancel each other out or make it worse ... not sure about long-term effects ... very high dosage.'

(Patient 7)

This contrasts with the patient with a possible ovarian primary site who referred several times to her treatment plan and the reassurance this gave her.

They said we're going to treat you for ovarian cancer as that is the direction the tests are pointing, so as far as I was concerned that was it, a plan was in place. Because I've got a plan I'm concentrating on that, not on the negative.

(Patient 10)

Healthcare professionals not knowing the answers

All patients referred to the healthcare professionals involved in their care 'not knowing.' The majority of patients accepted this, while acknowledging that they would like more information.

I do understand they are in the dark as much as me ... They don't know enough about this unknown primary situation. Perhaps that's why they don't tell you much because they are not sure of what they are telling you.

(Patient 2)

Some patients found it very difficult that the 'so-called experts' did not have any answers. One was worried that all the consultants were 'baffled' (Patient 8).

One patient acknowledged that the uncertainty must be hard for the healthcare professionals themselves.

You've got to let the doctors do their bit; I know it's difficult for them as well.

(Patient 2)

Several patients found it helpful that they had been given as much information as possible about their illness, and had been shown their scans.

Most patients felt well supported by the healthcare professionals that they had encountered; a few reported feeling abandoned by their oncology teams.

He said, well they don't particularly want you and they are passing you back to me, and don't worry; I will deal with you, even though it's not strictly my province
(Patient 4)

Difficulty explaining to others /not like other cancers

Several patients felt CUP was not like other cancers. Two patients found it difficult being told they were very young and unusual to have CUP.

It was quite upsetting to know that mine is a rare case
...
(Patient 7)

Some patients found it hard explaining CUP to their family and friends, whose own cancer experience seemed quite unlike their own.

I keep getting the normal questions can they tell where it is and I try to explain ... but people still can't understand it.
(Patient 9)

One patient had not found this a problem at all.

We've just told them that I have cancer, probably on the bone and in my lungs. I don't have any trouble explaining to people.
(Patient 8)

Coping strategies

Several different coping strategies were identified, which related to coping with any diagnosis of cancer. Many patients talked about trying to 'remain positive', though admitted this was 'easier said than done.' Some spoke of the benefits of taking 'one day at a time.' Support offered by family and friends was invaluable as well as support from healthcare professionals, particularly when at home. Some found talking about their illness and concerns helpful. Several tried to maintain a sense of control by organizing their affairs and making their own decisions.

Concerns

Many concerns patients identified were again related to having any metastatic cancer. Several talked of their disbelief and shock, often persisting long after the initial diagnosis. Some patients voiced anger and existential

questions such as 'why me?' Another common theme was fear of the future and the unknown, as well as concerns about becoming more dependent.

Many descriptions of patients' healthcare experiences were given. Most of these were positive, but some less so, including poorly broken bad news and a sense of being on 'a conveyor belt.'

Several gave detailed descriptions of physical symptoms. Some patients described adverse effects of the disease on their lifestyle – for example role changes and impact on holidays and insurance.

Quality of life data

The McGill QOL questionnaire assesses QOL across global, physical, psychological, existential and support domains. High scores denote good QOL. Global QOL scores are shown in Table 1.

There was no direct correlation between degree of concern expressed in the interviews and quality of life scores. One patient who talked of coping well and remaining very positive scored very low in the psychological and existential domains. Another who discussed similarly positive themes in the interview scored extremely highly in all domains.

There was no correlation between low QOL scores for physical symptoms and more negative themes in the interviews. Overall, patients scored lowest in the physical domain, slightly better in psychological and existential domains, and generally scored quite well for support.

Discussion

This is an exploratory qualitative pilot study performed with the intention of generating ideas and themes regarding patients' perceptions of having CUP rather than aiming to generalize the results. Patients in this study were younger than average (a median age of 60.5 compared to medians of 71 for men and 73 for women for all patients with CUP) and came from two treatment centres.

Patients in this study have limited understanding of CUP and most would welcome more information.

Many patients found the uncertain nature of CUP difficult, both in terms of its unpredictability and in the desire for a firmer diagnostic label. They struggled with the inability to predict the likely course and response to any treatment offered. In addition, they would welcome a clearer diagnostic 'label' to enhance their understanding and sense of control. A diagnosis such as breast cancer immediately allows patients to identify with others and to access support from site-specific clinical nurse specialists and patient support groups. CUP is such a heterogeneous group that patients share no common experience in terms of disease trajectory or treatments given. Even CUP

where the primary site is ultimately found shows a different pattern of metastases from the expected distribution of the same known primary cancer. For example, bone metastases are uncommon in prostate and lung cancers that initially present as CUP.²

Speculatively, having CUP with a suspected primary site is easier for both patient and clinician, in terms of increased predictability and ability to target treatment. Certainly in this study, the patient with CUP of possible ovarian origin acknowledged she had made a conscious decision to firmly believe it was an ovarian primary and focus on its treatment. In fact, CUP where there is a suspected primary site do not respond to treatment as effectively as a known primary cancer at that site.²

Patients varied in their ability to cope with this uncertainty. In this pilot study, there was no relationship between length of time from diagnosis, extent of disease, physical symptoms or performance status on ability to cope. All patients described good social support. Two patients felt that past experiences and coping strategies enabled them to cope well now. The variations may fit with the five identified common adjustment styles to a cancer diagnosis: fighting spirit, helplessness/hopelessness, fatalism, avoidance/denial and anxious preoccupation.¹⁰ Personality styles may also influence current coping strategies. Little research has been done in this area, though a recent paper described a significant association between neuroticism and end-of-life distress.¹¹ In addition the way information is given by oncologists at diagnosis may influence acceptance. One participant (Patient 7) said her oncologist explained that only the secondaries could be treated, not the unknown primary, so recurrence was inevitable (despite having chemotherapy). This contrasts with some oncologists who emphasize that chemotherapy reaches the primary as well as the secondaries.

It is also recognized that failure to make a definitive diagnosis may be a cause of anxiety for the physician,² which one patient in this study acknowledged. This topic alone would be worthy of further research.

All patients in this study felt that if the primary site were known treatment would be more effective. These are justified concerns – even with treatment, CUP has an extremely poor prognosis.

Patients universally described undergoing multiple investigations with little benefit. In a review of patients with CUP managed by one cancer network, patients with liver or multiple metastases underwent an average of 19 investigations.² It is suggested that investigations should be limited to those that will identify the more favourable prognostic subgroups of CUP, which may respond to treatment.^{1–3}

This study suggests that patients would like more information and opportunities to ask questions. Many patients welcomed inclusion in this research and said they found it very helpful to talk further about CUP. Several commen-

ted that this had been their only opportunity to discuss these issues. Most participants wanted to know how CUP arises, how common it is, why the primary cannot be found, in addition to as much detail as possible about their individual case, including seeing X-rays and scans. They would also like information to be available about other people's experience of having CUP.

This was a pilot study. By the nature of the disease, some patients were too unwell or had died before they could be seen. One patient was too confused to be included in the results. This meant convenience sampling was largely used, rather than purposive as originally planned. Most patients were known to specialist palliative care teams, which may have had some bearing on how well supported they felt, and in turn on their ability to cope. The study was not longitudinal, so changes in understanding, perception and coping over time could not be assessed. However, the patients who were included varied widely in time from diagnosis.

The study suggests that the concerns of these patients are different from those with an identified primary and this should be taken into account by those providing the clinical care for these patients.

It is planned to use this pilot study to inform further research. A larger longitudinal study is needed with further assessment of quality of life. Other areas for research include assessing the impact of patients' personalities and information given by oncologists on coping with CUP, and looking at effects of CUP on family and carers.

Conflict of interest

None declared.

Acknowledgements

We would like to thank Gerry Loden and David Wright for advice on the protocol, Nicky Gibbons for transcribing the interviews, Helen Elsey for independently reviewing a transcript and Angie Rogers for reviewing transcripts and the manuscript.

References

- 1 Culin, S, Kramar, A, Saghatchian, M, *et al.* Development and validation of a prognostic model to predict the length of survival in patients with carcinomas of an unknown primary site. *J Clin Oncol* 2002; **20**: 4679–4683.
- 2 Shaw, PHS, Adams, R, Jordan, C, Crosby, TDL. A clinical review of the investigation and management of carcinoma of unknown primary in a single cancer network. *Clin Oncol* 2007; **19**: 87–95.
- 3 Baron-Hay, SE, Tattersall, MHN. Cancer of unknown primary site. In: Souhami, RL, Tannock, I, Hohenberger, P, Horiot, J-C. (eds). *Oxford Textbook of*

- Oncology*. Oxford: Oxford University Press, 2002: 2837–2851.
- 4 Hoskin, P, Makin, W. Malignancy of unknown primary site. In: Hoskin, P, Makin, W. *Oncology for Palliative Medicine*. (eds). Oxford: Oxford University Press, 2003: 253–261.
 - 5 CancerBACUP2005:www.cancerbacup.org.uk/Cancer-type/Unknownprimary/Canceroftheunknownprimary.
 - 6 Rodary, C, Pezet-Langevin, V, Garcia-Acosta, S, *et al*. Patient preference for either the EORTC QLQ-C30 or the FACIT quality of life measures: a study performed in patients suffering from carcinoma of an unknown primary site. *Eur J Cancer* 2004; **40**: 521–528.
 - 7 Cohen, S R, Mount, BM, Bruera, E, *et al*. Validity of the McGill quality of life questionnaire in the palliative care setting: a multi-centre Canadian study demonstrating the importance of the existential domain. *Palliat Med* 1997; **11**: 3–20.
 - 8 Pratheepawanit, N, Salek, MS, Finlay, IG. The applicability of quality-of-life assessment in palliative care: comparing two quality-of-life measures. *Palliat Med* 1999; **13**: 325–334.
 - 9 Mays, N, Pope, C. Quality in qualitative health research. In: Mays, N, Pope, C. (eds). *Qualitative Research in Health Care*. London: BMJ Books, 1999: 89–103.
 - 10 Greer, S, Watson, M. Mental adjustment to cancer: its measurement and prognostic importance. *Cancer Surv* 1987; **6**: 439–453.
 - 11 Chochinov, HM, Kristjanson, LJ, Hack, TF, *et al*. Personality, neuroticism and coping towards the end of life. *J Pain Symptom Manage* 2006; **32**: 332–341.