

Case Report

Idiosyncratic reactions to methotrexate- A short case series

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ABSTRACT:

Pancytopenia and maturation arrest due to methotrexate are important hematological complications of drug therapy in rheumatoid arthritis and psoriasis. Two cases of these complications are described in the present case series. Hematologic monitoring at more frequent interval, especially in high risk groups, may help in early diagnosis and management of these complications.

Keywords- Pancytopenia, rheumatoid arthritis, psoriasis

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INTRODUCTION

Pancytopenia due to methotrexate is an important hematological complication of drug therapy in rheumatoid arthritis and psoriasis¹⁻⁴. Pancytopenia is generally seen after some duration of therapy and in the setting of well described risk factors. Granulocyte maturation arrest is, however a rare complication of this drug. Two cases of these complications are described in the present communication.

CASE 1

A 52 year old male patient was admitted to Medical emergency department with high grade fever, rash over arms and legs and ulcers in the mouth for 10 days. He had received single dose of methotrexate (7.5 mg) one month back for cutaneous lesions of psoriasis along with topical application of keratolytic agents. The patient was a smoker (10 packs a year) and alcoholic (200 ml a day) for 30 years.

On examination the patient was febrile, tachypneic and had pallor. He had erythematous lesions over arms, legs and painful ulcers with erosions in the mouth. His investigations are summarized in Table 1.

Table 1: Investigative details of case 1

| Investigation | Day 1 | Day 4 | Day 7 |
|--|-----------|--------|--------|
| Hb (gm/dl) | 10 | 10.2 | 10.4 |
| TLC(cells/ µl) | 700 | 600 | 550 |
| Platelets(cells/ µl) | 1.9 lakhs | 45,000 | 30,000 |
| ESR mm Ist hour | 40 | - | - |
| Na (mEq/L) | 133 | 136 | 137 |
| K(mEq/L) | 6.0 | 5.7 | 5.8 |
| Blood Urea(mg/dl) | 186 | 144 | 168 |
| Serum Creatinine(mg/dl) | 6.4 | 6.0 | 6.2 |
| PBF- mild degree of anisopoikilocytosis, few macrocytes and microcytes | | | |
| Urine examination: albumin ++ | | | |
| LFT-normal | | | |

| |
|-----------------------------|
| PT-increased APTT-normal |
|-----------------------------|

Due to persistent fever and pancytopenia, the bone marrow examination was done on 4th day of hospital admission. Bone marrow aspirates were aparticulate. Bilateral trephine showed markedly hypocellular marrow spaces with depression of all the three haematopoietic elements. A diagnosis of methotrexate induced pancytopenia with acute renal failure, toxic epidermal necrolysis and septicaemia was made.

Leucopenia persisted despite folinic acid therapy, antibiotics, dialysis and supportive care to the patient. He developed cardiorespiratory arrest on 7th day of hospital admission and died.

CASE 2

A 24 year old male, a known case of psoriatic arthritis for 15 years, was admitted to emergency department with complaints of fever, loose stools and pain in small and large joints for 20 days. He was on methotrexate (2.5 mg thrice weekly) for last one month. On examination, he was febrile, tachypneic and had candidiasis and psoriatic lesions all over the body. His previous and present hospital investigations are summarized in Table 2.

Table 2: Investigative details of case 2

| Investigation | Day 1 | Day 4 | Day 7 | Day 10 |
|---|-----------------------------|-------------|----------------|----------|
| Hb (gm/dl) | 6.9 | 7.5 | 8.0 | 9.1 |
| Retic | 0.5% | 0.3% | 1% | 2% |
| TLC(cells/ µl) | 1500 | 3000 | 90,000 | 49,400 |
| DLC | P4L19M0E2(25 cells counted) | MM8P30L60E2 | M37MM26P33L3E1 | M1MM3P88 |
| Platelets(cells/ µl) | 3.2 Lacs | 3.0 Lacs | 3.0 Lacs | 3.6 Lacs |
| ESR mm 1st hour | 48 | | | |
| Na (mEq/L)-normal K(mEq/L)- normal Blood Urea(mg/dl)- normal Serum Creatinine(mg/dl)- normal Blood culture- <i>Pseudomonas aeruginosa</i> PBF-mild degree of anisopoikilocytosis, moderate hypochromia, few macrocytes, macroovalocyte and microcyte Urine examination-20-30 RBC/hpf LFT- normal PT- normal APTT- normal | | | | |

In view of bicytopenia and persistent fever, bone marrow investigation was done on 5th day of hospital admission.

Bone marrow aspirates were cellular with slight depression of erythropoietic series (very few early forms). Myeloid series showed maturation arrest (myelocyte-56% and metamyelocyte-23%). Megakaryocyt were increased with presence of monolobated forms. Iron stores were normal. Bilateral trephine biopsy showed hypocellular marrow spaces. There was adequate representation of myeloid and megakaryocytic series with depression of erythroid series. Congo red stain for amyloid was negative. Based on these features, a diagnosis of methotrexate induced bicytopenia and maturation arrest was made. Patient received supportive treatment, steroids, anti inflammatory drugs and showed gradual recovery in one month.

DISCUSSION

Pancytopenia due to single dose of methotrexate has been well discussed in the literature. The factors

associated with high risk for hematological toxicity are elderly age, renal dysfunction, alcohol ingestion, folate deficiency, hypoalbuminemia, drug interaction with NSAIDs and other folate antagonists like trimethoprim, surgery and misunderstanding dosage instructions^{2,3}. The added risk factor in our first patient was alcohol ingestion. The occurrence of myeloid maturation arrest due to low dose of methotrexate is rare. This can be differentiated from leukaemoid reaction by presence of early immature forms in marrow with paucity of late mature forms⁵.

Blood counts are usually monitored 4-6 weeks after starting weekly low dose methotrexate therapy. Haematologic monitoring at more frequent interval, especially in high risk group, may help in early diagnosis of these complications. Idiosyncratic reactions can, however, occur anytime during the course of the disease. Both cases had severe stomatitis and painful erosions of psoriatic lesions which have been reported as presenting sign of methotrexate therapy⁶.

CONCLUSION

The present case series highlight the fact that prompt diagnosis and management is warranted to save the life of patient from these fatal complications.

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