Case Report

Pharmacological Management and Diagnostic Challenges in Adult-Onset Still's Disease

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ABSTRACT

Adult-Onset Still's Disease [AOSD] is a rare inflammatory condition that causes fevers spikes, arthritis and rashes. It can be difficult to diagnose because its symptoms are similar to other diseases. In the case of a 46 year old male with a history of high fever for one week, followed by five days of sore throat and dry cough and two days of multiple joint pains. The patient had no known comorbidities but had a previous hospitalization for brucellosis in 2020 and an amoxicillin allergy. Despite initial treatment with Moxifloxacin and Doxycycline therapy, followed by prophylactic administration of Meropenem, the fever persisted. Laboratory testing revealed leukocytosis, increased ESR and elevated ferritin levels. CT imaging showed hepatosplenomegaly and sub-pleural fibrotic spots. The AOSD diagnosis was confirmed based on Yamaguchi Criteria including salmon-coloured maculopapular rashes, elevated inflammatory markers, medical history, elevated ferritin levels and imaging findings. Treatment with anti-inflammatory medications and corticosteroids resulted in significant clinical improvement. The patient was discharged on the seventh day with prescriptions for pantoprazole, prednisolone and naproxen and was advised to follow up after one week. This case highlights the importance of early diagnosis and aggressive treatment for managing AOSD, highlighting the effectiveness of steroids for symptom relief.

Keywords: Hepatosplenomegaly, Maculopapular Rashes, Stills Disease, Yamaguchi Criteria.

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INTRODUCTION

Adult-Onset Still's Disease (AOSD) is an uncommon systemic inflammatory condition characterized by symptoms such as evanescent rash, high spiking fever, leukocytosis, joint pain or arthritis and multi-organ involvement, with a prevalence of 0.6/100,000 in the population.[1,2] AOSD presents diagnostic hurdles due to its varied clinical presentation and the lack of specific diagnostic tests. Understanding the pathophysiology and improving diagnostic accuracy are paramount for effective management of AOSD. While corticosteroids are typically the first- line treatment, Subsequently Disease-Modifying Anti-Rheumatic Drugs (DMARDs), the variability in treatment response underscores the need for tailored therapeutic approaches.[3,4] This case study seeks to explore the diagnostic criteria and clinical presentations for Adult-Onset Still's Disease (AOSD), focusing on distinguishing features from other febrile illnesses. It evaluates the effectiveness of corticosteroids, Disease-Modifying Anti-Rheumatic Drugs (DMARDs) and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in managing AOSD symptoms and improving patient outcomes. Additionally, the report explores the challenges and opportunities in the management of AOSD, emphasizing the optimization of diagnostic strategies and treatment regimens. Through these objectives, this case report hopes to improve our comprehension and treatment of AOSD, ultimately enhancing patient care and outcomes.

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CASE REPORT

A 46-year-old male, without any known underlying health conditions, reported experiencing fever, odynophagia,

a dry cough and generalized joint pain over the past week. Medical history showed a previous hospital admission for similar complaints and a diagnosis of brucellosis in 2020. Initial investigations revealed neutrophilic leukocytosis and peripheral smear showed toxic changes- started on IV antibiotics (Tables 1,2). Blood, urine and sputum culture did not reveal any significant growth. Infectious etiologies ruled out. CT Thorax and abdomen were done which showed sub-pleural fibrotic patch in posterior basal segment of right lower lobe, hepatosplenomegaly (Figures 1-3). Cardiology consultation was done to rule out infective endocarditis. Patient did not respond to IV antibiotics. Evaluated for other causes of pyrexia. Patient had similar kind of episode in the past for which they had evaluated extensively including bone marrow; everything was inconclusive except for the positive inflammatory markers. From there they considered one of the differentials as stills disease.

Table 1: Lab investigations relevant to AOSD.

Sample type	Test name	Result	Reference range
Blood	Haemoglobin	13.3 gm/dL	13.10-17
Blood	White blood cell [WBC]	14.78x1000 c/cu	4-11
Blood	Neutrophils	91%	35-75
Blood	Lymphocytes	06%	18-44
Blood	ESR	67 mm/hr	0-20
Serum	CRP	230.7 mg/L	<6
Serum	AST	33 U/l	8-33
Serum	ALT	90 U/l	4-36
Serum	Alkaline phosphatase	178 U/l	44-147
Serum	Ferritin	52500 ng/mL	30-400

Repeated peripheral smear showed no toxic changes. ANA-profile was negative, ferritin markedly elevated. Liver function showed mild derangement. Based on clinical evaluation including salmon-pink maculopapular rashes, arthritis and fever spikes, lab findings, previous history and Yamaguchi criteria possibility of still disease considered.

Treatment with corticosteroids (Dexamethasone) and anti-inflammatory drug (Naproxen) resulted in significant clinical improvement. Upon discharge, the patient was prescribed a tapering regimen of Prednisolone 20 mg, Pantoprazole 40 mg and Naproxen 750 mg sustained release, with follow-up instructions.

Table 2: ANA Profile.

Sample type	Test name	Result
Serum	nRNP/Sm	Negative
Serum	Sm	Negative
Serum	SS-A	Negative
Serum	Ro52	Negative
Serum	SS-B	Negative
Serum	PM Scl	Negative
Serum	Jo-1	Negative
Serum	CENP B	Negative
Serum	PCNA	Negative
Serum	Nucleosomes	Negative
Serum	Histones	Negative
Serum	Rib.P-Protein	Negative
Serum	AMA-M2	Negative
Serum	Scl-70	Negative
Serum	ds DNA	Negative
Serum	LEPTOSPIRA IgM and IgG ANTIBODY [CARD]	Negative

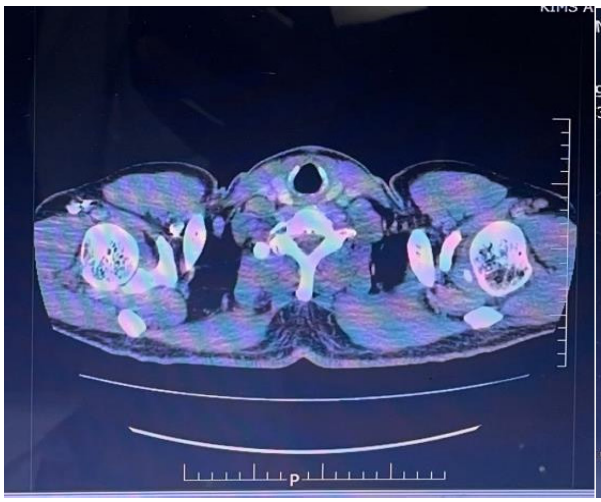

Figure 1: Transverse section of chest.

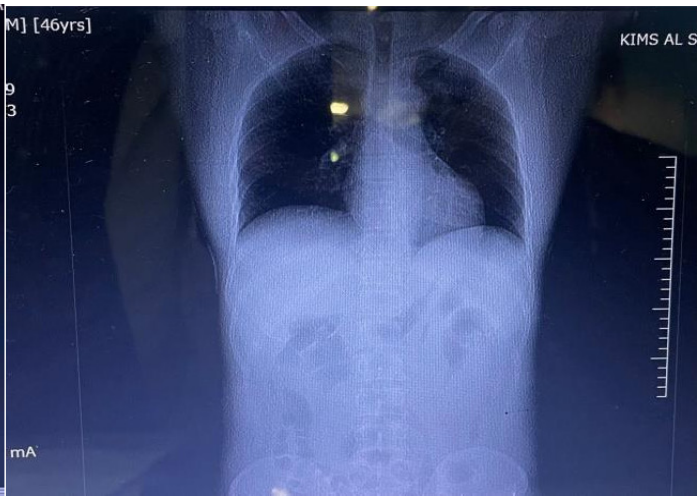

Figure 2: Chest and upper abdomen.

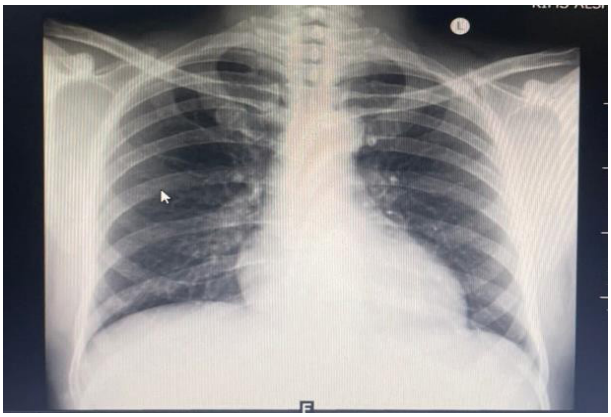

Figure 3: Chest X-ray.

DISCUSSION

This case highlights the difficulties in diagnosis and clinical intricacies associated with Adult-Onset Still's Disease (AOSD). The 46 year old male patient, presented with hallmark symptoms consistent with AOSD, including fever, sore throat, dry cough and multiple joint pains. These symptoms, along with his history of a similar episode requiring extensive hospitalization and critical care, raised suspicion for AOSD.

Initial investigations revealed abnormal leukocytosis, elevated inflammatory markers and sub- pleural fibrotic patches on CT imaging, which are commonly observed in patients with AOSD.[5,6] Despite extensive testing, including blood, urine and sputum cultures and an autoimmune panel, the definitive diagnosis of AOSD was delayed, underscoring the diagnostic challenges associated with this condition.[7] These findings emphasize the need for increased awareness among healthcare providers regarding the clinical features and diagnostic criteria of AOSD to facilitate timely diagnosis and appropriate management.

AOSD is primarily diagnosed by exclusion due to the lack of definitive biomarkers and its nonspecific clinical presentation, which overlaps with many infectious, neoplastic and other autoimmune conditions. The Yamaguchi criteria are a widely used set of guidelines for diagnosing adult-onset Still's disease.[8] In order to confirm the diagnosis, a patient must satisfy at least five criteria, with a minimum of 2 of those being major criteria. The major criteria consist of a fever surpassing 39ºC that lasts for a minimum of one week, arthralgia or arthritis persisting for two weeks or more, a characteristic salmon-colored rash and leukocytosis with a white blood cell count exceeding 10,000/mm^3, with more than 80% of the cells being polymorphonuclear. The minor criteria involve symptoms such as pharyngitis, notable recent enlargement of lymph nodes, hepatomegaly, abnormal liver enzyme levels and the absence of antinuclear antibodies and rheumatoid factor in diagnostic tests. These criteria help differentiate AOSD from other diseases with similar symptoms, ensuring a more accurate diagnosis and appropriate treatment plan.[9]

The clinical presentation of our patient was consistent with typical manifestations of AOSD. Subsequent evaluation and clinical features, including the presence of salmon-pink maculopapular rashes, arthritis and fever spikes, supported the diagnosis of AOSD. Additionally, the patient's medical history, including a prior hospital admission for similar symptoms and a diagnosis of brucellosis in 2020 highlights the importance of considering underlying autoimmune conditions in patients presenting with recurrent febrile episodes.

Managing Adult-Onset Still's Disease poses difficulties because of the limited availability of large-scale prospective trials, relying instead on empirical approaches derived from retrospective case series. Nonsteroidal anti-inflammatory drugs along with corticosteroids represent first-line treatment for mild cases of AOSD.[10] Corticosteroids, particularly at high dosages, control symptoms in about 65% of patients. Early introduction of steroid-sparing treatments such as Disease-Modifying Anti-Rheumatic Drugs like methotrexate, along with targeted biologic therapy such as IL-6 antagonists (e.g. tocilizumab) and IL-1β antagonists (e.g. Rilonacept) has improved outcomes in AOSD management, especially in refractory cases, although treatment strategies remain largely empirical.[10] In our case treatment with corticosteroids (Dexamethasone) and the anti-inflammatory drug Naproxen resulted in significant clinical improvement, highlighting the effectiveness of these agents in achieving symptom resolution in patients with AOSD.

Timely identification and proper treatment are crucial for improving outcomes in patients with AOSD. Future research endeavors should focus on larger-scale studies to validate the effectiveness of corticosteroids and anti-inflammatory drugs in the treatment of AOSD and elucidate the underlying mechanisms driving disease pathogenesis.[10]

SUMMARY

The case report presents a 46-year-old male with a one-week history of fever, sore throat, dry cough and multiple joint pains. Despite initial antibiotic treatment and extensive diagnostic workup, including blood, urine and sputum cultures and an autoimmune panel, the patient's condition deteriorated, leading to ICU

admission. Subsequent evaluation revealed clinical features consistent with Adult Onset Still's Disease (AOSD), including salmon-pink maculopapular rashes, arthritis and fever spikes. Treatment with corticosteroids and anti - inflammatory drugs resulted in significant clinical improvement and the patient was discharged with a tapering regimen. The case highlights the diagnostic challenges associated with AOSD and underscores the importance of early recognition and appropriate management in optimising patient outcomes.

CONCLUSION

Diagnostic challenges stem from various factors, including the increasing complexity of diseases, the need for rapid and accurate diagnoses and the evolving landscape of diagnostic technologies. Medical professionals face the daunting task of navigating these challenges to ensure accurate and timely diagnoses, leading to effective patient management.

The management role of medical professionals encompasses a wide range of responsibilities, including clinical decision-making, patient communication, resource allocation and quality improvement. They play a crucial role in coordinating care, collaborating with other healthcare providers and advocating for patient needs.

To address these challenges and fulfill their management responsibilities effectively, medical professionals must possess a strong foundation in clinical knowledge, critical thinking skills and effective communication abilities. They must also stay updated with the latest advancements in diagnostic technologies and treatment modalities.

In conclusion, diagnostic challenges and the management role of medical professionals are intertwined and require a comprehensive approach. By addressing these challenges and effectively fulfilling their management responsibilities, medical professionals can significantly improve patient outcomes and contribute to the overall quality of healthcare delivery.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this case report.

REFERENCES

1. Efthimiou P, Paik PK, Bielory L. Diagnosis and management of adult onset Still's disease. Ann Rheum Dis. 2006;65(5):564-72.
2. Bywaters EG. Still's disease in the adult. Ann Rheum Dis. 1971;30(2):121-33.
3. Jamilloux Y, Gerfaud-Valentin M, Henry T, Sève P. Treatment of adult-onset Still's disease: a review. Ther Clin Risk Manag. 2015;11:33-43.
4. Arlet JB, Le THD, Marinho A, Amoura Z, Wechsler B, Papo T, *et al*. Reactive haemophagocytic syndrome in adult-onset Still's disease: a report of six patients and a review of the literature. Ann Rheum Dis. 2006;65(12):1596-601.
5. Fautrel B. Adult-onset Still disease. Best Pract Res Clin Rheumatol. 2008;22(5):773-92.
6. Kadavath S, Efthimiou P. Adult-onset Still's disease-pathogenesis, clinical manifestations and new treatment options. Ann Med. 2015 Feb;47(1):6-14.
7. Maria ATJ, Le Quellec A, Jorgensen C, Touitou I, Rivière S, Guilpain P. Adult onset Still's disease [AOSD] in the era of biologic therapies: Dichotomous view for cytokine and clinical expressions. Autoimmun Rev. 2014;13[11]:1149-59.
8. Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, *et al*. Preliminary criteria for classification of adult Still's disease. J Rheumatol. 1992;19(3):424-30.
9. Pouchot J, Sampalis JS, Beaudet F, Carette S, Décary F, Salusinsky-Sternbach M, *et al*. Adult Still's disease: manifestations, disease course and outcome in 62 patients. Medicine (Baltimore). 1991;70(2):118-36.
10. Cavalli G, Farina N, Campochiaro C, Baldissera E, Dagna L. Current treatment options and safety considerations when treating adult-onset Still's disease. Expert Opin Drug Saf. 2020;19(12):1549-58.

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