Brief Communication

Tumour markers

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Introduction

Imagine a typical gynaecological or surgical outpatients in the West. The doctor sees a patient with non-specific persistent abdominal pain, with nothing remarkable on examination. Typically he would 'fire off' a battery of tests for tumour markers, 'in case something turns up'. In Sri Lanka this may not be so in the public sector because of lack of resources, but could possibly happen in the private sector.

In Europe, this is common practice; it is estimated that over 15 million such requests are made in the UK every year, whereas only 10% of those are appropriate. Clinical biochemists are getting fed up with such 'fishing expeditions' and have come up with authoritative guidelines for their appropriate use. This prompted an excellent review by Sturgeon et al. This article is essentially a summary of it[1].

Tumour markers are a diverse group of substances which are present in higher than normal concentrations in blood or body fluids, in patients with cancer. A given marker could be present in more than one cancer, and also in a variety of other non-malignant conditions (Table).

Table. Tumour markers and associations

Marker	*Principal organ*	*Other associated cancers*	*Associated non-malignant conditions*
CA 125	Ovary	Endometrial, cervix, breast peritonea lliver, pancreas, lung, non-Hodgkin's lymphoma	*Other gynae events and pelvic conditions*: Menstruation, pregnancy, endometriosis, fibroids, urinary retention, pelvic examination, hysteroscopy, laparoscopy, ovarian hyperstimulation *Acute conditions*: hepatitis, pancreatitis, pericarditis, peritonitis, pleurisy *Chronic conditions*: arthritis, colitis, SLE, CCF, non-malignant ascitis
CA 199	Pancreas	Colorectal, liver gastric, oesophagus ovary	Acute and chronic pancreatitis, acute cholangitis, Chronic liver disease IBS
CEA	Colorectal	Pancreas, gastric, oesophagus Lung, mesothelioma Breast	Chronic liver disease, chronic renal failure Colitis, diverticulitis, IBS
AFP	Germ cell/testicular Liver	Colorectal, lung, gastric	Pregnancy
HCG	Germ cell/testicular Gestational trophoblastic	Lung	Pregnancy, cannabis use (transient)
PSA	Prostate	None known	All types of benign prostatic conditions Acute urinary retention All interventions involving bladder/prostate

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Clinical uses

1. The most appropriate use is monitoring response to treatment. They are universally useful in this regard.
2. Assessing prognosis, (along with other factors): In ovarian cancer, it is being realised that CA 125 level by itself is a poor indicator of prognosis, and scoring systems are being developed using multiple variables.
3. Detecting recurrence: although technically possible, it is ethically justifiable only if effective second line treatments are available and appropriate.
4. Diagnosis: Most of the misuse of tumour markers arises in this area.

   'Blanket use' is not justified in cases with non-specific symptoms. A single and specific request must be made with a clear diagnosis in mind, backed up by good clinical indicators. For e.g., CA 125 must be requested only when considering the differential diagnosis of a pelvic tumour, and not in those with vague abdominal pain. (If the clinical examination is uncertain, the next logical step is imaging and not measurement of CA 125.)
5. Screening:
   This is a developing area; currently recommended only in carefully selected groups:

   a. six-monthly **AFP** in patients with high risk of hepato-cellular carcinoma.

   b. PSA in men: PSA is unique in that it is organ-specific; but it is not cancer-specific. Its use as a screening test for early prostatic cancer is controversial as preliminary results from large scale studies have produced conflicting results[2,3]. Hence, the current recommendation is that it is used on an individual basis, after adequate counselling.

   c. CA 125 (along with pelvic ultrasound) could be used in a limited way in patients at high risk for ovarian cancer, in a dedicated cancer centre. Its use in population screening is currently being studied in 208 638 women (UKCTOCS) 4; the final results are due in 2015. Hopefully a consensus would then emerge.

Improper use

There is very clear evidence of this, apart from sheer numbers of requests. The most obvious examples are that in one centre, 26% of requests for CA 15-3 (marker for breast cancer) 5 and in another, 26% of requests for CA 125[6], were for men!

Illogical use of tumour markers is not just a waste of resources. It causes anxiety, leads to unnecessary invasive interventions, delays correct diagnosis by leading the clinician astray, and sometimes could give false reassurance.

Improvement in practice

This could only come from adhering to carefully made authoritative guidelines, by regular audit of one's practice and by case-reflection. Some guidelines are available; most are in 'pipeline', awaiting the outcome of large-scale studies.

Conclusion

Tumour markers are a valuable aid in the management of cancer, if properly used. It is an emerging field, and more definitive guidelines await firmer evidence.

References

1. Sturgeon CM, *et al*. Serum tumour markers: how to order and interpret them. *BMJ* 2009; **339**: 852-8.
2. Andriole GL, *et al*. Mortality results from a randomised prostate cancer screening trial. *N Engl J Med* 2009; **360**: 1310-9.
3. Schroder FH, *et al*. Screening and prostate cancer mortality in a randomised European study. *N Eng J Med* 2009; **360**: 1320-8.
4. Menon U, *et al*. Sensitivity and specificity of multi-modal and ultrasound screening for ovarian cancer, and stage distribution of detected cancers; results of the prevalence screen of the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). *Lancet Oncol* 2009; **10**: 327-40.
5. McGinley PJ, Kilpatrick ES. Tumour markers: their use and misuse by clinicians. *Ann Clin Biochem* 2003; **40** (pt 6): 643-7.
6. Ntaios G, *et al*. An audit of tumour marker utilisation in Greece. *Eur J Intern Med* 2009; **20**(3): e 66-9.