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Guest Editorial

Tumor markers in clinical practice

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ABSTRACT

Tumor markers are assuming a growing role in all aspects of cancer care, starting from screening to follow-up after treatment, and their judicious application in clinical practice needs a thorough understanding of the basics of pathophysiology, techniques of identification or testing, reasons for out-of-range levels of tumor markers, as well as the knowledge of evidence of their role in any given malignancy. These are, at the most, just an adjunct to diagnosis, and establishing a diagnosis on the basis of tumor markers alone (especially a single result) is fraught with associated pitfalls because of the problem of non-specificity. An ideal tumor marker does not exist. Detection can be done either in tissue or in body fluids like ascitic or pleural fluid or serum. Clinical uses can be broadly classified into 4 groups: screening and early detection, diagnostic confirmation, prognosis and prediction of therapeutic response and monitoring disease and recurrence. In addition to variable sensitivity and specificity, the prevalence of a particular malignancy may be a major determinant in the application of a particular test as a screening tool. Serum levels, in certain situations, can be used in staging, prognostication or prediction of response to therapy. Monitoring disease is, perhaps, the most common clinical use of serum tumor markers. Rising trend in serum levels may detect recurrence of disease well before any clinical or radiological evidence of disease is apparent ("biochemical recurrence"). Sampling should ideally be repeated after 5-6 half-lives of the marker in question (or the marker with the longest half-life if multiple markers are being considered); but if found elevated, the next sampling after 2-4 weeks, for additional evidence, may be justified.

1. Introduction

Current clinical practice in oncology has a growing impetus on early diagnosis, proper prognostication and (of late) screening for malignancy in asymptomatic groups. Tumor markers are assuming a growing role in all aspects of cancer care, starting from screening to follow-up after treatment. Important clinical decisions are increasingly likely to be made on the basis of these results, whether for diagnosis, screening, prediction or treatment monitoring.[1]

Tumor markers include a variety of substances like cell surface antigens, cytoplasmic proteins, enzymes, hormones, oncofetal antigens, receptors, oncogenes and their products.[2] There have been numerous attempts to broaden the definition to accommodate the rapidly expanding set of identified tumor markers

Various guidelines Have been suggested for clinical application in various malignancies by professional bodies like American Society of Clinical Oncology, Canadian Task Force, American Association for Clinical Chemistry, etc., but only tumor marker that finds a place in any screening algorithm is prostate-specific antigen (PSA).

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Table 1: Characteristics of an ideal tumor marker[3]

Characteristics	Remarks
Highly specific	Detectable only in one tumor type
Highly sensitive	Non-detectable in physiological or benign disease states
Long lead-time	Sufficient time for alteration of natural course of disease
Levels correlate with tumor	Prognostic and predictive utility of
burden	The tumor marker
Short half-life	Frequent serial monitoring of the marker levels after 5-6 half lives
Simple and cheap test	Applicability as screening test
Easily obtainable specimens	Acceptability by target population

Table 2: Methods of detection of tumor marker[4]

Serology	Enzyme assays
Immunological	Immuno histo chemistry
	Radio immuno assay
	Enzyme-linked immuno sorbent assay
Flow cytometry	
Cytogenetic analysis	Fluorescent in-situ hybridization
	Spectral karyotyping
	Comparative genomic hybridization
Genetic analysis	Sequencing (automated)
	Reverse transcription
	Gel electrophoresis
	DNA micro-array analysis
Proteomics	Surface-enhanced laser desorption/Ionization

2. Recommendations for Ordering Tumor Marker Tests

It is imperative to remember that a single value or test is unreliable. It is noteworthy that in most situations, elevations of markers in nonmalignant diseases are often transient, whereas elevations associated with cancer either remain constant or continuously rise. Ordering serial testing can help detect falsely elevated levels due to transient elevation. Knowledge of the assay method is important in interpretation of either an abnormal value or a serial change in tumor marker values.[5–7] Various methods of detection have their own specific cut off values and sensitivities.[8] Thus, for any set of serial values to be meaningful, they have to come from the same assay methods and preferably from the same laboratory.

An important interfering factor to be considered before any interpretation is presence of a hook effect. This is especially true if the value of a tumor marker does not correlate to the clinical situation. Hook effect is an inherent flaw of certain methods of detection (specifically immunoassay) due to which the serum tumor marker levels may be reported to be falsely low if the concentration rises above a particular level.

3. Interpretation

According to guidelines published by Working Group on Tumor Marker Criteria, interpretation should take into account the therapy status of the patient

If the patient is under active treatment or has received treatment in the recent past, changes in marker levels may reflect the clinical progression of the disease. Partial remission is defined as a decrease in marker levels by at least 50%; and progressive disease, as an increase in marker levels by at least 25%, on the basis of the concept that tumor load is related to changes in serum tumor marker level

4. Conclusions

The use of tumor markers in clinical oncology has increased tremendously with rapid expansion of techniques of detection and identification of new markers in recent times, a trend that continues to grow as technology progresses and our understanding about our body and the disease processes increases. However, such use is not without its pitfalls; in fact, injudicious application of tumor markers is fraught with risks of mistreatment (under-treatment or over-treatment) and its consequence

Judicious application of tumor markers to clinical practice needs a thorough understanding of the basics of pathophysiology, the techniques of identification or testing, reasons (in cases of both benign and malignant tumors) for out-of-range levels of tumor markers, as well as the knowledge of evidence of their role in any given malignancy

5. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

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