OPINION REVIEW

7620  Whipple’s operation with a modified centralization concept: A model in low-volume Caribbean centers
Cawich SO, Pearce NW, Naraynsingh V, Shukla P, Deshpande RR

REVIEW

7631  Role of micronutrients in Alzheimer’s disease: Review of available evidence
Fei HX, Qian CF, Wu XM, Wei YH, Huang JY, Wei LH

MINIREVIEWS

7642  Application of imaging techniques in pancreaticobiliary maljunction
Wang JY, Mu PY, Xu YK, Bai YY, Shen DH

7653  Update on gut microbiota in gastrointestinal diseases
Nishida A, Nishino K, Ohno M, Sakai K, Owaki Y, Noda Y, Imaeda H

7665  Vascular complications of pancreatitis
Kalas MA, Leon M, Chavez LO, Canalizo E, Sarani S

ORIGINAL ARTICLE

Clinical and Translational Research

7674  Network pharmacology and molecular docking reveal zedoary turmeric-trisomes in Inflammatory bowel disease with intestinal fibrosis
Zheng L, Ji YY, Dai YC, Wen XL, Wu SC

Case Control Study

7686  Comprehensive proteomic signature and identification of CDKN2A as a promising prognostic biomarker and therapeutic target of colorectal cancer
Wang QQ, Zhou YC, Zhou Ge YJ, Qin G, Yin TF, Zhao DY, Tan C, Yao SK

Retrospective Cohort Study

7698  Is anoplasty superior to scar revision surgery for post-hemorrhoidectomy anal stenosis? Six years of experience
Weng YT, Chu KJ, Lin KH, Chang CK, Kang JC, Chen CY, Hu JM, Pu TW

Retrospective Study

7708  Short- (30-90 days) and mid-term (1-3 years) outcomes and prognostic factors of patients with esophageal cancer undergoing surgical treatments
Shi MK, Mei YQ, Shi JL
**Contents**

**Thrice Monthly Volume 10 Number 22 August 6, 2022**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7720</td>
<td>Effectiveness of pulsed radiofrequency on the medial cervical branches for cervical facet joint pain</td>
<td>Chang MC, Yang S</td>
</tr>
<tr>
<td>7738</td>
<td>Correlation between the warning symptoms and prognosis of cardiac arrest</td>
<td>Zheng K, Bai Y, Zhai QR, Du LF, Ge HX, Wang GX, Ma QB</td>
</tr>
<tr>
<td>7749</td>
<td>Serum ferritin levels in children with attention deficit hyperactivity disorder and tic disorder</td>
<td>Tang CY, Wen F</td>
</tr>
<tr>
<td>7760</td>
<td>Application of metagenomic next-generation sequencing in the diagnosis of infectious diseases of the central nervous system after empirical treatment</td>
<td>Chen YY, Guo Y, Xue XH, Pang F</td>
</tr>
<tr>
<td>7785</td>
<td>Prospective single-center feasible study of innovative autorelease bile duct supporter to delay adverse events after endoscopic papillectomy</td>
<td>Liu SZ, Chai NL, Li HK, Feng XX, Zhai YQ, Wang NJ, Gao Y, Gao F, Wang SS, Linghu EQ</td>
</tr>
</tbody>
</table>

**Clinical Trials Study**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7794</td>
<td>Performance of Dexcom G5 and FreeStyle Libre sensors tested simultaneously in people with type 1 or 2 diabetes and advanced chronic kidney disease</td>
<td>Ölafsdóttir AF, Andelin M, Saeed A, Sofizadeh S, Hamoodi H, Jansson PA, Lind M</td>
</tr>
</tbody>
</table>

**Observational Study**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7808</td>
<td>Complications of chronic pancreatitis prior to and following surgical treatment: A proposal for classification</td>
<td>Murruste M, Kirschmägi Ü, Kase K, Veršinina T, Talving P, Lepner U</td>
</tr>
<tr>
<td>7825</td>
<td>Effects of comprehensive nursing on postoperative complications, mental status and quality of life in patients with glioma</td>
<td>Dong H, Zhang XL, Deng CX, Luo B</td>
</tr>
</tbody>
</table>

**Prospective Study**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7832</td>
<td>Predictors of long-term anxiety and depression in discharged COVID-19 patients: A follow-up study</td>
<td>Boyraz RK, Şahan E, Boylu ME, Karpuzar İ</td>
</tr>
</tbody>
</table>

**META-ANALYSIS**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Page</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>7859</td>
<td>Rectal nonsteroidal anti-inflammatory drugs, glyceryl trinitrate, or combinations for prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis: A network meta-analysis</td>
<td>Shi QQ, Huang GX, Li W, Yang JR, Ning XY</td>
</tr>
<tr>
<td>7872</td>
<td>Effect of celecoxib on improving depression: A systematic review and meta-analysis</td>
<td>Wang Z, Wu Q, Wang Q</td>
</tr>
<tr>
<td>7883</td>
<td>Rectal mature teratoma: A case report</td>
<td>Liu JL, Sun PL</td>
</tr>
<tr>
<td>7890</td>
<td>Antibiotic and glucocorticoid-induced recapitulated hematological remission in acute myeloid leukemia: A case report and review of literature</td>
<td>Sun XY, Yang XD, Yang XQ, Ju B, Xu NN, Xu J, Zhao XC</td>
</tr>
<tr>
<td>7899</td>
<td>Non-secretory multiple myeloma expressed as multiple extramedullary plasmacytoma with an endobronchial lesion mimicking metastatic cancer: A case report</td>
<td>Lee SB, Park CY, Lee HJ, Hong R, Kim WS, Park SG</td>
</tr>
<tr>
<td>7906</td>
<td>Latamoxef-induced severe thrombocytopenia during the treatment of pulmonary infection: A case report</td>
<td>Zhang RY, Zhang JJ, Li JM, Xu YY, Xu YH, Cai XJ</td>
</tr>
<tr>
<td>7913</td>
<td>Multicentric reticulohistiocytosis with prominent skin lesions and arthritis: A case report</td>
<td>Xu XL, Liang XH, Liu J, Deng X, Zhang L, Wang ZG</td>
</tr>
<tr>
<td>7931</td>
<td>Primary hypertension in a postoperative paraganglioma patient: A case report</td>
<td>Wei JH, Yan HL</td>
</tr>
<tr>
<td>7936</td>
<td>Long-term survival of gastric mixed neuroendocrine-non-neuroendocrine neoplasm: Two case reports</td>
<td>Woo LT, Ding YF, Mao CY, Qian J, Zhang XM, Xu N</td>
</tr>
<tr>
<td>7944</td>
<td>Percutaneous transforaminal endoscopic decompression combined with percutaneous vertebroplasty in treatment of lumbar vertebral body metastases: A case report</td>
<td>Ran Q, Li T, Kuang ZP, Guo XH</td>
</tr>
<tr>
<td>7950</td>
<td>Atypical imaging features of the primary spinal cord glioblastoma: A case report</td>
<td>Liang XY, Chen YP, Li Q, Zhou ZW</td>
</tr>
<tr>
<td>7960</td>
<td>Resection with limb salvage in an Asian male adolescent with Ewing’s sarcoma: A case report</td>
<td>Lai CY, Chen KJ, Ho TY, Li LY, Kuo CC, Chen HT, Fong YC</td>
</tr>
<tr>
<td>Page</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>------</td>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------</td>
</tr>
<tr>
<td>7973</td>
<td>Delayed arterial symptomatic epidural hematoma on the 14th day after posterior lumbar interbody fusion: A case report</td>
<td>Hao SS, Gao ZF, Li HK, Liu S, Dong SL, Chen HL, Zhang ZF</td>
</tr>
<tr>
<td>7982</td>
<td>Clinical and genetic analysis of nonketotic hyperglycinemia: A case report</td>
<td>Ning JJ, Li F, Li SQ</td>
</tr>
<tr>
<td>7994</td>
<td>Occurrence of MYD88L265P and CD79B mutations in diffuse large b cell lymphoma with bone marrow infiltration: A case report</td>
<td>Huang WY, Weng ZY</td>
</tr>
<tr>
<td>8003</td>
<td>Rare case of compartment syndrome provoked by inhalation of polyurethane agent: A case report</td>
<td>Choi JH, Oh HM, Hwang JH, Kim KS, Lee SY</td>
</tr>
<tr>
<td>8009</td>
<td>Acute ischemic Stroke combined with Stanford type A aortic dissection: A case report and literature review</td>
<td>He ZY, Yao LP, Wang XK, Chen YJ, Zhou J, Zhou Q, Yang XF</td>
</tr>
<tr>
<td>8018</td>
<td>Compound-honesuckle-induced drug eruption with special manifestations: A case report</td>
<td>Zhou LF, Lu R</td>
</tr>
<tr>
<td>8025</td>
<td>Spontaneous internal carotid artery pseudoaneurysm complicated with ischemic stroke in a young man: A case report and review of literature</td>
<td>Zhong YL, Feng JP, Luo H, Gong XH, Wei ZH</td>
</tr>
<tr>
<td>8034</td>
<td>Microcystic adnexal carcinoma misdiagnosed as a &quot;recurrent epidermal cyst&quot;: A case report</td>
<td>Yang SX, Mou Y, Wang S, Hu X, Li FQ</td>
</tr>
<tr>
<td>8040</td>
<td>Accidental discovery of appendiceal carcinoma during gynecological surgery: A case report</td>
<td>Wang L, Dong Y, Chen YH, Wang YN, Sun L</td>
</tr>
<tr>
<td>8045</td>
<td>Intra-ampullary papillary-tubular neoplasm combined with ampullary neuroendocrine carcinoma: A case report</td>
<td>Zavrtanik H, Lucar B, Tomažič A</td>
</tr>
</tbody>
</table>

**LETTER TO THE EDITOR**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8054</td>
<td>Commentary on &quot;Primary orbital monophasic synovial sarcoma with calcification: A case report&quot;</td>
<td>Tokur O, Aydın S, Karavas E</td>
</tr>
</tbody>
</table>
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CASE REPORT

Antibiotic and glucocorticoid-induced recapitulated hematological remission in acute myeloid leukemia: A case report and review of literature

Xiao-Yun Sun, Xiao-Dong Yang, Xiao-Qiu Yang, Bo Ju, Nuan-Nuan Xiu, Jia Xu, Xi-Chen Zhao

BACKGROUND
Leukemic hematopoietic cells acquire enhanced self-renewal capacity and impaired differentiation. The emergence of symptomatic leukemia also requires the acquisition of a clonal proliferative advantage. Untreated leukemia patients usually experience an aggressive process. However, spontaneous remission occasionally occurs in patients with acute myeloid leukemia (AML), most frequently after recovery from a febrile episode, and this is generally attributed to the triggering of antineoplastic immunity. There may be another explanation for the spontaneous remission as implicated in this paper.

CASE SUMMARY
A 63-year-old Chinese man presented with high fever, abdominal pain and urticaria-like skin lesions. He was diagnosed with AML-M4 with t(8;21)(q22;q22)/RUNX1-RUNX1T1 based on morphological, immunological, cytogenetic and molecular analyses. He had a complex chromosome rearrangement of 48,XY,t(8;21)(q22;q22),+13,+13[9]/49,idem,+mar[9]/49,idem,+8[2]. He also had a mutated tyrosine kinase domain in fms-like tyrosine kinase 3 gene. He was treated with antibiotics and glucocorticoids for gastrointestinal infection and urticaria-like skin lesions. The infection and skin lesions were quickly resolved. Unexpectedly, he achieved hematological remission along with resolution of the febrile episode, gastrointestinal symptoms and skin lesions. Notably, after relapse, repeating these treatments resulted in a return to hematological remission. Unfortunately, he demonstrated strong resistance to antibiotic and glucocorticoid treatment after the second relapse and died of sepsis from...
bacterial infection with multidrug resistance. The main clinical feature of this patient was that symptomatic AML emerged with flaring of the gut inflammatory disorder and it subsided after resolution of the inflammation. Learning from the present case raises the possibility that in a subgroup of AML patients, the proliferative advantage of leukemia cells may critically require the presence of inflammatory stresses.

CONCLUSION
Inflammatory stresses, most likely arising from gastrointestinal infection, may sustain the growth and survival advantage of leukemic cells.

Key Words: Acute myeloid leukemia; Fms-like tyrosine kinase 3 tyrosine kinase domain; Glucocorticoid; Antibiotic; Spontaneous remission; Gastrointestinal infection; Case report

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Core Tip: Untreated leukemia patients usually experience an aggressive process. However, spontaneous remission occasionally occurs in a small number of patients with acute myeloid leukemia. Here, we report an acute myeloid leukemia (AML) patient with t(8;21) translocation who achieved recapitulated spontaneous remissions after antibiotic and dexamethasone treatments for febrile episodes and skin lesions. These antibiotic and dexamethasone treatment-induced spontaneous remissions indicated that inflammatory stresses, most likely arising from gastrointestinal infection, sustained the growth and survival advantage of the leukemia cells. Inflammation-sustained proliferation may represent a specific subgroup of AML.

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INTRODUCTION
Acute myeloid leukemia (AML) is a highly heterogeneous group of malignant hematological diseases caused by somatic mutations in multipotential hematopoietic cells. Leukemic hematopoietic cells acquire enhanced self-renewal capacity and impaired differentiation. The emergence of symptomatic leukemia not only requires the acquisition of enhanced self-renewal capacity but also critically requires the acquisition of clonal growth and survival advantages. It is the growth and survival advantages that lead to the accumulation and infiltration of transformed hematopoietic cells in the bone marrow, taking up the hematopoietic pool, inhibiting normal hematopoiesis and ultimately resulting in a reduced capacity to produce mature blood cells.\[1-4\].

Chemotherapy is currently the main initial treatment for AML, the aim of which is to reduce the number of leukemia cells and to achieve complete hematological remission. Untreated AML patients usually experience an aggressive process.\[1\]. However, spontaneous remission occasionally occurs in a small number of AML patients, which frequently follows a febrile episode and is generally attributed to the overproduction of proinflammatory cytokines and the activation of antineoplastic activities.\[5\]. This spontaneous remission could occur not only in patients with fused genes in recurrent chromosome rearrangements and other cytogenetic abnormalities but also in patients with mutated genes in recurrent molecular abnormalities and other transcription factors. Here, we report an AML patient with the recurrent chromosome rearrangement t(8;21)(q22;q22)/RUNX1-RUNXIT1 who achieved unexpected spontaneous remission after antibiotic and glucocorticoid treatment for his gastrointestinal infection and urticaria-like skin lesions. After relapse, repeating this treatment resulted in a second remission. The recapitulated treatment responses confirmed the spontaneous remissions to be induced by the antibiotic and glucocorticoid treatments. Learning from the present case raises the possibility that in a subgroup of AML patients, the proliferative advantage of leukemia cells may critically require the presence of inflammatory stresses.
CASE PRESENTATION

Chief complaints
Abdominal pain and fever for 3 d and pruritic skin lesions for 2 d.

History of present illness
A 63-year-old Chinese man presented with abdominal pain and fever for 3 d in the absence of headache, chest pain, dyspnea, cough and sputum. The highest body temperature was 39.7 °C. Oral administration of antibiotics could not resolve the febrile episode or gastrointestinal symptoms. Urticaria-like pruritic skin lesions occurred 2 d before, and treatment with astemizole could partially relieve the pruritus but could not completely resolve the skin lesions. Within the last month, his performance status exacerbated, with gradually aggravated fatigue, dizziness and palpitation.

History of past illness
The patient had no history of diseases in the hematological or other systems.

Personal and family history
No family history of hematological diseases, autoimmune diseases or malignant diseases was recorded.

Physical examination
His height was 1.71 m, body weight 74.5 kg. His body temperature was 38.3 °C, breathing rate 21 bp per minute, heart rate 92 bp per minute, and blood pressure 17.6/10.4 Kpa (132/78 mmHg). Upon physical examination, prominent signs were panabdominal tenderness and urticaria-like skin lesions. Conspicuous mucocutaneous hemorrhage and jaundice were not found. No significant signs in the nervous system, respiratory system, cardiovascular system, urogenital system or skeletal musculature system were identified.

Laboratory examinations
Routine laboratory examinations: On admission, complete blood count (CBC) revealed the following results: White blood cells (WBCs), 19.13 × 10^9/L; absolute neutrophil count (ANC), 4.55 × 10^9/L; absolute monocyte count (AMC), 8.88 × 10^9/L; red blood cells (RBCs), 2.38 × 10^12/L; hemoglobin level (Hb), 80 g/L; platelets (Plts), 32 × 10^9/L; absolute reticulocyte count (Ret), 5.61 × 10^9/L; and C-reactive protein (CRP), 142.7 mg/L. The coagulation profile and the urine examination did not show any abnormalities. Fecal examination revealed the presence of increased pyocytes. Biochemical analysis found elevated serum levels of lactate dehydrogenase (2834 IU/L), hydroxybutyric dehydrogenase (2394 IU/L) and β2-microglobulin (47.3 mg/L) in the absence of abnormalities in liver and renal functions. Pathogenic culture of his blood was sterile. Serological tests for hepatitis A, B, and C virus and human immunodeficiency virus were negative. Biomarkers of neoplasms were also negative.

Morphological, immunophenotyping, cytogenetic and molecular biological analysis of leukemic hematopoietic cells: Morphological evaluation of the bone marrow smears showed a heavily hypercellular bone marrow, with substantially increased percentages of monoblasts (accounting for 44.5% of the total nucleated hematopoietic cells) and premonocytes (24.5%). Morphological evaluation
of the blood smears showed a highly increased number of WBCs, with substantially increased percentages of premonocytes (accounting for 44% of the total nucleated cells) and monocytes (46%) (Figure 1). Two groups of abnormal myeloid precursors were detected in the bone marrow samples by flow cytometric immunophenotyping analysis. One group (accounting for 32.53% of the total nucleated cells) expressed CD13, CD33, CD14, CD11b, CD36, CD64, CD123 and human leukocyte antigen-DR (HLA-DR); another group (accounting for 48.95% of the total nucleated cells) expressed CD34, CD117, CD38, HLA-DR, CD13, CD33, CD11b, CD56 and CD123. Cytogenetic analysis by culturing the bone marrow cells reported a karyotype of 48,XY,t(8;21)(q22;q22),+13,+13[9]/49,idem,+mar[9]/49, idem,+8[2] (Figure 2). Molecular biological analysis revealed the presence of a fused AML1–ETO gene and a mutated tyrosine kinase domain in fms-like tyrosine kinase 3 (FLT3-TKD) gene.

**Imaging examinations**

No positive findings were observed in the chest computed tomography (CT) images. However, abdominal CT imaging revealed striking bowel wall thickening in the small and large intestines, abnormally gas-filled small intestine, and paper-like dilation of the small intestines and sigmoid colon with perienteric hypervascular fat proliferation, together with the symptoms and signs of the gastrointestinal tract indicating the presence of gut inflammatory lesions.

**FINAL DIAGNOSIS**

He was made a definitive diagnosis of AML-M4 with the recurrent chromosome arrangement of t(8;21)(q22;q22)/RUNX1-RUNX1T1.

**TREATMENT**

Because of the presence of obvious gastrointestinal infection and his poor performance status, cytostatic therapies were deferred. He was treated with piperacillin-tazobactam and etimicin for his febrile disease and with dexamethasone for his urticaria-like skin lesions. He was also prescribed an oral administration of polyglycol electrolyte solution (1500 mL daily for 2 d) followed by rifaximin (200 mg, four times daily) and berberine (0.3 g, three times daily) in an attempt to quickly eliminate the pathogens and their metabolites from the intestines.

**OUTCOME AND FOLLOW-UP**

**Unexpected hematological remission by antibiotic and glucocorticoid treatment**

The febrile episode, gastrointestinal symptoms and urticaria-like skin lesions quickly resolved after antibiotic and glucocorticoid treatment. Unexpectedly, his hematological parameters gradually improved. Along with a decline in the AMC and CRP, the ANC, Plts and Ret rapidly increased, and the RBCs and Hb steadily increased. On day 31, CBC showed the following results: WBCs, 10.83 × 10^9/L; ANC, 6.24 × 10^9/L; AMC, 6.24 × 10^9/L; RBCs, 2.74 × 10^12/L; Hb, 93 g/L; Plts, 253 × 10^9/L; and Ret, 112.45 × 10^9/L. When the blood smears were examined, there were no evident morphological abnormalities in the blood cells except for the left shift in neutrophils. The significantly improved hematological parameters and the absence of leukemia cells on blood smears indicated clearance of the leukemia cells from the peripheral blood and an achievement of clinical hematological remission. Because he declined chemotherapy and hypomethylation therapy, he was discharged from our center.

**Recapitulated hematological remission by antibiotic and glucocorticoid treatment after relapse**

He maintained a good performance status for approximately three weeks since he was discharged from our center. On day 51, he was sent to our center with identical symptoms as when he was first hospitalized. The CBC results and the morphological evaluation of the blood smears confirmed disease recurrence. Because of the history of the achievement of a hematological response to antibiotic and glucocorticoid treatment and because of the existence of an obvious gastrointestinal infection, he was tentatively treated with the same modality as when he was first hospitalized. As we anticipated, repeating the treatment resulted in a second clinical and hematological remission. He refused chemotherapy and hypomethylation therapy again, and he was discharged. During the follow-up, he experienced a second relapse on day 105 with the same symptoms, but this time, he demonstrated strong resistance to antibiotic and glucocorticoid treatment and eventually died of an overwhelming infection at another hospital. Pathogenic culture of his blood samples reported a positive result for *Acinetobacter baumannii* infection with multidrug resistance.
Figure 2 Cytogenetic analysis for the bone marrow culture. Cytogenetic analysis by culture of the bone marrow sample reported a karyotype of 48,XY,t(8;21)(q22;q22),+13,+13[9]/49,idem,+mar[9]/49,idem,+8[2].

Results of CBCs during the treatments in our center
Hematological examinations of WBCs, ANC, AMC, Hb, Plt and Ret levels during the treatments in our center are outlined in Figure 3.

DISCUSSION
In the present case, the presence of increased percentages of blasts and CD34+ progenitors, the identification of the chromosome rearrangement of t(8;21)(q22;q22) and the fused AML1-ETO gene fulfilled the diagnostic criteria for AML with the recurrent chromosome rearrangement of t(8;21)(q22;q22)/RUNX1-RUNXIT1[1,4]. On admission, he presented with the major complaints of high fever, overt gastrointestinal symptoms and urticaria-like skin lesions. In this setting, chemotherapy was deferred. He was prescribed antibiotics to treat the febrile episode, dexamethasone to treat urticaria-like skin lesions and a gut-cleansing preparation to remove gastrointestinal pathogens and their metabolites. His gastrointestinal infection and skin lesions were quickly resolved. Along with the resolution of the gastrointestinal infection and the skin lesions, his hematological profile significantly improved. The disappearance of the leukemia cells from his blood smears suggested an achievement of clinical hematological remission, although bone marrow aspiration was not performed at that time.

Because he declined chemotherapy and hypomethylation therapy, we had the opportunity to observe the recapitulated treatment response after disease relapse. The relapse-remission regularity was that symptomatic AML emerged with flaring of the gastrointestinal infection, and symptomatic AML subsided after resolution of the gastrointestinal infection by antibiotic and glucocorticoid treatments. These recapitulated treatment responses indicated that hematological remission was induced by antibiotic and glucocorticoid treatments. This raises the possibility that the clonal growth and survival advantage of the leukemia cells were sustained by the inflammatory stresses, probably derived from the gut inflammatory condition. With effective treatment of the gut inflammatory condition, the leukemia cells lost their proliferative advantage, and normal hematopoiesis was restored.

AML is highly heterogeneous in clinical presentation and treatment responses, which results from the high diversity of impaired genes, not only driving genes in the transformation of hematopoietic progenitors and in the acquisition of proliferative advantage but also nondriving genes affecting the clinical and biological activities of transformed leukemia cells. To date, hundreds of genes have been found to be associated with leukemia pathogenesis, each of which has a distinctive impact on disease development, progression and treatment responses[1-4]. The natural history of AML is generally aggressive, leading to death usually within weeks to months after the emergence of symptomatic disease in the absence of specific treatments[1,4]. However, spontaneous remission occasionally occurs in a small number of AML patients[5].

Although spontaneous remission is a rare event, more than 100 adult AML cases have been recorded. Spontaneous remission was reported in AML patients with various recurrent cytogenetic abnormalities, such as t(8;21)(q22;q22)/RUNX1-RUNXIT1[6-9], t(15;17)(q31;q22)/PML-RAR-α[10], t(v;11q23)/KMT2A rearrangement[11-13], inv(16)(p13;q22) or t(16;16)(p13;q22)/CBFB-MYH11[14,15] and t(8;16)(p11;p13)/MOZ-CBP[16]. Spontaneous remission was also reported in AML patients with a normal karyotype and other cytogenetic abnormalities, with +8 being the most frequently observed cytogenetic abnormality [17-21]. Spontaneous remission has been reported in AML patients with recurrent gene mutations such
as nucleophosmin 1 and RUNX1[22-24], with gene mutations in epigenetic modulation such as Ten-Eleven Translocation-2, BCOR, isocitrate dehydrogenase 1 and 2; splicing factors such serine/arginine-rich splicing factor 1, U2AF1 and pre-mRNA processing factor 8; and cell growth receptors and their signaling pathway components such as FLT3-ITD, BRAF, NRAS, KRAS and neurofibromatosis type 1 (NF1)[22-26]. Spontaneous remission even occurs in relapsed AML patients many years after allogeneic hematopoietic stem cell transplantation[13,27]. These AML patients encompassed M0-M6 subtypes with monocytoid differentiation accounting for approximately half of the reported cases[6,10,11,14,16]. Patient bone marrow may be either hypercellular or hypopcellular, and WBCs may be either elevated or reduced, with reduced WBCs occurring in a large proportion of reported cases.

In the majority of reported cases, the emergence of AML was concomitant with the flaring of an infectious episode, and spontaneous remission occurred after recovery from the infectious disease by treatment with antibiotics, corticosteroids, recombinant human granulocyte colony stimulating factor (rH-GSF) and/or surgical drainage. Infections range from localized infections[5,6,28-30] to fulminant sepsis[5,6,28-30]. Several extrapolations have been proposed to explain the occurrence of spontaneous remission in AML: (1) Overproduced inflammatory cytokines suppress the proliferation and promote the apoptosis of leukemia cells[31-33]; (2) Restored or acquired cellular and innate immune responses target leukemia cells[11,34]; (3) Restored or acquired humoral immune response targets leukemia cells [8,35]; (4) Acquired graft-versus-leukemia effects suppress the proliferation of leukemia cells[13,21,27]; (5) Glucocorticoids promote the apoptosis of leukemia cells[9]; and (6) Granulocyte CSF promotes the differentiation of leukemia cells[7,10,17]. However, these mechanisms do not legitimately explain the features of spontaneous remissions in our present case. This raises the possibility that an inflammation-sustained proliferative advantage of leukemia cells promotes the emergence of symptomatic disease, which may be the best explanation for these antibiotic and glucocorticoid treatment-induced hematological remissions. Symptomatic AML emerged when the inflammatory stresses flared, and the symptomatic AML subsided after the inflammatory stresses had been resolved by effective treatments. In other reported cases, spontaneous remissions occurred frequently after recovery from a febrile episode in response to diverse treatments rather than during the flaring of the infectious episode, also indicating an inflammation-sustained proliferative advantage, at least in a fraction of the reported cases.

It is generally accepted that constitutionally activated growth factor receptor signaling pathways are responsible for the growth and survival advantage of leukemic stem cells. Activated growth factor receptors and their signaling pathway components, such as the formation of fused genes involving ABL, FGFR1 and platelet-derived growth factor receptor and mutated genes involving FLT3, KIT, interleukin-3R, RAS, CBL, PTPN11 and NF1, result in autonomous proliferation[1-4]. In some AML patients, activation of certain mutated genes may not be autonomous but instead ligand-dependent, resembling mutated genes in the B-cell receptor signaling pathway during lymphoma pathogenesis in which the antigen-dependent growth and survival advantages have been well described[36-39]. In this setting, mutated genes in growth factor receptor signaling pathways may play a tonic role in intensifying prolif-

Figure 3 Sequential hematological changes following the antibiotic and dexamethasone treatments. Following the antibiotic and dexamethasone treatments, the white blood cells (× 10^9/L) and the absolute monocytes counts (× 10^9/L) gradually decreased, and the absolute neutrophil counts (× 10^9/L), hemoglobin levels (× 10 g/L), platelets (10 × 10^10/L) and the absolute reticulocytes counts (10 × 10^10/L) gradually increased. The patient rapidly relapsed due to the discontinuation of the antibiotic and dexamethasone treatment. After relapse, repeating the same treatment resulted in the recapitulated hematological remission.

WBC: White blood cell; ANC: Absolute neutrophil count; AMC: Absolute monocytes count; Hb: Hemoglobin; Plts: Platelets; Ret: Reticulocytes.
erative signaling after ligands bind to their receptor, thereby acquiring growth and survival advantages. While clonal B cells proliferate in response to antigens binding to B-cell receptors[36-39], myeloid hematopoietic progenitors proliferate in response to ligands binding to pattern recognition receptors, cytokine receptors and colony-stimulating factor receptors[40-42]. Inflammatory cytokines and colony-stimulating factors could directly promote the growth and survival of leukemia cells[43-47]. In our present case, the FLT3-TKD mutation was identified, which might be responsible for the proliferative advantage in inflammatory conditions.

This study has several limitations. First, the diagnosis of spontaneous remission was dependent on hematological improvements and the disappearance of leukemia cells from blood smears, lacking morphological evaluation of bone marrow smears and cytogenetic and molecular monitoring. Second, the exact ligands responsible for the proliferative advantage were not identified. Therefore, additional studies are merited to confirm the extrapolation.

CONCLUSION

The recapitulated hematological remissions provide strong evidence for the treatment responses being induced by antibiotic and glucocorticoid treatments. AML is a highly heterogeneous hematological malignancy. In our present case, removing the underlying infection could induce a transient hematological remission, suggesting that the growth and survival advantage in this subgroup of leukemia cells may be sustained by inflammation. The ligands may be infection-related components such as microbes or their metabolites, inflammatory cytokines or colony-stimulating factors produced in response to infection. This phenomenon warrants further investigation and may aid in investigating AML pathogenesis and in improving therapeutic outcomes in this subgroup of AML patients.

FOOTNOTES

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REFERENCES


Mozafari R, Moeinian M, Asadollahi-Amin A. Spontaneous Complete Remission in a Patient with Acute Myeloid Leukemia after Severe Pneumonia Treated with High-Dose Methotrexate.

Sun XY et al. Spontaneous remissions in AML.


