Avens Publishing Group
J Surgery
February 2016 Vol:4, Issue:1

Open Access Research Article

Journal of Surgery

Studied of CD14 and CD15 Gene Expressions for Myeloid Derived Suppressor Cell Profile at the RNA Level as a Predictor for Progressivity in Nasopharyngeal Carcinoma

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Submission: 20 November 2015
Accepted: 27 January 2016
Published: 01 February 2016

Keywords: Myeloid derived suppressor cell; CD14; CD15; Nasopharyngeal carcinoma; 2-ΔΔCt Methods; qRT-PCR; Predictor of progression

Abstract

Background: Nasopharyngeal carcinoma (NPC) is a disease in which malignant cells formed in the tissue of the nasopharynx, which is a frequent cancer in Indonesia. Estimated of NPC in Indonesia at 6.2/100.000 or about 12.000 new cases per year. Developments of tumors are influenced by many factors, generally an interaction between genetic, environmental and immune system. There is a role of myeloid derived suppressor cells in the process of immune suppression.

Objective: The aim of this study is to clarify the profile of MDSC encoded by CD14 and CD15 genes expression to find the predictor for progressivity of nasopharyngeal carcinoma. Peripheral blood specimen and biopsy from primary tumor were collected from 16 nasopharyngeal carcinoma patients. The samples collected underwent qRT-PCR. Data were analyzed by 2-ΔΔCt methods and statistical analysis.

Results: There were up regulation of CD14 and CD15 m-RNA level in blood at advanced stage (52.42 and 38.03) using 2-ΔΔCt methods. The expression of CD14 and CD15 genes was strongly correlated with clinical stage.

Conclusion: MDSC can be used as a predictor of progression in NPC.

Introduction

Nasopharyngeal carcinoma (NPC) is a disease in which malignant cells formed in the tissue of the nasopharynx [1-4]. NPC is the most common malignancy in the head and neck and frequent cancer in Indonesia, rating as a fourth most common tumor of all malignancies. Overall incidence estimated of NPC in Indonesia at 6.2/100.000 or about 12.000 new cases per year [5].

Frequent cases are progressive NPC at the time of diagnosis; NPC patients generally come with an advanced disease that gives unsatisfactory therapeutic result. Difficulties arising in the NPC after getting the full treatment are when there are residual or recurrent and distant metastases, consequently survivals of NPC will decrease. We're looking for other tools for diagnosis, therapeutic efficacy, and predictor of progression based on the molecular pathogenesis.

Developments of tumors are influenced by many factors, generally an interaction between genetic, environmental, and immune system. There is a role of myeloid derived suppressor cells (MDSC) in the process of immune suppression.

Myeloid derived suppressor cells are a heterogeneous population of immature myeloid cells that are increased in states of cancer, inflammation, and infection with induced by tumor secreted growth factors in malignancy and play an important role in suppression of immune responses through several mechanisms such as production of arginase-1, release of reactive oxygen species (ROS) and nitric oxide (NO) and secretion of immune-suppressive cytokines [6]. This leads to a permissive immune environment necessary for the growth of malignant cells. MDSC may also contribute to angiogenesis and tumor invasion [6]. In the normal people, MDSC can be found in the bone marrow, whereas in pathologically states can be found in the spleen, blood circulation as much as 20-40%, tumor tissue, and lymph nodes [7-12].

Morphologically, MDSC can be divided into two types, namely monocytic (MO)-MDSC and granulocytic/polymorph nuclear (PMN)-MDSC [7-9,12,13]. In Humans, CD15+ population in the peripheral blood circulation can identify MDSC [9]. In a healthy individual, immature myeloid cell (IMC) can be seen around 0.5% in peripheral blood mononuclear cells. Markers that typical for PMN-MDSC is CD15 in blood circulation, while for MO-MDSC are CD14 [9,11,12,14,15].

Tumor progression due to tumor-derived factors (TDF) can be associated with severe progressive accumulation of IMC in the blood, lymph nodes, spleen, and primary tumor site. This aberrant balance between immature and mature myeloid cells is a hallmark of cancer and may be one of the central mechanisms of tumor evasion from the immune system and subsequent tumor progression [7]. Immature myeloid cells activations leads to up regulation of immune suppressive factors such as arginase (which is encoded by ARG1), induced nitric oxide synthase (iNOS, also known as NOS_2), increases the production of NO and ROS. Then accumulations of MDSC