

Leukemoid Reaction in a Case of Chronic Cholecystitis With Focal Mild Acute Inflammation

Likhasit Sanglutong¹, Somchai Insiripong², Taweechai Wisanuyothin³

¹ Department of Medicine, Bangkok Hospital Muangraj, Ratchaburi, Thailand

² Department of Medicine, Saint Mary's Hospital, Nakhon Ratchasima, Thailand

³ Department of General Surgery, Saint Mary's Hospital, Nakhon Ratchasima, Thailand

Leukemoid reaction is a rare condition of marked increase of the white blood cells (WBC) in the peripheral blood, mostly more than $50 \times 10^9/L$. Although its most common cause is infection, acute or chronic cholecystitis has been hardly mentioned. This report aimed to present the leukemoid reaction found in a Thai who had chronic cholecystitis with focal acute inflammation. A 74-year-old woman had low-graded fever and generalized vague abdominal discomfort for 2 days. The physical examination showed the body temperature $37.7^\circ C$ and unremarkable abdominal signs. Her blood tests showed: hemoglobin 9.0 g/L, WBC $52.48 \times 10^9/L$, neutrophil 91%, band form 1%, platelet $434 \times 10^9/L$, and alkaline phosphatase (ALP) 290 U/L. The blood cultures yielded no growth. The computed tomography of the abdomen revealed 2 stones in the common bile duct (CBD) causing obstruction; the gall bladder (GB) showed mild dilatation with thin wall containing multiple small gall stones; no pericholecystic fluid and normal size of spleen. She promptly underwent operative cholecystectomy, CBD choledochoscopy, stones removal and T-tube choledochostomy. Along with the surgery, intravenous ertapenem was also administered. The pathology of the gall bladder was chronic cholecystitis with focal mild acute inflammation. With these therapies, fever daily decreased and finally disappeared within 5 days meanwhile the WBC count also gradually diminished every day till $8.04 \times 10^9/L$ within 7 days. The WBC count was still normal one month later. The diagnosis of leukemoid reaction was concluded and it was presumably be associated with chronic calculous cholecystitis with focal acute inflammation although the BCR-ABL translocation had never been explored.

Keywords: Cholecystitis, Leukemoid reaction, White blood cell

Rama Med J: doi:10.33165/rmj.2021.44.3.250706

Received: June 11, 2021 **Revised:** July 13, 2021 **Accepted:** August 31, 2021

Corresponding Author:

Likhasit Sanglutong
Department of Medicine,
Bangkok Hospital Muangraj,
59/3 Phetchakasem Road,
Na Muang, Muang Ratchaburi,
Ratchaburi 70000, Thailand.
Telephone: +668 4911 5775
E-mail: Lickhasit1986@gmail.com



Introduction

Leukemoid reaction is a condition of marked increase of the white blood cell (WBC) count in the peripheral blood with the different cut point of more than $30 \times 10^9/L$,¹ $40 \times 10^9/L$,² or $50 \times 10^9/L$ in most authorities.³⁻⁵ And the main WBCs involved are mature neutrophil possibly with the left shift. However all authorities agree the leukemoid reaction does not include the hematologic malignancy. For the definition of $30 \times 10^9/L$, its common causes include 47.9% of infection, 27.7% of ischemia/stress, 6.9% of inflammation and 6.9% of the obstetric diagnosis. And its common underlying conditions/diseases are the history of cardiovascular disease, diabetes and chronic lung disease. It posts the in hospital mortality rate of 38.1%. Factors that affect the degree of leukocytosis are positive blood culture, positive *Clostridium difficile* toxin and prolonged duration of leukocytosis. The kinds of infections commonly reported include sepsis, pneumonia, the urinary tract infection, disseminated tuberculosis, *C. difficile* colitis, shigellosis salmonellosis, brucellosis, cryptogenic abscess^{4,6} while the unusual infections include diarrhea, cellulitis, and gangrene.³

In Thailand, leukemoid reaction has been illustrated in 2 Thai children with acute hemolytic uremic syndrome associated with shigellosis dysentery, WBC $45 - 50.6 \times 10^9/L$.⁷ Herein we presented one case of leukemoid reaction that was recognized in an old Thai woman who experienced acute on top of chronic calculous cholecystitis.

Case Report

A 74-year-old Thai woman was admitted because of low-graded fever without chill for 2 days. Other symptoms included vague and mild generalized abdominal discomfort but severe anorexia, dysgeusia, early satiety, nausea, constipation and significant weight loss for 10 kg in 2 months. The physical examination revealed the body temperature $37.7^\circ C$, pulse rate 80/min, moderate pallor, no jaundice and no significant abdominal signs.

The initial blood tests included: hemoglobin 9.0 g/L; hematocrit 0.26 proportion of 1.0; WBC $52.48 \times 10^9/L$;

neutrophil 91%; lymphocyte 3 %; monocyte 5%, band form 1%; platelet $434 \times 10^9/L$, mean corpuscular volume (MCV) 81.5 fL; mean corpuscular hemoglobin (MCH) 27.8 pg/cell; mean corpuscular hemoglobin concentration (MCHC) 34.1 g/L; red blood cell distribution width (RDW) 19.5%; serum ferritin 1461.4 $\mu g/L$; serum iron 7.52 $\mu mol/L$ (normal 10 - 32); total iron binding capacity (TIBC) 30.79 $\mu mol/L$ (normal 38 - 73); transferrin saturation 24.4%; leukocyte alkaline phosphatase (LAP) activity 88; creatinine 99 $\mu mol/L$; estimated glomerular filtration rate (eGFR) 0.81 mL/sec/1.73m²; albumin 2.6 g/L; globulin 4.8 g/L; normal serum electrolyte ranges; indirect bilirubin 0.9 $\mu mol/L$; direct bilirubin 0.3 $\mu mol/L$; aspartate aminotransferase (AST) 38 U/L; alanine aminotransferase (ALT) 41 U/L; alkaline phosphatase (ALP) 290 U/L (normal 30 - 120); hemoglobin A_{1c} (Hb A_{1c}) 5.3%; and normal coagulogram. The blood cultures yielded no growth.

The multidetector computed tomography (MDCT) of the upper abdomen revealed: normal liver size with normal parenchyma; 2 gall stones, 0.7 cm and 0.8 cm in diameter at the mid and the distal portions of the common bile duct (CBD) causing the CBD obstruction and dilatation of bilateral intrahepatic bile ducts with the wall thickening; the gall bladder (GB) showed mild dilatation with thin wall containing multiple small gall stones; no pericholecystic fluid; and normal size of spleen.

The preoperative clinical diagnoses included leukemoid reaction, acute and chronic calculous cholecystitis, gall stones in the CBD with CBD obstruction, multiple gall stones in the GB, severe sepsis and anemia of chronic inflammation. She was immediately treated with parenteral ceftriaxone, metronidazole, and amoxicillin/clavulanic acid and blood transfusion. Her clinical manifestations seemed not respond to antibiotics. She accepted the surgical treatment, hence underwent the operative cholecystectomy, choledocostomy of the CBD, biliary stones removal and choledochostomy under the general anesthesia, on the second day of admission. She recovered well after the operation. All preoperative antibiotics were changed to be intravenous ertapenem (Invanz[®], Merck & Co, Inc, USA). After the operation, her low-graded fever gradually subsided and completely

disappeared in 5 days. The CBC was tested nearly every day since the first day after the operation. And the total WBC counts were shown to gradually diminish every test until finally became normal in 7 days: day 1, $43.23 \times 10^9/L$; day 2, $24.6 \times 10^9/L$; day 3, $22.18 \times 10^9/L$; day 4, $14.2 \times 10^9/L$; day 5, $10.02 \times 10^9/L$; day 7, $8.04 \times 10^9/L$.

The microscopic pathology of the resected gall bladder was chronic cholecystitis with focal mild acute inflammation, and numerous small gall stones.

One month after the operation, she had neither fever nor abdominal discomfort while her WBC count was still within the normal range.

The diagnosis of leukemoid reaction was definitely concluded and presumably associated with mild acute and chronic calculous cholecystitis as well as CBD stones and CBD obstruction therefore the BCR-ABL translocation gene was not studied.

Discussion

Leukemoid reaction associated with cholecystitis was found in a Thai woman. Its important differential diagnosis is chronic myeloid leukemia (CML). Because the strikingly high total WBC count in this case was mostly mature neutrophil, not all stages of myelopoietic development that is the morphologic characteristic of CML⁸ and it was not persistent.⁹ Moreover, LAP activity was normal,¹⁰ instead of marked decrease, the common characteristic of CML¹¹ therefore CML could be simply excluded although the BCR-ABL translocation, the important and specific gene for CML,¹²⁻¹³ was not explored yet. The WBC of CML should not become normal without tyrosine kinase inhibitor, bone marrow transplantation or chemotherapy.¹⁴

The far more difficulty for differential diagnosis is chronic neutrophilic leukemia (CNL) because both leukemoid reaction and CNL share most morphological features predominantly mature neutrophils in peripheral blood, increased LAP activity¹⁵ and the absence of the BCR-ABL translocation.¹⁶ However both entities mainly have different prognosis, mortality is found in

only one-third of leukemoid reaction patients³ but in nearly all of CNL patients.¹⁷

The WBC count in this case was markedly high at the initial presentation and became normal after proper management including both antibiotics and surgical intervention. It was opposed to those of cases of chronic myelomonocytic leukemia of who the WBC turned from $5.48 - 20.3 \times 10^9/L$ to $104 - 346.9 \times 10^9/L$ after operation for nonhematologic diseases.¹⁸ Therefore, chronic myelomonocytic leukemia could be simply excluded in this case.

In general, leukocytosis ($WBC > 10 \times 10^9/L$) can be found in only 52.7 % of acute cholecystitis and only 11.6 % of chronic cholecystitis.¹⁹ The mean (standard deviation) of WBC in acute cholecystitis is $13.2 (4.8) \times 10^9/L$ or $13.3 (5.5) \times 10^9/L$ in acute but $8.8 (2.8) \times 10^9/L$ in chronic cholecystitis.²⁰⁻²² If patients with acute cholecystitis were classified according to age into less than 65 years and 65 years or more groups, WBC greater than $10.5 \times 10^9/L$ is found in only 26.4% of the former but 41.2% in the latter.²³ The WBC may be found higher, up to $17.4 \times 10^9/L$ in a case of more severe cholecystitis or gangrenous form.²⁴ The maximal leukocytosis of $20.3 \times 10^9/L$ was recorded in a case with acute on top of chronic cholecystitis.²⁵ On the contrary, in patients with non-gangrenous acute cholecystitis, up to 32% had no leukocytosis, and 28% had neither fever nor leukocytosis whereas in patients with gangrenous acute cholecystitis, 27% lacked leukocytosis, and 16% lacked fever and leukocytosis.²⁶ To our knowledge, the WBC greater than $50 \times 10^9/L$ in the case of chronic calculous cholecystitis with focal mild acute inflammation and CBD obstruction seen in this case has never been mentioned before.

Conclusions

A 74-year-old Thai woman was incidentally found to have very high count, more than $50 \times 10^9/L$, mostly mature neutrophils or leukemoid reaction due to chronic cholecystitis with focal mild acute inflammation and CBD obstruction. She was recovered well and leukemoid reaction became normal after cholecystectomy and antibiotics therapy. Hence chronic myeloid or CNL could be simply excluded.

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ภาวะเม็ดเลือดขาวสูงคล้ายมะเร็งเม็ดเลือดขาวในผู้ป่วยถุงน้ำดีอักเสบเรื้อรังร่วมกับการอักเสบเฉียบพลันเป็นหย่อม

ลิขสิทธิ์ แสงลู่ทอง¹, สมชาย อินทศิริพงษ์², ทวีชัย วิษณุโยธิน³

¹ กลุ่มงานอายุรกรรม โรงพยาบาลกรุงเทพมหานครเมืองราช ราชบุรี ประเทศไทย

² กลุ่มงานอายุรกรรม โรงพยาบาลเซนต์แมรี นครราชสีมา ประเทศไทย

³ กลุ่มงานศัลยกรรมทั่วไป โรงพยาบาลเซนต์แมรี นครราชสีมา ประเทศไทย

ภาวะเม็ดเลือดขาวสูงคล้ายมะเร็งเม็ดเลือดขาว หรือปฏิกิริยาลิวคิมอยด์ (Leukemoid reaction) เป็นภาวะที่เม็ดเลือดขาวในเลือดเพิ่มขึ้นสูงมาก ส่วนมากใช้เกณฑ์เกินกว่า $50 \times 10^9/L$ พบได้ไม่บ่อย และพบมากที่สุด ในโรคติดเชื้อ แต่สาเหตุที่เกิดจากถุงน้ำดีอักเสบเฉียบพลันหรือเรื้อรังยังพบน้อยมาก รายงานฉบับนี้นำเสนอภาวะเม็ดเลือดขาวสูงคล้ายมะเร็งเม็ดเลือดขาวในผู้ป่วยไทยที่ถุงน้ำดีอักเสบเรื้อรังร่วมกับการอักเสบเฉียบพลันเป็นหย่อม ผู้ป่วยเป็นหญิงไทย อายุ 74 ปี รับตัวไว้ในโรงพยาบาลด้วยไข้ต่ำ ปั่นป่วนท้องเล็กน้อย 2 วัน ตรวจร่างกายอุณหภูมิ 37.7 องศาเซลเซียส อาการทางหน้าท้องไม่ชัดเจน ตรวจเลือดพบปริมาณฮีโมโกลบิน 9.0 g/L เม็ดเลือดขาว $52.48 \times 10^9/L$ นิวโทรฟิล 91% แบนด์นิวโทรฟิล 1% เกล็ดเลือด $434 \times 10^9/L$ ค่าเอนไซม์อัลคาไลน์ฟอสฟาเตส 290 U/L การเพาะเชื้อจากเลือดให้ผลลบ ภาพเอกซเรย์คอมพิวเตอร์ช่องท้องส่วนบนพบนิ่วในท่อน้ำดี 2 เม็ด และมีภาวะท่อน้ำดีอุดตัน ถุงน้ำดีขยายขนาดเล็กน้อย แต่ผนังถุงน้ำดียังบาง ไม่มีของเหลวรอบถุงน้ำดี และมีนิ่วขนาดปกติ ผู้ป่วยได้รับการผ่าตัดถุงน้ำดีส่องกล้องท่อน้ำดี เอานิ่วในท่อน้ำดีออก และคาสาयरูปตัว T ระบายน้ำดีจากท่อน้ำดี ผู้ป่วยได้รับยา Ertapenem เข้าเส้นไปด้วย โดยการรักษาทั้งหมดนี้ ไข้ลดลงทุกวัน จนหายใน 5 วัน ขณะที่เม็ดเลือดขาวลดลงจนเหลือเพียง $8.04 \times 10^9/L$ ภายใน 7 วัน ผลจุลพยาธิสภาพของถุงน้ำดีคือ มีการอักเสบเรื้อรังร่วมกับการอักเสบแบบเฉียบพลัน เม็ดเลือดขาวยังอยู่ในเกณฑ์ปกติในอีก 1 เดือน จึงสรุปว่าเป็นภาวะเม็ดเลือดขาวสูงคล้ายมะเร็งเม็ดเลือดขาว ซึ่งเกี่ยวข้องกับถุงน้ำดีอักเสบเรื้อรังร่วมกับการอักเสบเฉียบพลันเป็นหย่อมจากการมีนิ่วในถุงน้ำดี แม้ว่าไม่ได้ศึกษาความผิดปกติของยีน BCR-ABL (BCR-ABL translocation) ซึ่งเป็นยีนจำเพาะของโรคมะเร็งเม็ดเลือดขาวเรื้อรัง

คำสำคัญ: ถุงน้ำดีอักเสบ ปฏิกิริยาลิวคิมอยด์ เม็ดเลือดขาว

Rama Med J: doi:10.33165/rmj.2021.44.3.250706

Received: June 11, 2021 Revised: July 13, 2021 Accepted: August 31, 2021

Corresponding Author:

ลิขสิทธิ์ แสงลู่ทอง

กลุ่มงานอายุรกรรม

โรงพยาบาลกรุงเทพมหานครเมืองราช

59/3 ถนนเพชรเกษม

ตำบลหน้าเมือง อำเภอเมือง

ราชบุรี 70000 ประเทศไทย

โทรศัพท์ +668 4911 5775

อีเมล Lickhasit1986@gmail.com

