

## Non-Hodgkin Lymphoma after Acute Myocardial Infarction: A Case Report

Somchai Insiripong, M.D.\*,  
Watcharin Yingsitsiri, M.D.\*,  
Juree Boondumrongsagoon, M.D.\*,  
Jirawadee Noiwanakul, M.D.\*

### Abstract

Acute myocardial infarction (MI) has never been mentioned as the risk factor for Non-Hodgkin lymphoma (NHL) development. But both of them may have some risk factors in common. Herein we report a case of 43-year-old Thai man who was diagnosed as acute inferior wall myocardial infarction based on the findings of the pathologic Q waves in leads II, III, aVF and coronary thrombosis on angiography three years ago. His risk factors consisted of hyperlipidemia, hypertension and long term smoking. He was successfully treated with the coronary intervention and medicated stenting and his regular medications included aspirin, atenolol, amlodipine, gemfibrozil, losartan and ranitidine. He had been well until developed progressive cervical lymph nodes enlargement for one month without fever or significant weight loss. And also multiple lymphadenopathies were found in the chest on the computerized tomogram of the chest. The cervical lymph node biopsy showed diffuse large B cell lymphoma. His clinical diagnosis was NHL stage IIA and he was treated with chemotherapy, CHOP regimen. He responded well to treatment, no relapse of NHL or acute MI. Although the direct association between acute MI and NHL has never been mentioned, both have one risk factor in common that is the current smoking.

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\*Hematology Unit, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima 30000

**บทคัดย่อ:** Non-Hodgkin Lymphoma หลังจากกล้ามเนื้อหัวใจตายเฉียบพลัน: รายงานผู้ป่วย 1 ราย  
 สมชาย อินทศิริพงษ์, พ.บ.\*, วชรินทร์ ยิ่งสิทธิ์ศิริ, พ.บ.\*,  
 จุรี บุญดำรงสกุล, พ.บ.\*, จิราวดี น้อยวัฒนกุล, พ.บ.\*,  
 \* หน่วยโลหิตวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา จ.นครราชสีมา 30000  
 เวชสาร โรงพยาบาลมหาราชนครราชสีมา 2559; 38: 53-7.

โรคกล้ามเนื้อหัวใจตายเฉียบพลัน ยังไม่ถือว่าเป็นปัจจัยเสี่ยงของการเป็นมะเร็งต่อมน้ำเหลืองชนิด non-Hodgkin lymphoma (NHL) โดยตรง แต่ทั้งสองโรคอาจจะมีปัจจัยเสี่ยงบางชนิดร่วมกันก็ได้ ในรายงานนี้เป็นผู้ป่วยชาย อายุ 43 ปี เคยเป็นกล้ามเนื้อหัวใจตายเฉียบพลันที่ผนังด้านล่างเมื่อ 3 ปีก่อน วินิจฉัยได้โดยการตรวจ EKG พบ Q wave ใน lead II, III, aVF และ angiography พบการอุดตันของเส้นเลือดหัวใจจริง ผู้ป่วยมีปัจจัยเสี่ยงคือ ไขมันในเลือดสูง ความดันโลหิตสูง และสูบบุหรี่มานาน ได้รับการรักษาด้วยการขยายหลอดเลือดซึ่งประสบความสำเร็จด้วยดี และใส่ขดลวดเคลือบยาให้ด้วย และให้รับประทานยา aspirin, atenolol, amlodipine, gemfibrozil, losartan, ranitidine มาตลอด ผู้ป่วยสบายดีจนมาตรวจอีกครั้งด้วยอาการต่อมน้ำเหลืองที่คอค่อย ๆ โตขึ้นภายใน 1 เดือน และพบต่อมน้ำเหลืองโตในทรวงอกจากเอกซเรย์คอมพิวเตอร์ร่วมด้วย ไม่มีไข้ ไม่มีน้ำหนักลด ผลตรวจชิ้นเนื้อต่อมน้ำเหลืองเป็นมะเร็งต่อมน้ำเหลืองชนิด diffuse large B cell lymphoma ให้การวินิจฉัยว่าเป็นมะเร็งต่อมน้ำเหลืองชนิดไม่ใช่ฮอดจกิน ระยะที่ IIA ให้การรักษาด้วยยาเคมีสูตร CHOP ซึ่งผู้ป่วยตอบสนองดี ไม่มีการกลับเป็นซ้ำอีกไม่ว่าโรคมะเร็งต่อมน้ำเหลือง หรือโรคกล้ามเนื้อหัวใจตาย เฉียบพลัน แม้โรคกล้ามเนื้อหัวใจตายเฉียบพลันจะไม่มี ความเกี่ยวข้องโดยตรงกับโรคมะเร็งต่อมน้ำเหลืองก็ตาม แต่ทั้งสองโรคก็มีหนึ่งปัจจัยเสี่ยงที่ร่วมกันอยู่นั่นคือ การสูบบุหรี่

## Background

Non-Hodgkin lymphoma (NHL) is a malignant disease of the lymphoid tissue. However it can also originate primarily outside the lymphoid tissue, the so called extranodal lymphoma. Moreover, it is basically multicentric disease therefore it can disseminate to distant various organs including the heart as the late manifestation<sup>(1)</sup>. The common site in the heart involved by the NHL is the pericardium, and the common cell type is high grade B cell NHL, not Hodgkin's disease<sup>(2)</sup>.

The NHL primarily originating at the heart has been very rarely reported<sup>(3)</sup> and it used to be reported as the rare and unusual cause of acute myocardial infarction (MI) by compressing the coronary artery by the lymphomatous deposit<sup>(4)</sup>. But the MI has never been mentioned as the direct risk factor for NHL development. However among various modifiable risk factors for MI including hypertension, diabetes mellitus (DM), lack of physical activity, dyslipidemia, current smoking, abdominal obesity, high risk diet,

and psychosocial stress<sup>(5)</sup>, only smoking appears to be weakly associated with risk of follicular NHL<sup>(6)</sup>.

Although the exact etiologies in the majority of the patients with NHL have not been known, they are more frequently found in cases with the immune defects, congenital or acquired conditions, post-transplantation, some infectious agents: HIV, EBV, *Helicobacter pylori*, human T-lymphotropic virus type 1, human herpesvirus 8, the autoimmune diseases such as rheumatoid arthritis, SLE or smoking<sup>(6)</sup>. Herein, we report one case of the chronic smoker who develops diffuse large B cell NHL after he was diagnosed as acute MI and has been treated with the coronary intervention and oral aspirin as well as clopidogrel for three years.

### Case Report

A 43-year-old Thai man presented with progressive cervical lymph nodes enlargement for one month, without pain. During this period, he had no constitutional symptoms such as fever or significant weight loss. His nodes were around 1-2 cm in diameter, firm, no tenderness. The chest and neck computerized tomography showed multiple lymphadenopathies 1-2 cm at the bilateral paratracheal, precarinal, para-aortic, cervical, axillary, submandibular, jugular and submental regions while the ultrasonography of the upper abdomen showed only the prominent size of the spleen.

Three years ago, he was definitely diagnosed as acute inferior wall myocardial infarction (MI) from the evidence of the pathologic Q waves in leads II, III, aVF and atrial fibrillation with rapid ventricular response on EKG and the occlusion of

the coronary vessels on the coronary angiography, and was successfully treated with the percutaneous coronary intervention (PCI) and stenting with the medicated coil. The echocardiogram revealed the ejection fraction of 62 %. His current modifiable risk factors for acute MI consisted of smoking, hyperlipidemia and hypertension. The drugs he took regularly comprised amlodipine, atenolol, cholestyramine, folic acid, gemfibrozil, losartan, ranitidine, clopidogrel and aspirin.

Laboratory investigations: Hb 12.9 g%, MCV 84.1 fL, MCH 28.0 pg, WBC 13,400/mm<sup>3</sup>, platelet 152,000/mm<sup>3</sup>, creatinine 1.2 mg%, uric acid 5.5 mg%, cholesterol 136 mg%, triglyceride 236 mg%, HDL 21 mg%, LDL 68 mg%, FBS 87 mg%, AST 40 IU/L, ALT 53 IU/L, alkaline phosphatase 88 U/L, LDH 358 IU/L.

VDRL and viral studies including HBsAg, anti-HCV, and anti-HIV were all negative.

The pathological diagnosis of the submental lymph node was diffuse large B cell lymphoma (DLBCL), positive CD20, negative CD3. The bone marrow study showed normal trilineage without NHL involvement.

He was definitely diagnosed as DLBCL, clinical stage IIA with the former diagnosis of acute inferior wall MI and the CHOP regimen was offered to him. He could tolerate and responded well to chemotherapy. After completing 6 courses of chemotherapy, he had no recurrence of NHL or acute MI. He could survive for few years in spite of the continuity of all mentioned drugs while this paper was being written.

## Discussion

Acute MI per se has never been mentioned to be directly associated with NHL. However, among the lists of various risk factors for MI and for NHL, current smoking is the only one factor that appears in both lists. Smoking can contribute the odd ratios of 2.87 for acute MI<sup>(7)</sup> and of 2.0 for NHL<sup>(8)</sup> and 1.31 with 95% confidence interval (CI) of 1.12-1.52 for follicular lymphoma<sup>(9)</sup>, as compared with the nonsmokers. Our case has regularly smoked the cigarettes since the early adulthood and never stopped even after the attack of acute MI.

For DM, the meta-analysis shows the risk ratio (RR) of developing NHL in patients with DM is 1.19 (95% CI 1.04-1.35). Based on prospective studies, patients with DM have an RR of developing NHL of 1.41 (95% CI 1.07-1.88), without heterogeneity among studies ( $I(2) = 34.3\%$ ;  $P > 0.10$ ). Based on case-control studies, patients with DM have an RR of 1.12 (95% CI 0.95-1.31) of developing NHL, compared with people without DM, with some heterogeneity among studies ( $I(2) = 36.28\%$ ;  $P = 0.09$ )<sup>(10)</sup>. However our case is proved to be free from DM.

The association of aspirin usage and NHL development is still controversial, women using aspirin exclusively (RR 1.71; 95% CI 0.94-3.13), non-aspirin NSAIDs exclusively (RR 2.39; 95% CI 1.18-4.83), or both types of drugs (RR 1.97; 95% CI 1.06-3.68) are at increased risk of NHL. And this positive association is independent of rheumatoid arthritis history<sup>(11)</sup>. But later, the case-control study of the patients with rheumatoid arthritis demonstrates that risk of NHL depends on the inflammatory activity of the disease rather than the treatment effect<sup>(12)</sup> and no association of aspirin and NHL is confirmed<sup>(13,14)</sup>.

On the contrary, aspirin usage is found to be inversely associated with total cancer incidence (multivariable-adjusted RR 0.84; 95% CI 0.77-0.90)<sup>(15)</sup>, moreover, regular aspirin usage may be associated with decreased NHL risk among men (adjusted OR 0.82, 95%; CI 0.65-1.04), but not among women (adjusted OR 0.93; 95% CI, 0.71-1.23)<sup>(16)</sup> and aspirin, not other NSAIDs, in the population-based case-control study, is found to be protective factor for Hodgkin's lymphoma development (OR 0.7, 95% CI 0.5-1.2)<sup>(17)</sup>.

## Conclusion

A 43-year-old Thai man presents with multiple lymphadenopathies for a month. The pathology of the lymph node is diffuse large B cell lymphoma. His former diagnosis is acute inferior wall myocardial infarction treated with coronary intervention and aspirin. Although the direct association between acute MI and NHL has never been mentioned, among various risk factors for MI, smoking is the only one that can also contribute the higher odd ratio to NHL development. But the association between the long term aspirin use for MI and NHL is controversial.

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