Clinical and haematological characteristics of autoimmune haemolytic anemia: retrospective analysis of 10 cases

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Abstract

Background: Autoimmune haemolytic anemia (AIHA) is a disease of red cell destruction due to different antibody types. They are of two types: warm antibody AIHA (IgG type) and cold agglutinin disease (IgM type). Direct Coombs test is the cornerstone for diagnosis of AIHA.

Methods and results: A retrospective analysis of ten cases diagnosed with DAT were included. The cases showed female predilection (M: F = 1:9). Fatigue and breathlessness was the commonest presentation (90%) and Pallor was the most common (90%) physical examination finding. MCV (>100 fl) was seen in 9 cases (90%). Direct antiglobulin test (DAT) was positive in all ten cases (100%).

Conclusion: AIHA is common in females and patients mainly present with anemia. Secondary cold AIHA was more common than primary and warm type of AIHA. Secondary AIHA was associated with connective tissue disorders.

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Introduction

Autoimmune haemolytic anemia (AIHA) is one of the most common causes of acquired haemolytic anemia caused by circulating antibodies against antigens on the red cell membrane.[1] Depending on the nature of the antibodies they are of two major types: warm antibody AIHA (IgG type) and cold agglutinin disease (IgM type). [2] Direct Coombs test is the cornerstone for diagnosis of AIHA. Clinical presentation is mainly attributed to the rate of hemolysis thereby, manifesting anemia like fatigue, breathlessness and also systemic symptoms like fever, joint pains and bleeding.[1] With this background, a clinico – haematological profile of patients with AIHA were assessed using a retrospective study of 10 patients.

Materials and Methods

A retrospective analysis was performed on patients diagnosed with AIHA by direct antibody test (DAT) from December 2012 to February 2013. The details pertaining to the disease status which included presenting complaints and physical examination findings were retrieved. The laboratory parameters including haematological, serological and immunological findings were then correlated. Other tests including bone marrow aspiration biopsy, lymph node biopsy and ANA profile was performed wherever necessary.

Result

A total of 10 cases were evaluated. The age at presentation ranged from 26 to 80 years and there was a female predilection (M: F = 1:9). Fatigue and breathlessness was the commonest presentation (90%) in our patients. [Fig 1]Pallor was the most common (90%) physical examination finding. Organomegaly (splenomegaly, hepatomegaly and hepatosplenomegaly) was seen only in AIHA – cold type. [Fig 2]
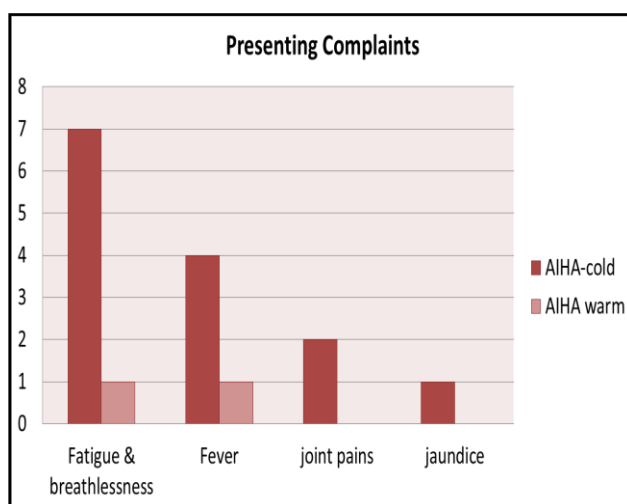

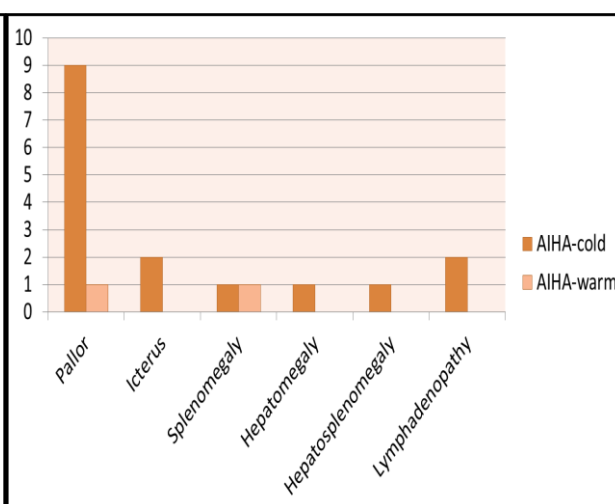Fig 1: Modes of clinical presentation   Fig 2: Physical examination findings

Laboratory findings was correlated and in our study moderate anemia (Hb 6-10 gm%), raised indirect bilirubin (>2mg/dl), raised Lactate dehydrogenase (>450 Units) was observed in all ten cases. Raised MCV (>100 fl) was seen in 9 cases (90%) and raised ESR (>50mm/hr) was seen in 6 cases (60%). [Table 1]

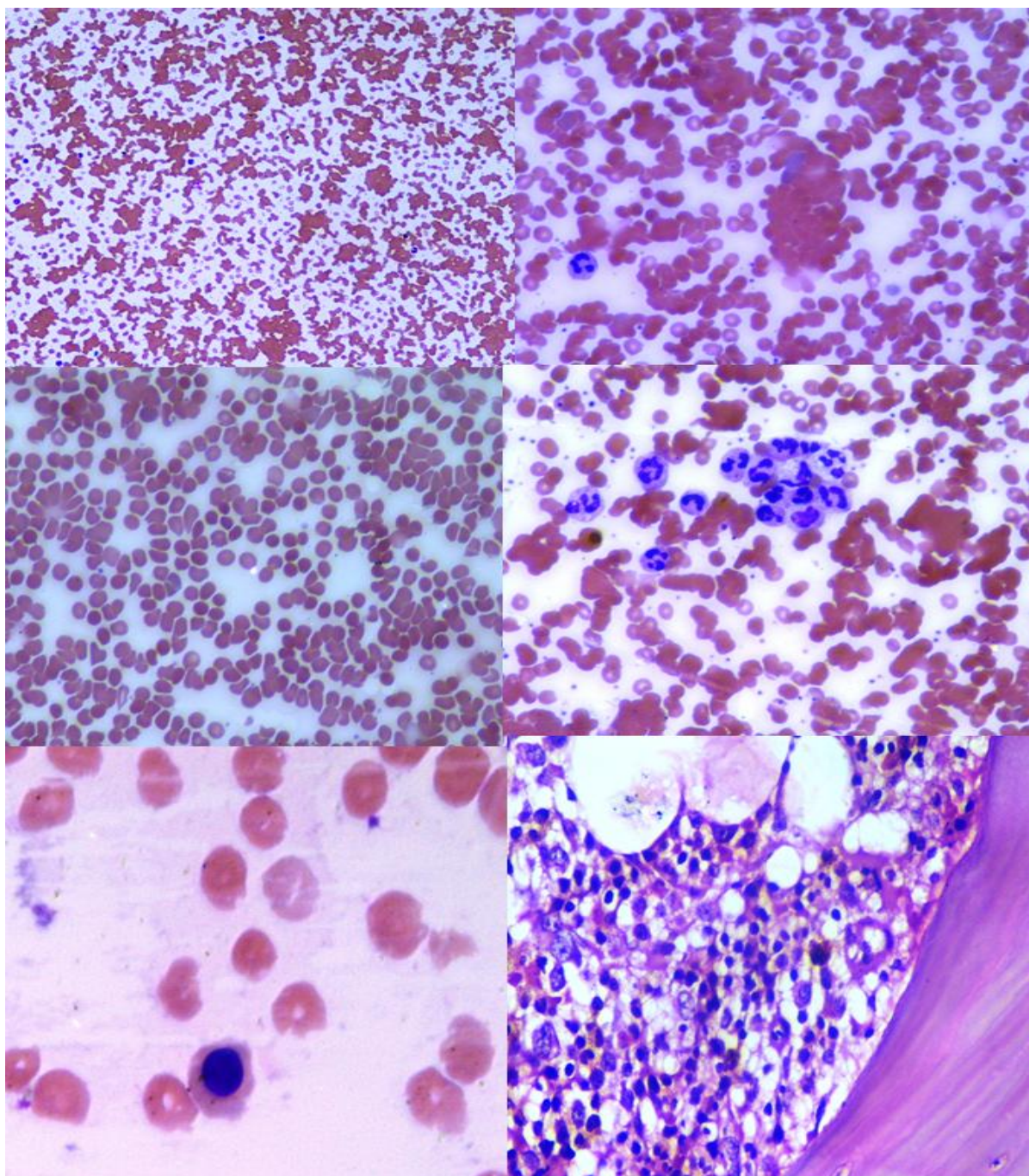| Investigations	Present study (10cases)
Hb <10 gm/dl	10 cases (100 %)
MCV >100 fl	9 cases (90%)
ESR > 50mm/hr	6 cases (60%)
Indirect Bilirubin>2mg/dl	10 cases (100%)
LDH> 450U	10 cases (100%)
DAT- Positive	10 cases (100%)
IAT- positive	none
ANA positive	4 cases (40%)
AntidsDNA positive	2 cases (20%)

Figure 1: (A) Microscopy Low Power: RBC agglutinates seen. (B) High power : RBC agglutinates; (C) Microscopy peripheral smear: Spherocytes & Polychromatophils; (D). High power (40x): Leukoagglutinates seen (E). High power (40x): Nucleated RBC seen. (F). Case of plasma cell dyscrasia: Bone marrow biopsy, Plasma cells and scattered hemosiderin laden macrophages seen

Morphological features on peripheral smear examination revealed RBC agglutinates, spherocytes and polychromasia. Nucleated RBC and leukoagglutinates were also seen. [Figure 3: A-E]

Serologically, Direct antiglobulin test (DAT) was positive in all ten cases (100%). Other tests included four cases (40%) of ANA positive, two cases (20%) of AntidsDNA positive and bone marrow biopsy in a case of plasma cell dyscrasia revealed abundant plasma cells.

This clinico-hematological correlation revealed that nine out of ten cases were of cold AIHA and one was of warm AIHA. Four out of ten cases are secondary AIHA associated with connective tissue disorder (two cases confirmed SLE). Other cases were plasma cell dyscriasis with AIHA on bone marrow biopsy (1/10), [Figure 3: F] primary AIHA (1/10), essential thrombocytosis (1/10), malaria (1/10), Mycoplasma pneumonia (1/10) and hypothyroidism (1/10).

Discussion

Cold agglutinins are polysaccharide antibodies that react with the red cells at lower temperature ($<37^0$ C) and are almost always IgM type. This type of AIHA requires accurate diagnosis as it heralds a therapeutic challenge. Hence understanding its clinical manifestations and laboratory diagnosis is very much essential for accurate therapeutic options.

Few vital studies have been undertaken in Indian population on AIHA. Alwar et al, studied 175 cases, the commonest presentation was fatigue and breathlessness attributed to anemia (36%). Pallor (98%) was a universal finding. Serologically, 45% of primary AIHA cases showed both DAT and IAT positivity. Cold agglutinin titer was significantly raised in two cases.[1]

Choudhry et al, studied 21 cases, in which pallor (89%) was the most common feature, splenomegaly (81%) was higher than hepatomegaly (76%). DAT positivity was seen in 19 cases, while IAT was positive in 7 cases.[3] In a study by Baek et al, Coomb's test was positive in 96% of the cases. Out of 32 cases, 32 were warm and 1 case was cold antibody type. MCV was raised with range of 107 +/- 22. Thus MCV is considered an important index for AIHA.[4]

The diagnosis of CAD mainly depends on typical DAT findings. Specific DAT for IgG is usually, but not always, negative.[5,6] Other investigations include complement assessments (C3, C4 and CH50), electrophoresis with immunofixation, trephine biopsy including immunohistochemistry, flow cytometry of aspirate, chest X ray and abdominal ultrasonography.[7,8]

The cornerstone for CAD management is nonpharmacological measures which include avoiding cold exposure and increasing warm clothing. Pharmacological therapies are mainly aimed to suppress aberrant IgM protein production and mainly include corticosteroid therapy.[9] Drugs such as Cladribine, Rituximab, Fludarabine and Eculizumab are all under evaluation. It is also important to note that splenectomy is contraindicated in CAD as hemolysis occurs outside the spleen.[10]

Conclusion

In a retrospective analysis performed on 10 cases, AIHA was common in females and patients mainly presented with anemia. An increased MCV in a background of a haemolytic blood picture should raise a suspicion of cold AIHA. Secondary cold AIHA was more common than primary and warm type of AIHA. Secondary AIHA was associated with connective tissue disorders.

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