

## **Case study**

### **‘A CASE OF OVERLAPPING AUTOIMMUNE SCLEROSING CHOLANGITIS AND AUTOIMMUNE HEMOLYTIC ANEMIA’**

#### ***Abstract***

A 14-year old female patient, who appeared to be otherwise healthy and normal, was brought to the hospital. This female patient had complaints of fever, sore throat, severe abdominal pain, and generalized body aches for the last two days.

She appeared to be lethargic and weak. Her condition had made her fatigued and a yellowish tinge of the face and sclera pointed towards jaundice. There was also hepatomegaly and splenomegaly present, and the muscles appeared to be tender as well.

The girl was admitted to the hospital, where her lab investigations revealed that she was anemic. Other investigations revealed that her liver enzymes and bilirubin levels were significantly elevated. Her DAT was positive and there was a presence of high eosinophilia.

However, her Hepatitis A, B, and C screening came out to be negative. She was kept as a suspected case of Autoimmune Hemolytic Anemia as it appeared to be the most probable diagnosis, but following a biopsy she was also confirmed as a case of Autoimmune Sclerosing Cholangitis.

Once the diagnosis was confirmed, the girl was treated accordingly. This was a unique case because it involved a significant overlap in the presence of two diseases. Both of the diseases, although similar in appearance, could have caused great havoc if they were not separately

diagnosed and treated accordingly. However, it was the timely diagnosis and appropriate screening which led to the accurate diagnosis in this scenario.

The events leading to this outcome have been discussed in the preceding sections. The case study also highlights how both of these diseases present in a patient of the younger population, and how they need to be managed effectively and efficiently to ensure that there are no complications that might alter the already deteriorating state of the patient.

Key words: Autoimmune Hemolytic Anemia, Autoimmune Sclerosing Cholangitis, DAT

## INTRODUCTION

Autoimmune Hemolytic Anemia is a rare heterogeneous disorder that is hereditary in nature. In this disorder, there is an acquired premature destruction of red blood cells (RBCs) by the body's own immune system that seems to have generated antigens against the premature RBCs. <sup>[1]</sup>

However, just like in the case of any other undiagnosed yet suspected anemia, there is also a systematic way of approaching this particular type of anemia.

Since hemolysis is the initiating factor in Autoimmune Hemolytic Anemia, it is not difficult to guess that why hemolysis would be the first warning or alerting sign that would ultimately lead the physician to carry out further investigations to establish this diagnosis.

However, the commonly noticed signs in Autoimmune Hemolytic Anemia include either a normocytic or macrocytic anemia, raised reticulocyte count, raised unconjugated bilirubin levels, and the presence of spherocytes or agglutination on blood smears, as well as reduced haptoglobin levels. All these factors are confirmed signs that lead one to the diagnosis of Autoimmune Hemolytic Anemia in a given patient. <sup>[2]</sup>

Once a confirmed diagnosis has been established and the patient has been informed about their illness, the next step is to deduce a treatment option that is deemed appropriate according to the clinical picture of the patient. There is no final treatment that puts an end to this disease or resolves it completely, and so in every case, supportive measures need to be continued for the rest of the patient's life. <sup>[3]</sup>

The patient whose case is being discussed also presented with complaints that were consistent with Autoimmune Sclerosing Cholangitis. This condition is often referred to as 'Overlap Syndrome', mainly because it is seen to commonly overlap with both the clinical and morphological features of Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis. <sup>[4]</sup>

The key factor here is the involvement of the immune system. Being an autoimmune disease, there is no clear initiating or triggering factor for this disease. It clearly seems to stem from disturbances or problems in the immune system of a patient, who is most commonly of a young age. <sup>[5]</sup>

Because of the presence of an obvious and confusing overlapping clinical picture, it is often difficult to diagnose this condition, and thus, delays are often encountered. The final solution to tackle this issue is to only rely upon the cholangiographic diagnosis on the presence of structures within the biliary tree to establish the diagnosis. <sup>[6]</sup>

## CASE STUDY

This case revolves around a 14-year old female child. The child was previously in a healthy and normal state. However, she was brought to the hospital with presenting with complaints of fever, sore throat, and generalized body pains for the last three days. She also had severe abdominal pain and because of this condition, she appeared to be generally unwell and fatigued.

In response to the severity of her condition, she was directly admitted to the hospital.

### *Examinations:*

Upon examining her in detail, it was found that the patient appeared pale. She had obvious signs of jaundice as her face and sclera both had a yellowish tinge. She also complained about passing darker than normal urine.

Her vitals were as follows: temperature 37.1C, peripheral pulse 88, blood pressure 108/72 mm Hg, oxygen saturation 100%.

The girl also complained of muscle tenderness and this was confirmed by her general physical examination.

Her abdominal examination revealed that she also had hepatomegaly (extending 3 cm below the costal margin) and splenomegaly.

## Laboratory Analysis:

The laboratory investigations that were carried out on the patient along with their respective results have been summarized as follows:

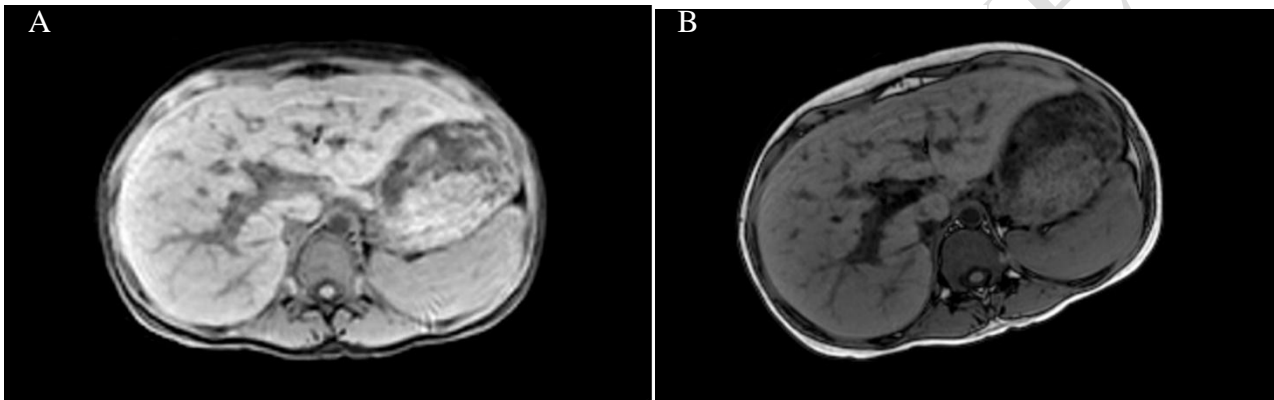
**Table 1.** laboratory investigations

Hepatitis Bs Ag Screen	Negative		PT	15.0 sec(s)	(12.0 - 15.0)
Hep Bs Ab	Negative		INR	* 1.2	(0.7 - 1.1)
Hep Bs Ab Titer	6.950 IU/L		APTT	* 44.8 sec(s)	(27.7 - 42.1)
Hep Be Ag	Negative	(Negative -)	Fibrinogen Lvl	3.20 g/L	(2.00 - 4.00)
Hep B Core Ab	Negative		Anticoagulant?	None	
Hep B Core IgM Ab	Negative	(Negative -)	D-Dimer Auto	* 0.43 mcg/mL	( - <=0.50)
Hepatitis C Ab Screen	Negative		Hepatitis Bs Ag Screen	Negative	(Negative -)
Hep A Ab	Negative		ANA	* Negative	
DAT Poly	Positive		CMV IgG	Positive	(Negative -)
Glucose Random	6.56 mmol/L	( - <=8.80)	CMV IgG Abs	* >250.0 AU/mL	
Total Protein	72.3 g/L	(60.0 - 80.0)	CMV IgM	Negative	(Negative -)
Albumin Lvl	39.1 g/L	(35.0 - 50.0)	CMV IgM Titer	0.080	
Bili Total	52.1 micromol/L	(0.0 - 17.1)	EBV Capsid Antigen IgG	Positive	(Negative -)
Bili Direct	44.8 micromol/L	(0.0 - 3.4)	EBV Capsid Antigen IgM	Negative	(Negative -)
Alk Phos	510.8 IU/L	( - <=187.0)	EBV Nuclear Antigen IgG	Positive	(Negative -)
AST	279.3 IU/L	(0.0 - 32.0)	Hep B Core IgM Ab	Negative	(Negative -)
ALT	223.2 IU/L	(0.0 - 31.0)	HSV 1/2 IgM	Negative	(Negative -)
EBV Capsid Antigen IgG	Positive	(Negative -)	LKM Abs	* Negative	
EBV Capsid Antigen IgM	Negative	(Negative -)	Parvo B19 IgG	Positive	(Negative -)
EBV Nuclear Antigen IgG	Positive	(Positive -)	Parvo B19 IgG abs	* 36.27 IU/mL	
Albumin Lvl	30 g/L	(35 - 52)	Parvo B19 IgM	Negative	(Negative -)
Bili Total	39.4 micromol/L	( - <=17.0)	Rubella IgM Ab	Negative	(Negative -)
Bili Direct	27.4 micromol/L	( - <=5.0)	SMA Screen	* Negative	
AST	236 IU/L	( - <=32)	Hep A IgM Ab	Negative	(Negative -)
ALT	194 IU/L	( - <=33)	Anti Tissue Transglutaminase IgA	* <1.9 CU	( - <=19.9)
WBC	15.0 x10 <sup>9</sup> /L	(4.5 - 13.5)	DAT Interp	DAT Interp	
RBC	* 3.26 x10 <sup>12</sup> /L	(3.80 - 5.00)	DAT Poly	Positive	
Hgb	74 g/L	(115 - 150)	IgG BB	4+	
Hct	0.24 L/L	(0.34 - 0.44)	IgM BB	0	
MCV	74.2 fL	(73.0 - 95.0)	IgA BB	* 1+	
MCH	22.7 pg	(26.0 - 32.0)	C3d	0	
MCHC	306 g/L	(320 - 360)	C3c	0	
Platelet	366 x10 <sup>9</sup> /L	(140 - 400)	Ctrl	0	
Ammonia Lvl	* 32.1 micromol/L	(15.0 - 51.0)			
Ceruloplasmin	0.45 g/L	(0.16 - 0.45)			
A-1-AT	2.05 g/L	(0.90 - 2.00)			
Amino Acid Quant	Amino Acid Quant				

***MRI MRCP:***

The MRI MRCP report of the child revealed the following results:

‘Presence of hepatosplenomegaly was noted. There was a diffuse irregular biliary dilatation of thickened wall with periportal lymph nodes and T2W hyperintensity in keeping with the suspected clinical diagnosis of sclerosing cholangitis.’



***Figure 1. MRI MRCP report***

***Liver Biopsy:***

The liver biopsy results of the girl revealed the following analysis:

“This biopsy showed moderate portal inflammation with interface hepatitis noted in some of the portal tracts. No definite plasma cells are identified. Diffuse bile duct injury is noted. No periductal fibrosis is seen. No granuloma or lymphoid aggregates/follicles are seen.

The above features along with the MRCP/MRI findings are suggestive of overlap syndrome (AIH/PSC). The histological features are probably affected due to the steroid intake and

treatment. Another possibility that can not be completely excluded is autoimmune cholangitis. Correlation with serology markers, radiology and laboratory results.”

***Patient's Progress:***

On the very next day of her admission to the ward, the girl's hemoglobin dropped to 70 g/L along with positive antibodies. As a suspected case of Autoimmune Hemolytic Anemia and primarily to avoid complications from taking place, the girl was started on Prednisone right away. In the meantime, it was also excluded that there was no history of any other autoimmune disease present or diagnosed in this patient.

However, her abnormal liver enzymes combined with her clinical presentation helped reveal the fact that she was suffering from a case of Autoimmune Hepatitis associated with Cholangitis. This diagnosis was confirmed under the observation of a Pediatric GI.

Therefore, she was continued on Prednisolone and remained admitted due to her ongoing fever. Currently, after some tapering and dose adjustments, she is now on Prednisolone 20 mg during the day and 15 mg at night.

When the CBC was repeated, it revealed the following results:

Table 2 : Pathological report

<b>White Blood Cells</b>	12.4
<b>Hemoglobin</b>	108
<b>Hematocrit</b>	0.34
<b>Platelets</b>	537,000 (Differentials were normal)
<b>Direct Coombs' Test</b>	Positive

***Management & Treatment Plan:***

After the Pediatric GI confirmed that the patient was indeed suffering from Autoimmune Hepatitis associated with Autoimmune Hemolytic Anemia, the matter revolved around suggesting an appropriate treatment plan for her.

The hepatology team were brought on board. Here, her LFTs were seen to worsen over time, her jaundice had now become well-manifested, and hemoglobin continued to drop down, attaining a level of 51 at the time. At this point, the patient was being maintained on Ursodiol and Azathioprine.

Because of her worsening anemia, Prednisone was restarted. It was later stopped when she was discharged.

She was also started on IV Methylprednisolone 2 mg/kg/day along with 2 doses of IVIG.

When she was discharged, she was prescribed Sirolimus 2 mg PO daily. As per the last update taken in April 2022, it was found that her response to Sirolimus was acceptable. Her hemoglobin levels were also satisfactory and the reticulocyte count had significantly dropped. Steroids were stopped and she was advised to continue taking Folic Acid 5 mg PO on a weekly basis for the time being.

## DISCUSSION

Pediatric autoimmune diseases pose a great negative impact on the morbidity and mortality of the pediatric population around the world. Due to the lack of this target population describing their complaints properly in detail, it often becomes difficult to diagnose these diseases in children. There are currently an estimated 26 autoimmune diseases that present in the pediatric population across the different ages of their age group. All of these diseases are among the prevalent diseases that are seen in this age group.<sup>[7]</sup>

Autoimmune Hepatitis is one such autoimmune disease that is found to occur in the pediatric population. It was commonly seen to occur in the female pediatric population. More frequently, it has been seen to occur as part of the 'Overlap Syndrome'.

The Overlap Syndrome is a name given to a condition where a patient presents with similar and 'overlapping' features of both Autoimmune Hepatitis and Primary Sclerosing Cholangitis, as seen in this patient. The management of these types of cases is usually confusing, mainly because it becomes difficult to diagnose the actual condition amidst the confusing symptoms.<sup>[8]</sup>

Autoimmune Hepatitis is a progressive form of autoimmune disease where there is a noticeable inflammation of the liver due to an unknown cause.<sup>[9]</sup>

It is thought to stem from a combination of genetic and environmental factors and so, the affected individual has to suffer from a myriad of symptoms in return. 60% of the patients are diagnosed without any obvious symptoms or causes. Out of all the cases diagnosed, 80% belong to the Type I category, which is diagnosed on the basis of anti-smooth muscle antibodies (ASMA) with or without any antinuclear antibodies. (ANA).<sup>[10]</sup>

The most common symptoms that present in this condition are malaise, fatigue, jaundice, abdominal pain, and sometimes, arthralgias. The treatment options for Autoimmune Hepatitis keep evolving and changing as per the intensity and severity of the disease.

So far, the most widely accepted regimen is where the disease is stopped from progressing towards liver cirrhosis and other complicated and irreversible stages.

The given patient was also seen to be suffering from Autoimmune Hemolytic Anemia. This is a rare, hereditary condition in which a hemolysis or breakdown of the premature red blood cells (RBCs) occurs due to the immune system dysfunctioning against the body's red blood cell antigens.<sup>[11]</sup>

Autoimmune Hemolytic Anemia could either be primary or secondary depending on the presence or absence of an underlying illness. The diagnosis is largely based on the abnormalities that could be seen on the peripheral smear and the complete blood picture.

Just like with any other autoimmune disease, there is no treatment for it. Supportive blood transfusions are given to the patient to make sure that their hemoglobin levels remain within the optimal range. Hematopoietic stem cell transplantation is also recommended in some cases, but

the cost of this is often too expensive for people to afford, so they usually prefer transfusions and other supportive treatment options. <sup>[11]</sup>

## CONCLUSION

In this case, the patient presented with confusing symptoms. A prompt diagnosis was made, and in accordance with that, further evaluation and management was carried out.

The patient has now been discharged and is on maintenance treatment. There is no doubt that it was due to the timely diagnosis and appropriate treatment protocol that in this case saved her life and prevented complications.

### **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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