## Contents

### EDITORIAL

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2686</td>
<td>Antifungal pipeline: Is there light at the end of the tunnel?</td>
<td>Schinas G, Spernovasilis N, Akinosoglou K</td>
</tr>
<tr>
<td>2692</td>
<td>Cracking the silent gallstone code: Wait or operate?</td>
<td>Goswami AG, Basu S</td>
</tr>
<tr>
<td>2698</td>
<td>Metabolic dynamics in chronic gastritis: Examining urinary profiles post <em>Helicobacter pylori</em> eradication</td>
<td>Musharaf I, Nashwan AJ</td>
</tr>
<tr>
<td>2701</td>
<td>Pearls of meta-analyses and systematic review in scientific evidence</td>
<td>Au SCL</td>
</tr>
</tbody>
</table>

### MINIREVIEWS

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2704</td>
<td>Advanced nanomedicines and immunotherapeutics to treat respiratory diseases especially COVID-19 induced thrombosis</td>
<td>Wu J, Zheng Y, Zhang LN, Gu CL, Chen WL, Chang MQ</td>
</tr>
</tbody>
</table>

### ORIGINAL ARTICLE

#### Retrospective Cohort Study

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>

#### Retrospective Study

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2722</td>
<td>Multimodal imaging in the diagnosis of bone giant cell tumors: A retrospective study</td>
<td>Kou MQ, Xu BQ, Liu HT</td>
</tr>
<tr>
<td>2729</td>
<td>Treatment for paraganglioma with stereotactic radiotherapy</td>
<td>Pontoriero A, Critelli P, Zeppieri M, Angileri FF, Ius T</td>
</tr>
<tr>
<td>2738</td>
<td>Effect of endoscopic full-thickness resection assisted by distal serosal turnover with floss traction for gastric submucosal masses</td>
<td>Liu TW, Lin XF, Wen ST, Xu JY, Fu ZL, Qin SM</td>
</tr>
<tr>
<td>2745</td>
<td>Relationship between ultrasound parameters of the umbilical and middle cerebral arteries and intrauterine fetal distress</td>
<td>Chen J, Liu FX, Tao RX</td>
</tr>
</tbody>
</table>
### Contents

**Thrice Monthly Volume 12 Number 16 June 6, 2024**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2751</td>
<td>Effect of psychological nursing interventions on effectiveness and quality of life in schizophrenia patients receiving modified electroconvulsive therapy</td>
<td>Lu J</td>
</tr>
<tr>
<td>2758</td>
<td>Effect of percutaneous electrical stimulation at the Baliao point on preventing postpartum urinary retention after labor analgesia</td>
<td>Wang XQ, Guan LS</td>
</tr>
<tr>
<td>2765</td>
<td>Perceptions and factors influencing exercise interventions in elderly patients with debilitating spinal surgery and healthcare professionals: A qualitative study</td>
<td>Cheng RR, Li R</td>
</tr>
<tr>
<td>2789</td>
<td>Causal association between 25-hydroxyvitamin D status and cataract development: A two-sample Mendelian randomization study</td>
<td>Wang CH, Xin ZK</td>
</tr>
<tr>
<td>2803</td>
<td>Iron and ferritin effects on intensive care unit mortality: A meta-analysis</td>
<td>Yang DC, Zheng BJ, Li J, Yu Y</td>
</tr>
<tr>
<td>2813</td>
<td>Secondary diabetes due to different etiologies: Four case reports</td>
<td>Song WR, Xu XH, Li J, Yu J, Li YY</td>
</tr>
<tr>
<td>2822</td>
<td>Giant cavernous aneurysms occluded by aneurysmal thrombosis, calcification, parent artery occlusion: A case report and review of literature</td>
<td>Wang MX, Nie QB</td>
</tr>
</tbody>
</table>
## Contents

**World Journal of Clinical Cases**  
**Thrice Monthly** 
**Volume 12 Number 16** 
**June 6, 2024**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2831</td>
<td>Computed tomography three-dimensional reconstruction in the diagnosis of bleeding small intestinal polyps: A case report</td>
<td>Zhang SH, Fan MW, Chen Y, Hu YB, Liu CX</td>
</tr>
<tr>
<td>2837</td>
<td>Managing adult-onset Still's disease in pregnancy: A case report</td>
<td>Kang JH</td>
</tr>
<tr>
<td>2847</td>
<td>Conversion therapy of a giant hepatocellular carcinoma with portal vein thrombus and inferior vena cava thrombus: A case report and review of literature</td>
<td>Song WJ, Xu J, Nie Y, Li WM, Li JP, Yang L, Wei MQ, Tao KS</td>
</tr>
<tr>
<td>2856</td>
<td>Migration of varicocele coil leading to ureteral obstruction and hydronephrosis: A case report</td>
<td>Alamri A</td>
</tr>
<tr>
<td>2869</td>
<td>Giant vascular malformations invading the skull: A case report</td>
<td>Xie MC, Wang FX, Xu J</td>
</tr>
<tr>
<td>2876</td>
<td>Uterine epithelioid trophoblastic tumor with the main manifestation of increased human chorionic gonadotropin: A case report</td>
<td>Huang LN, Deng X, Xu J</td>
</tr>
<tr>
<td>2881</td>
<td>Dynamically changing antineutrophil cytoplasmic antibodies in granulomatosis with polyangiitis: A case report</td>
<td>Zhang Y, Dai QD, Wang JX, Xu LP, Chen Q, Jin YZ</td>
</tr>
<tr>
<td>2887</td>
<td>Clinicopathological analysis of EWSR1/FUS::NFATC2 rearranged sarcoma in the left forearm: A case report</td>
<td>Hu QL, Zeng C</td>
</tr>
<tr>
<td>2894</td>
<td>Thoracic giant cell tumor after two total en bloc spondylectomies including one emergency surgery: A case report</td>
<td>Liang HF, Xu H, Zhan MN, Xiao J, Li J, Fei QM</td>
</tr>
<tr>
<td>2904</td>
<td>Primary thoracolumbar intraspinal malignant melanoma: A case report</td>
<td>Huang JB, Xue HJ, Zhu BY, Lei Y, Pan L</td>
</tr>
</tbody>
</table>
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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Managing adult-onset Still's disease in pregnancy: A case report

Ji-Hyoun Kang

Abstract

BACKGROUND
Adult-onset Still’s disease (AOSD) is a rare systemic inflammatory disorder characterized by fever, arthritis, skin rash, and systemic symptoms. The etiology of AOSD is unknown; however, it is thought to be related to immune dysregulation. Although a rare disease, AOSD can significantly impact reproductive health, particularly during pregnancy. This case study assesses the implications of pregnancy in a patient with AOSD, as well as the potential for heredity of the disease. Neonatal hemophagocytic lympho-histiocytosis (HLH) is a rare and life-threatening disorder characterized by hyperinflammation and uncontrolled activation of immune cells, leading to multiple organ dysfunction. This case report aimed to introduce neonatal HLH from a mother with AOSD.

CASE SUMMARY
This case study presents a 29-year-old female with AOSD who became pregnant and gave birth to a premature infant who was diagnosed with neonatal HLH. AOSD can significantly impact pregnancy and childbirth, as it may become more severe during pregnancy, with an increased risk of fetal loss and preterm birth. The management of AOSD during pregnancy involves the use of nonsteroidal anti-inflammatory drugs and glucocorticoids, as well as immunosuppressive agents in severe cases. However, the use of immunosuppressive agents during pregnancy may be associated with potential risks to the fetus. The hereditary implications of AOSD are unclear; however, available evidence suggests that genetic factors may play a role in the disease development.

CONCLUSION
AOSD can have significant implications for pregnancy and childbirth, including an increased risk of fetal loss and preterm birth. Neonatal HLH, a complication of AOSD in pregnancy, requires prompt diagnosis and management. Women with AOSD who are considering pregnancy should discuss their options with their healthcare provider and develop a management plan that addresses the potential risks to both mother and fetus.
Core Tip: This case study explores the intricate challenges faced by a 29-year-old woman with adult-onset Still’s disease (AOSD) during pregnancy, resulting in the premature birth of an infant diagnosed with neonatal hemophagocytic lymphohistiocytosis. Pregnancy exacerbates the risks associated with AOSD, including heightened chances of fetal loss and preterm birth. The management of AOSD during pregnancy involves utilizing nonsteroidal anti-inflammatory drugs, glucocorticoids, and, in severe cases, immunosuppressive agents despite potential fetal risks such as low birth weight and preterm birth, highlighting the delicate balance required in addressing the complexities of AOSD during gestation.

INTRODUCTION
Adult-onset Still’s disease (AOSD) is a rare inflammatory condition with uncertain origins, likely stemming from immune dysregulation[1], posing significant considerations during pregnancy. Given its potential impact on reproductive health, understanding the implications of pregnancy in patients with AOSD and the potential hereditary aspects of the disease are crucial. Additionally, neonatal hemophagocytic lymphohistiocytosis (HLH), a severe disorder characterized by immune hyperactivation, presents a rare but life-threatening complication in newborns born to mothers with AOSD, warranting further investigation and clinical attention.

Neonatal HLH is a rare and life-threatening disorder characterized by hyperinflammation and uncontrolled activation of immune cells, leading to multiple organ dysfunction. This case report aimed to introduce neonatal HLH from a mother with AOSD.

CASE PRESENTATION

Chief complaints
In the first trimester of pregnancy, she was maintained in a stable state with a low-dose steroid and tacrolimus. From the second trimester, she was hospitalized due to sudden elevation of liver function test markers, including aspartate aminotransferase, alanine transaminase, and bilirubin, fever, and rash. Due to frequent recurrent flares, she was admitted repeatedly and was treated with intravenous steroid injections. At 32 wk of gestation, she suddenly went into labor and gave birth through emergent delivery by cesarean section. The male infant was born prematurely and was cared for in the neonatal intensive care unit. At 5 d of age, the male infant developed fever, pancytopenia, hepatosplenomegaly, and hypofibrinogenemia (Figure 1).

History of present illness
The male infant was born prematurely and was cared for in the neonatal intensive care unit. At 5 d of age, he developed fever, pancytopenia, hepatosplenomegaly, and hypofibrinogenemia.

History of past illness
A 29-year-old female reported to the emergency room with complaints of a prolonged high fever for more than 1 month, a non-pruritic, salmon pink-colored rash in the trunk, sore throat, multiple lymphadenopathies including both axillary and left para-aortic areas, and splenomegaly. Her white blood cell count was 20100/μL, including 92.5% of neutrophils. Her ferritin level was 14602 ng/mL, and her C-reactive protein level was 15.66 mg/dL. A biopsy finding of the left axillary lymph node presented reactive lymphadenopathy, and the blood culture results were negative. Her laboratory test results for rheumatoid factor, anti-neutrophil cytoplasmic antibody, and anti-nuclear antibody, were negative. According to the criteria by Yamaguchi et al[2], this patient was diagnosed with AOSD (Figure 1). The patient was prescribed intravenous methylprednisolone 1 mg/kg for 3 wk. Moreover, her symptoms improved, and her dosage of steroids was tapered while undergoing additional treatment with oral methotrexate. She was maintained in the outpatient department for more than 3 years without any flares. Then, she was suddenly hospitalized with fever, myalgia, and arthralgia. She was treated with 2-wk high-dose intravenous methylprednisolone therapy, with no effect. Her symptoms, including fever, rash, and arthralgia, were not controlled, and cyclosporin (100 mg once daily) was added to her therapy during hospitalization. Despite receiving high doses of intravenous methylprednisolone, methotrexate, and cyclosporin for 6 months post-diagnosis, her symptoms, including fever, skin rash, and
arthritis, persisted intermittently and remained uncontrolled. Consequently, the patient underwent monthly intravenous administration of tocilizumab, an interleukin (IL)-6 inhibitor. Following tocilizumab therapy, her symptoms improved, and this positive response was sustained. After 1 year, the tocilizumab therapy was discontinued, and she became pregnant after marriage.

**Personal and family history**

The patient has no specific family or personal history.

**Physical examination**

The newborn presented with symptoms of high fever and distress, accompanied by labored breathing, prompting immediate medical attention.

**Laboratory examinations**

The hemoglobin level of the male infant was $7.9 \text{ g/dL}$, and the platelet count was $34 \times 10^9/L$. His ferritin level was $12825 \text{ ng/mL}$, and he had hypofibrinogenemia.

**Imaging examinations**

The abdominal ultrasound of the male infant showed hepatosplenomegaly.

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**FINAL DIAGNOSIS**

According to the modified 2009 diagnostic criteria of familial HLH\cite{3}, the male infant satisfied seven parameters, including fever, splenomegaly, anemia and thrombocytopenia, hypofibrinogenemia, hyperferritinemia, elevated soluble IL-2 receptor, and evidence of phagocytosis on bone marrow biopsy (Figure 1).

**TREATMENT**

The infant was treated with dexamethasone, immunosuppressive therapy, and intravenous immunoglobulin (IVIG).

**OUTCOME AND FOLLOW-UP**

After 3 wk of intensive treatment, the baby improved and was discharged, while follow-up at the outpatient clinic continued. Moreover, his symptoms were well-controlled 6 months after therapy discontinuation.

**DISCUSSION**

AOSD can significantly affect pregnancy and childbirth, as the disease may become more severe during pregnancy due to hormonal changes and immune dysregulation. Similarly, patients with AOSD have an increased risk of fetal loss and preterm birth. In a study of 40 pregnant patients with AOSD, 10 (25%) had fetal loss, and 14 (35%) had preterm delivery. Additionally, patients with AOSD may have an increased risk of preeclampsia and gestational diabetes\cite{3}. Therefore,
Management of AOSD during pregnancy may involve the use of nonsteroidal anti-inflammatory drugs and glucocorticoids, as well as disease-modifying antirheumatic drugs (DMARDs) in severe cases. However, the use of DMARDs during pregnancy may be associated with potential risks to the fetus, including fetal malformations and growth retardation[4]. Therefore, the use of DMARDs should be carefully considered and balanced against the potential benefits of controlling disease activities.

The hereditary implications of AOSD are not well understood; however, evidence suggests that genetic factors may play a role in disease development. In a study of 11 patients with AOSD, 5 had a family history of rheumatologic diseases, suggesting a potential genetic predisposition to the disease. Additionally, several genetic variants have been associated with AOSD, including human leukocyte antigen-DRB1 and IL1 polymorphism[5].

Neonatal HLH is a rare and life-threatening disorder characterized by hyperinflammation and uncontrolled activation of immune cells, leading to multiple organ dysfunction. Early diagnosis and prompt treatment are essential for improving outcomes in affected infants. Genetic testing should be performed to identify underlying mutations and guide appropriate management strategies. The management of neonatal HLH typically involves a combination of chemotherapy, immunosuppressive therapy, and IVIG. However, the prognosis of neonatal HLH remains poor, with high mortality rates reported in many case series[6].

The risk of heredity in AOSD is not well-defined; however, the disease is likely multifactorial, with genetic and environmental factors contributing to its development. Therefore, the risk of heredity may be influenced by the genetic background of the patient, as well as environmental factors such as infections and stress.

This case serves as evidence that the intricate interplay of genetic predisposition, the unique circumstances of pregnancy in a mother with AOSD, and various environmental factors can collectively contribute to the development of neonatal HLH[7]. The underlying genetic background of AOSD in the mother, compounded by pregnancy-induced physiological changes, may influence the fetal environment, potentially predisposing the newborn to HLH. Moreover, the management of AOSD during pregnancy, including the use of medications like glucocorticoids and immunosuppressive agents, could further influence the fetal immune response. Additionally, environmental factors such as infections and stressors during pregnancy may exacerbate the risk of HLH development in the newborn. Overall, this case underscores the complex nature of disease pathogenesis, highlighting the need for a comprehensive understanding and management of genetic and environmental factors in similar clinical scenarios.

CONCLUSION

Pregnancy in patients with AOSD can be associated with significant risks, including fetal loss, preterm birth, and maternal complications. Therefore, close monitoring and management of disease activity during pregnancy are essential to ensure the best possible outcome for both mother and child. Additionally, the hereditary implications of AOSD are not well understood; however, evidence suggests genetic factors may play a role in disease development. Further research is necessary to understand the underlying mechanisms of AOSD and develop appropriate management strategies for pregnant patients with AOSD.

Learning points: (1) AOSD can have significant implications for pregnancy and childbirth, including an increased risk of fetal loss and preterm birth; (2) Neonatal HLH can be a complication of AOSD in pregnancy and requires prompt diagnosis and management; and (3) Women with AOSD who are considering pregnancy should discuss their options with their healthcare provider and develop a management plan that takes into account the potential risks to both the mother and the fetus.

FOOTNOTES

Author contributions: Kang JH designed the research study, performed the research, and analyzed the data and wrote the manuscript; Kang JH has read and approved the final manuscript.

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REFERENCES


