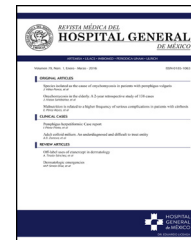




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ORIGINAL ARTICLE

Expression of cancer testis antigens in patients with Hodgkin's lymphoma and their clinical correlation

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KEYWORDS

Hodgkin's lymphoma;
Testis antigens;
MAGE-A gene family;
MAGE-A3 expression;
RT-PCR

Abstract

Objective: To determine the frequency of expression of cancer testis antigens and their clinical correlation in patients with Hodgkin lymphoma.

Methodology of the study: In this analytical, experimental and ambispective study, the MAGE A-3 and NY-ESO-1 antigen expression was correlated with clinical prognostic variables such as clinical stage, response to treatment, and relapse, in a total of 70 patients diagnosed with Hodgkin's lymphoma at the Hodgkin's Lymphoma Clinic of the General Hospital of Mexico "Dr. Eduardo Liceaga", from December 2000 to December 2015. Twenty-four patients were evaluated using RT-PCR, following extraction of RNA, to detect MAGE-A3 and NY-ESO1 expression. Cellular RNA was extracted from frozen tissue and controls using trizol (Life Technologies, Paisley, UK). 1 µg of RNA was used for cDNA synthesis by M-MLV reverse transcriptase (Life technologies, Paisley, UK).

Results: We studied 24 patients with a median age of 28 years, a minimum age of 16 years and a maximum age of 48 years, mostly male. 50% of patients presented complete response to the first line of treatment and 27% of patients presented relapse, 37.5% in relation to the expression of MAGE-A3. Expression of the NY-ESO-1 gene was not found in the study group. Twelve percent of patients died during the study, 8.33% of whom were also positive for MAGE-A3 ($p=0.264$, 95% CI). No significant correlation was found between MAGE-A3 expression and major clinical prognostic variables.

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Conclusion: Although the expression of MAGE-A3 in the study group was 37.5% (higher than reported in international studies), we found no correlation with the main clinical prognostics variables. Considering that the expression of MAGE-A3 in the cases studied does not confer prognostic value, making it impossible to use as a prognostic tool in peripheral blood, we are leaving the doors open to continue with this line of research, possibly increasing the number of patients as well as prolonging the follow-up time.

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PALABRAS CLAVE

Linfoma Hodgkin;
Antígenos testiculares;
Familia de genes MAGE A;
Expresión de MAGE A-3;
RT-PCR

Expresión de antígenos testiculares de cáncer en pacientes con linfoma Hodgkin y su correlación clínica

Resumen

Objetivo: Determinar la frecuencia de expresión de los antígenos testiculares de cáncer y su correlación con la clínica en pacientes con linfoma Hodgkin.

Metodología de estudio: Estudio de tipo analítico, experimental, ambispectivo, La expresión de antígenos MAGE A-3 y NY-ESO1 fue correlacionada con variables de pronóstico clínico tales como estadio clínico, respuesta a tratamiento, recaída, de un total de 70 pacientes diagnosticados con linfoma Hodgkin en la clínica de linfoma Hodgkin del Hospital General de México "Dr. Eduardo Liceaga" en el periodo comprendido entre DIC 2000 a DIC 2015. Fueron evaluados 24 pacientes a los que se les realizó mediante RT-PCR previa extracción de RNA la expresión de MAGE A-3 y NY-ESO1, el RNA celular fue extraído del tejido congelado y de los controles por medio de trizol (life technologies, paisley, uk) se utilizó 1 µg de RNA para la síntesis de cDNA por medio de la reverso transcriptasa M-MLV (life technologies, paisley, uk).

Resultados: se estudiaron 24 pacientes con una mediana de edad de 28 años, con una mínima de 16 años y una edad máxima de 48 años, predominio de sexo masculino, 50% de pacientes presentó respuesta completa a primera línea de tratamiento y un 27% de pacientes presentaron recaída, en relación con la expresión del gen MAGE A-3 fue de 37.5%, no encontrando en el grupo de estudio expresión para el gen NY-ESO1, El 12% de pacientes fallecieron en el periodo de estudio, de estos 8.33% fueron también positivos para MAGE A-3 (p=0.264, 95% IC). No se encontró correlación significativa entre la expresión de MAGE A-3 y las principales variables clínicas pronósticas.

Conclusión: A pesar de que la expresión de MAGE A-3 en el grupo de estudio fue de 37.5% (mayor a lo reportado en estudios internacionales), no encontramos correlación con las principales variables clínicas pronósticas, considerando que la expresión de MAGE A-3 en los casos estudiados no confiere valor pronóstico, por lo que no es posible utilizarlo como herramienta pronóstica en sangre periférica, dejamos puertas abiertas para continuar con esta línea de investigación considerando el incrementar número de pacientes así como prolongar el tiempo de seguimiento.

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Hodgkin's lymphoma (LH) is a neoplasm characterised by lymphatic infiltration of both Hodgkin cells and Reed-Sternberg cells surrounded by an inflammatory cell infiltrate composed of plasma cells, eosinophils and histiocytes.⁵ Factors associated with its onset have been described as familial factors, immunosuppression and association with viruses, the association with Epstein Barr virus being reported in more than 50% of cases.⁶

The majority of patients present with lymphadenopathy, with cervical lymphadenopathy being the most frequent, followed by axillary and, less frequently, inguinal lymphadenopathy, extra-nodal manifestations, either by direct

invasion or haematogenous dissemination, more frequently involving the spleen, lung and liver, and less frequently involving the bone marrow. Systemic symptoms occur in up to one third of patients, and include fever, night sweats, weight loss and chronic itching.

The diagnosis is made by excisional biopsy of the affected lymphatic tissue. Risk stratification is performed using the Ann Arbor staging system based on the involved lymph node area, the presence or absence of bulky mass, extranodal disease and present B symptoms.

The standard of treatment includes the use of the ABVD chemotherapy regimen (doxorubicin, bleomycin, vinblastine

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