Cellular Immunology and Serum Biology

OMMEGA Publishers
Answering Intelligence

Editorial Open Access

Radioimmunoscintigraphy of Breast Cancer

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Abstract

Breast cancer has become one of the leading causes of death in women today. Many researches are ongoing to develop more effective imaging methods for early diagnosis of breast cancer. The application of nuclear medicine techniques to study patients with breast cancer has recently raised its profile, particularly in the investigation 'indeterminate mammographic lesions'. Radio labeled monoclonal antibodies can add a new dimension to diagnostic imaging and staging of metastatic breast cancer known as radioimmunoscintigraphy.

Keywords: Breast cancer; Radioimmunoscintigraphy; Monoclonal antibody

Received Date: August 16, 2016
Accepted Date: August 17, 2016
Published Date: August 19, 2016

Citation: Salouti, M. Radioimmunoscintigraphy of Breast Cancer. (2017) Cell Immunol Serum Biol 2(2): 48- 49.

Introduction

This review briefly points out some difficulties encountered with other conventional imaging modalities and describes radioimmunoscintigraphy method in the investigation of patients with breast cancer.

Mammography is the gold standard for diagnosing minimal, non-palpable breast carcinoma with a relatively high sensitivity in the range of 85 - 90%. It is, however, unreliable in cases involving dense breasts, augmented breast or in patients evaluated following breast surgery or radiotherapy with a false-negative rate of 25 - 45%. Ultrasonography is another common imaging technique to study breast cancer. It usually follows mammography, is non-invasive, easily available, relatively cheap and useful to differentiate cystic and solid lesions. However, as a screening tool it is limited by its low sensitivity and specificity, when applied to general population, and furthermore it is operator-dependent. Magnetic resonance imaging (MRI) is useful for further evaluation when mammography and sonography are indeterminate for the presence or location of a suspect abnormality, where previously mammographic surveillance was the only remaining option. However, the disadvantage of MRI is its unavailability and relatively high cost at present.

In recent years nuclear medicine has become involved in the detection of breast cancer in patients with indeterminate mammographic lesions. One of the novel approaches for specific detection and selective treatment of cancer is the use of monoclonal antibodies (MAbs) conjugated with radionuclides. The efficacy of this technique depends on antigen expression on tumor cells relative to normal tissues. Affinity, specificity, pharmacokinetics, properties of the radionuclide and imaging techniques has influence on the efficacy of radioimmunoscintigraphy (RIS). Numerous antigens like CEA, MUC1 and TAG72 have been discovered in breast cancer and antibodies against them are in the developmental phase. During the last few years, different types of monoclonal antibodies have been used in breast tumor imaging in the animal models and human.

Technical limitations of RIS

***Antibody*:** MAbs are used currently, are not entirely sensitive to malignant tissues.

***Antigen*:** The majority of antigens represent tumor-associated antigens, not only present on the tumor tissues, but also detectable on normal tissues. Other factors influencing the suitability of antigens for tumor targeting are internalization and shedding into the blood stream.

***Background radioactivity*:** A high background level of radiation due to radioactivity in normal tissues reduces the tumor/background (T/B) ratio which reduces the success of imaging.

***Human anti-mouse antibodies*:** Almost all of the MAbs used in RIS are of the IgG class and are murine in origin. Administration of a murine MAb to a patient usually results in a human anti-mouse antibody (HAMA) response. This is due to the Fc portion of the antibody. A significant HAMA response will limit the efficacy of RIS in several ways. To decrease the immunogenicity, the MAb molecule can be reshaped to human–mouse chimeric (cMAbs) or even humanized (hMAbs) versions by using recombinant DNA techniques.

Improvement in RIS technique

Background subtraction: Subtraction has led to improved results in patients in whom tumors have not been seen, though the potential for false results should be remembered.

Second antibody: The background can be reduced by removing radioactivity from the blood circulation. The use of active second antibody is a good way to achieve a clear picture.

Targeting agents: The fragments of antibodies can be used instead of whole antibodies to target tumors to improve the delivery of radioactivity to tumor sites.

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