**CASE STUDY HA-MO-22-04:**

**Microangiopathic Haemolytic Anaemia**

53 year old female for follow-up testing.

WCC: 3.7 x10^9/L,

RCC: 3.6 x 10^12/L,

Hb: 104 g/L,

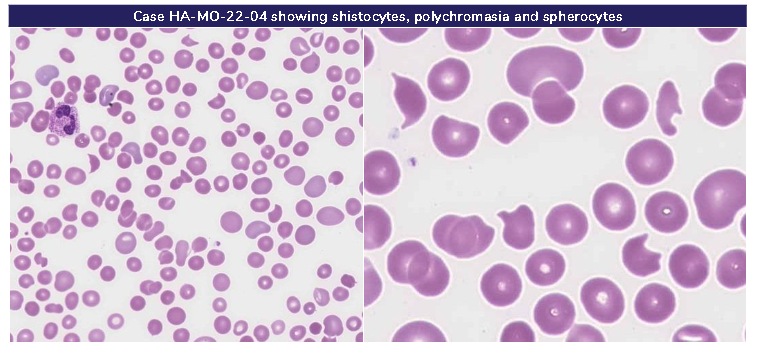
MCV: 92fL,

MCH: 29 pg,

MCHC: 312g/L,

PLT: 65 x10^9/L.

This blood film showed a variety of red cell changes, including schistocytes, spherocytes, nucleated RBC and increased polychromasia. The white cells showed mild left shift while the platelets appeared to have normal morphology. Considering the morphological features described and the reduced platelet count, the most likely diagnosis was microangiopathic haemolytic anaemia (MAHA).



The majority of participants reported the presence of schistocytes, which were considered the essential diagnostic feature. Schistocyte is a general term for a fragmented RBC which are formed when erythrocytes are forced through a vessel blocked with interlacing fibrin strands and the red cells are sliced into fragments. The presence of schistocytes indicates a disorder which is potentially life-threatening, and must be treated as a medical emergency. Bite cells were also present in this film, however, participants are cautioned to evaluate the significance of the bite cells in an overall MAHA picture. In this case the bite cells were of lesser significance in the presence of the thrombocytopenia with schistocytes (indicating a MAHA), and hence the bite cells were scored lower.

MAHA and Fragmentation Haemolysis, the most likely diagnoses, were assessed as concordant. Haemolytic uraemic syndrome / thrombotic thrombocytopenic purpura (HUS/TTP) were more specific diagnoses with the described features present and were also considered concordant.

Disseminated intravascular coagulation (DIC) was considered less likely, because of the marked increase in schistocytes and no significant features of response to sepsis, however, due to its morphological similarities to MAHA, this diagnosis was considered an appropriate differential diagnosis.

MAHA is a descriptive term denoting the features of red cell fragmentation haemolysis (ie Coombs-negative, intravascular) seen on peripheral blood (PB) film examination. Conditions in which schistovcytes are seen on PB examination include red cell fragmentation occurring either as a result of microvascular damage, physical fragmentation of red cells in small blood vessels, or physical fragmentation related to large vessels and prosthetic heart valves.

Thrombotic microangiopathy (TMA) is a specific group of disorders, where abnormalities in the small vessels lead to microvascular thrombosis. There is an overlap between thrombotic microangiopathy (TMA) and MAHA, however not all instances where a TMA-a primarily histopathological diagnosis-is present will result in a finding of MAHA and not all cases where a MAHA is detected will have an underlying TMA. The commonest clinical scenario however is one where MAHA, as detected on the PB film, is associated with underlying microvascular damage and thrombocytopenia. MAHA can also be present without significant thrombocytopenia. Again, the morphological finding of MAHA with or without thrombocytopenia is a critical result, and the clinician should be notified immediately and the film referred to the Haematology registrar or Haematologist. The presence of schistocytes on the blood film is a typical feature of MAHA, and occasionally, microspherocytes. Increased polychromasia and nucleated RBC may also be present, depending on the severity of the anaemia.1

Characteristic laboratory features are a negative direct antiglobulin test, an increased lactate dehydrogenase (LDH) level, increased indirect bilirubin, and low haptoglobin with an increased reticulocyte count.

Various systemic disorders can present with MAHA-type features, including TTP,HUS, DIC, systemic infections, and autoimmune disorders. Its occurrence in cases of widespread metastasis of malignant tumours -cancer-related MAHA (CR-MAHA) -has also been reported.2

CR-MAHA with thrombocytopenia can occasionally be a presenting feature that leads to the diagnosis of the underlying cancer, particularly in adenocarcinomas of the stomach and gastrointestinal tract. This is less likely with gynaecological adenocarcinomas which usually have clinical symptoms. The pathophysiology of CR-MAHA has not been fully elucidated; the mechanism by which haemolysis progresses due to the mechanical fragmentation of red blood cells as blood flows through the vascular lumen narrowed by such tumour thrombi has been proposed. Accordingly, the use of antineoplastic agents as an effort to reduce tumour burden, in addition to supportive measures, are considered the most important in improving MAHA in this scenario.2 The presence of MAHA related to either known or undiagnosed malignancy is usually associated with a very poor outcome.

This patient had a known history of metastatic gastric cancer. Her LDH was markedly elevated (776 U/L), haptoglobin reduced (<0.15 g/L), direct antiglobulin test negative, reticulocyte count increased (454 x 109/L, C-reactive protein elevated (94 mg/L) and bilirubin increased (25 μmol/L).

1. Cancer-associated thrombotic microangiopathy, Govind Babu K and Gita R Bhat, ecancer2016, 10:649 DOI: 10.3332/ecancer.2016.649

2. Microangiopathic hemolytic anemia associated with metastatic breast cancer:case report and literature review, Daisuke Takabatake and Kazuyuki Oishi,SpringerPlus,2016, 5:684, DOI 10.1186/s40064-016-2312-

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|  | **HA-MO-22-04** | | | | | | | | | | | |
| RBC Features | Schistocytes | Polychromasia increased | Schistocytes | Bite cells | Polychromasia increased | Polychromasia increased | Bite cells | Polychromasia increased | Bite cells | Spherocytes | Irregularly contracted cells | Spherocytes |
| Bite cells | Spherocytes | Spherocytes | Spherocytes | Spherocytes | Schistocytes | Polychromasia increased | Spherocytes | Spherocytes | Polychromasia increased | Polychromasia increased | Bite cells |
| Polychromasia increased | Schistocytes | Polychromasia increased | Dimorphism / Dimorphic red blood cells | Schistocytes | Bite cells | Spherocytes | Blister cells | Polychromasia increased | Schistocytes | Spherocytes | Polychromasia increased |
| Nucleated red blood cells | Nucleated red blood cells |  | Nucleated red blood cells | Nucleated red blood cells | Spherocytes | Nucleated red blood cells | Schistocytes | Schistocytes | Bite cells | Schistocytes | Schistocytes |
| WBC Features | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Band form | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Neutrophils - hypergranulation | Band form |
| Band form |  | Band form |  | Promyelocytes / metamyelocytes / myelocytes | Neutrophils - hypergranulation | Band form | Band form |  | Döhle bodies | Band form | Neutrophils - hypergranulation |
|  |  |  |  |  | Promyelocytes / metamyelocytes / myelocytes |  |  |  |  |  |  |
| Platelet Features | No significant morphological platelet abnormality | No significant morphological platelet abnormality | No significant morphological platelet abnormality | Giant platelets / significant numbers of large platelets | No significant morphological platelet abnormality | No significant morphological platelet abnormality | No significant morphological platelet abnormality | No significant morphological platelet abnormality |  | No significant morphological platelet abnormality | No significant morphological platelet abnormality | No significant morphological platelet abnormality |
| Primary Diagnosis | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Fragmentation haemolysis | Oxidative haemolysis | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Oxidative haemolysis | Oxidative haemolysis | Microangiopathic haemolytic anaemia | Autoimmune haemolytic anaemia - warm | Microangiopathic haemolytic anaemia |

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| Highest scoring response | Moderate scoring response | Lowest scoring response | Response given no score |

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|  | **HA-MO-22-04** | | | | |  |  | **RCPA Report 30/06/2022** | | |  |  |
| RBC Features | Polychromasia increased | Spherocytes | Nucleated red blood cells | Polychromasia increased | Polychromasia increased |  | RBC Features | Schistocytes | Polychromasia increased | Bite cells |  |  |
| Schistocytes | Polychromasia increased | Polychromasia increased | Spherocytes | Schistocytes |  |  | Spherocytes |  |  |  |
|  | Schistocytes | Schistocytes | Schistocytes | Irregularly contracted cells |  |  | Nucleated red blood cells |  |  |  |
|  | Nucleated red blood cells | Spherocytes | Nucleated red blood cells |  |  |  |  |  |  |  |
| WBC Features | Neutrophils - hypergranulation | Promyelocytes / metamyelocytes / myelocytes | Band form | Neutrophils - hypergranulation | Neutrophils - hypergranulation |  | WBC Features | Neutrophils - hypergranulation |  |  |  |  |
|  | Neutrophils - hypergranulation | Promyelocytes / metamyelocytes / myelocytes | Döhle bodies |  |  | Promyelocytes / metamyelocytes / myelocytes |  |  |  |  |
|  |  | Neutrophils - hypergranulation | Promyelocytes / metamyelocytes / myelocytes |  |  | Band form |  |  |  |  |
| Platelet Features | No significant morphological platelet abnormality | No significant morphological platelet abnormality | No significant morphological platelet abnormality | Inaccurate platelet count | No significant morphological platelet abnormality |  | Platelet Features | No significant morphological platelet abnormality |  |  |  |  |
| Primary Diagnosis | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia | Microangiopathic haemolytic anaemia |  | Primary Diagnosis | Microangiopathic haemolytic anaemia | Haemolytic uraemic syndrome / thrombotic thrombocytopenic purpura | Fragmentation haemolysis | Differential Diagnosis | Disseminated intravascular coagulation |

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| Highest scoring response | Moderate scoring response | Lowest scoring response | Response given no score |

