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ORIGINAL ARTICLE

Role of epidermal growth factor receptor in malignant pleural mesothelioma and its value for successful chemical pleurodesis

A. El-Hosainy [a], H. Hosny [a], S. Gabal [b], S. Ahmed [a,*], Y. El-Hinnawy [a]

[a] Chest Department, Faculty of Medicine, Cairo University, Kasr Alainy, Manyl, Cairo, Egypt
[b] Department of Pathology, Faculty of Medicine, Cairo University, Egypt

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KEYWORDS

Malignant pleural mesothelioma;
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Abstract *Background:* The most common primary malignant tumor of the pleura is malignant mesothelioma. It is a highly aggressive tumor that has become a very important issue over recent years. Evidence suggests that EGFR is involved in the pathogenesis and progression of different carcinomas.

Aim of the work: To study the role of EGFR in MPM and to investigate its value for successful chemical pleurodesis.

Patients and Methods: This study included 53 patients with exudative pleural effusion. All were subjected to full history taking, clinical examination, CT chest, pleural biopsy histopathological analysis and EGFR Ab immunostaining. According to pleural biopsy histopathology, the patient population was divided into 3 subgroups; subgroup I (19 patients diagnosed benign pleural effusion); subgroup II (21 patients diagnosed MPM) and subgroup III (13 patients diagnosed malignant pleural effusion other than MPM).

Results: Regarding comparison between the 3 subgroups in the demographic data, there was no statistically significant difference in age, sex and smoking prevalence. Regarding pleural fluid analysis, there was no statistically significant difference in protein and LDH levels but there was

Abbreviations: EGFR, epidermal growth factor receptor; CT, computed tomography; MPM, malignant pleural mesothelioma; Ab, antibody; LDH, lactate dehydrogenase; SD, standard deviation; USA, United States of America; BTS, British Thoracic Society; dl, decilitre; IU, international unit; ErbB, erythroblastosis oncogene B; NSCLC, non small cell lung cancer; TKI, tyrosine kinase inhibitors

* Corresponding author. Mobile: +20 01116444422.
E-mail address: samohamedoctober@yahoo.com (S. Ahmed).

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statistical significance in sugar levels between subgroups I and II. There was statistical significance regarding predominant cell pattern during pleural fluid cytology. Also there was statistical significance regarding immunostaining for the detection of EGFR in pleural biopsy among study subgroups. However, there was no statistical significance regarding comparison between success of chemical pleurodesis and expression of EGFR among malignant subgroups of pleural effusion.

Conclusion: There is evidence that EGFR is frequently overexpressed in MPM and therefore may be used as a potential therapeutic target.

Introduction

The most common primary malignant tumor of the pleura is malignant mesothelioma. It arises from mesothelial surfaces of the pleural and peritoneal cavities, as well as from the tunica vaginalis and pericardium [1].

Malignant pleural mesothelioma is a highly aggressive tumor that has become a very important issue over recent years [2].

Epidermal growth factor receptor exists on the cell surface and is activated by binding of its specific ligands, including epidermal growth factor and others [3]. The resulting signaling network initiates diverse cellular pathways leading to proliferation, migration, gene transcription, cell cycle progression and cell survival [4].

Evidence suggests that the EGFR is involved in the pathogenesis and progression of different carcinoma types. In vivo and in vitro studies have shown that these proteins are able to induce cell transformation [5].

Subjects

The present study included fifty three patients who were selected from the Chest Department inpatients, Kasr Alainy Hospital. The selected patients had either exudative pleural effusion according to the light's criteria [6], pleural thickening or pleural masses that allows pleural biopsy to be performed. Patients with transudative pleural effusion, bleeding disorders or unfit for pleural biopsy procedures were excluded from the study.

The included patients were divided into 3 subgroups according to histopathological examination of the pleural biopsy:

- Group I: included 19 patients with benign pleural effusion.
- Group II: included 21 with MPM.
- Group III: included 13 patients with malignant pleural effusions other than mesothelioma.

Methods

All included patients were subjected to written informed consent, full history taking, detailed clinical examination, plain chest X-ray, CT chest, and thoracentesis with chemical and cytological analysis of the pleural fluid samples. Pleural biopsy was also obtained and sent for histopathological examination to reach a final diagnosis and to search for the presence of mesothelial cells in pleural biopsy. Then immunohistochemical staining was done in the pleural biopsy specimens that showed the presence of mesothelial cells for the detection of epidermal growth factor receptor.

Finally chemical pleurodesis was performed for malignant cases only, when the pleural fluid drainage was less than 100 cc/day and the lung was clinically and radiologically fully expanded.

Out of the 53 patients who formed the study population, 48 cases were diagnosed by medical thoracoscopic pleural biopsy, one case was diagnosed by sonar guided pleural biopsy and another one was diagnosed by Abram's needle. Also 3 patients underwent open thoracotomy and decortication.

Histopathological examination of the pleural biopsy

All tissue samples were routinely processed, fixed in 10% buffered formalin, dehydrated, cleared and embedded in paraffin wax according to the routine processing procedure. Two sections (5 microns thick) were prepared from each tissue paraffin block. One was stained by Hematoxylin and Eosin (H&E) staining for routine histopathologic examination and the other sections were on charged slides and subjected to immunohistochemical staining by mouse anti-EGFR.

Then all patients were classified according to the results of the routine histopathological analysis of the pleural biopsy into 3 subgroups as mentioned previously.

Immunohistochemical staining for detection of EGFR in pleural biopsy

Immunohistochemical staining by labeled streptavidin–biotin method of immunohistochemistry for EGFR by mouse anti-EGFR clone 31G7, antibody conc. 357 μg/ml serial number 20718528L, manufacturer: Genemed biotech USA, REF: 61-0027-2 and dilution of 1:50–1:100 for 30–60 min at room temperature).

After deparaffinization and rehydration, sections were placed in 3% hydrogen peroxide for 20 min to inactivate endogenous peroxidase and treated by microwave at 121 °C in citrate buffer (10 mM, pH 6.0) for 10 min as an antigen retrieval method. After cooling to room temperature for 30 min, specimens were non-specifically blocked by incubation with normal rabbit serum for 15 min at room temperature. Sections were incubated with the primary antibodies for one hour at room temperature. The sections were then subjected to a three-step labeling procedure, with the use of streptavidin biotin complex using 3,3′-diaminobenzidine as the chromogen and the sections were faintly counterstained with Hematoxylin.

The positive control for EGFR consisted of sections from metaplastic carcinoma of the breast known as positive for