The sixty fourth case of pediatric Churg Strauss syndrome

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Abstract

Pediatric Churg Strauss syndrome is a rare disorder that is extremely rare during childhood. A total of 63 cases of pediatric Churg Strauss syndrome have been reported in the world.

The aim of this paper is to describe the 64th case of pediatric Churg Strauss syndrome and the first case of Churg Strauss syndrome in Iraq. The patient illness was misdiagnosed as tuberculosis and the use of anti-tuberculosis medication was associated with life threatening complications and the development of serious corneal opacity because of delay in receiving the appropriate therapy.

It is an unnecessary and unfortunate experience for the patient to receive management that is very inappropriate in the presence of a therapeutic intervention that can induce remission of the disease.

This case illustrates the difficulty and importance of the awareness to reach a diagnosis in a rare syndrome or disorder for which there is an effective therapy.

Introduction

Pulmonary eosinophilia including eosinophilic pneumonia is characterized by significant systemic and pulmonary manifestations such as fever, sweating at night, cough, difficulty breathing, weight loss, blood eosinophilia, peripheral infiltrates on chest radiograph, and a good response to corticosteroid therapy [1,2].

Pulmonary eosinophilia which can be caused by Churg Strauss syndrome is rare in children and can be misdiagnosed by pediatricians [1,2].

Chronic eosinophilic pneumonia was first described by Carrington in 1969. Tuberculosis was the initial diagnosis in most of Carrington cases, However, the patients’ condition deteriorated on chemotherapy [2].

Churg Strauss syndrome was first described by Jacob Churg and Lotte Strauss in 1951. They called the condition "allergic granulomatosis.” The syndrome is associated with the development of autoimmune systemic necrotizing vasculitis with inflammation of small and medium-sized blood vessels. It has highly variable presentation and course. The condition was sometimes called eosinophilic granulomatosis with polyangiitis [1].

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Case report

A six-year old girl with convergent squint (abducent nerve palsy) and corneal opacity on the right eye (Figure 1) was seen early during November, 2016, because of evidence of recent hepatitis B infection which developed following the receive of several blood transfusions.

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Table 1 shows the results of tests for hepatitis B virus which were performed on the 20th of October 2016. HBs, antigen HBe antigen, HBc antigen were all positive despite they were negative several weeks earlier.

Liver enzymes were shown to be elevated on earlier on the eighth of October while the serum albumin was normal. SGOT was 119 iu/L (Normally less than 50), SGPT was 121 iu/L (Normally less than 5), and serum albumin was 4.5g/L. The child had history of cough and wheezing more than one year earlier.

Her illness was first started at the age of five years with the development of keratitis in association with respiratory symptoms. She had fever, night sweats, cough and dyspnea with pulmonary infiltrates on chest radiographs. She also had hepatomegaly. Marked eosinophilia was demonstrated on blood counts.

Tuberculosis was considered despite it cannot account for marked eosinophilia and despite that spumum test for acid fast bacilli was negative. Hepatitis Anti-genes and anti-bodies for hepatitis B virus were negative during that time. The keratitis which was causing blurring of the cornea was considered to be viral and was treated by ophthalmologist accordingly. The corneal inflammation was treated mainly with acyclovir ophthalmic preparations. Anti-tuberculosis therapy was used for several weeks, but without any benefit.

She received triple anti-tuberculosis therapy (INH, rifampicin, and pyrazinamide). Anti-tuberculosis therapy was initiated on the second of November 2015. On the second of January 2016, pyrazinamide was stopped, and all anti-tuberculosis therapy was discontinued on the tenth of January 2016.

During January 2016, she developed pallor, jaundice, and lethargy. She was afebrile and had hepatosplenomegaly. Liver was palpable 10 cm below the subcostal margin, and the spleen was palpable 8 cm below the subcostal margin. There was no lymphadenopathy, and the rest of physical examination was not significant.

Laboratory was performed on the eleventh of January 2016. Hemoglobin was 4.4 g/dl with normochromic normocytic red blood cells. There was also neutrophil leukocytosis with white cell count of 16,800/ml and neutrophil count was 67% while the lymphocyte count 20%. Platelet count was 167,000/ml and no abnormal cell was seen on blood film. She received blood transfusion daily for seven days.

A bone marrows specimen was examined on the 13th of January 2016. The bone marrow was hypercellular with myelopisosis hyperplasia. There was predominance of intermediate stage in giant forms. There was also neutrophil leukocytosis with white cell count of 19,400/ ml and neutrophil count was 62% while the lymphocyte count 24%.

| Table 1. The results of tests for hepatitis B virus (October, 20, 2016) |
|---------------------------------------------------------------|
| Serum HBs antigen | Chromatographic immunoassay for the qualitative detection of hepatitis B virus surface antigen. |
| Positive |
| Serum HBe antibody | Chromatographic immunoassay for the qualitative detection of hepatitis B virus envelope antibody. |
| Negative |
| Serum HBc antibody | Chromatographic immunoassay for the qualitative detection of hepatitis B virus core antibody. |
| Positive |
| Serum HBe antigen | Chromatographic immunoassay for the qualitative detection of hepatitis B virus envelope antigen. |
| Positive |
| Serum HBs antibody | Chromatographic immunoassay for the qualitative detection of hepatitis B virus surface antibody. |
| Negative |

Hemoglobin was 5.1g/dl with normochromic red blood cells, and the presence of spherocytes, polychromatic macrocytes, and nucleated blood cells (2 per 100 blood cells).

There was also neutrophil leukocytosis with white cell count of 19.400/ml and neutrophil count was 62% while the lymphocyte count 24%.

Reticulocyte count was 18% and the corrected reticulocyte count was 7%.

Platelet count was adequate.

Total bilirubin was 8.2 mg/dl with the indirect bilirubin 5.7mg/dl.

SGPT was 38 iu/L and SGOT was 25 iu/L.

Test for G-6-PD was negative, but direct Coombs was positive.

On the 17th of January 2016 laboratory tests showed the followings:

- Hemoglobin was 6.5g/dl with normochromic red blood cells, and autoagglutination.
- Normal white cell count of and morphology; white blood cell count 4.600/ ml, neutrophil count was 68% while the lymphocyte count 22%.
- Platelet count was 167,000/ml.
- Total bilirubin was 8 mg/dl with the indirect bilirubin 5 mg/dl.
- SGPT was 47 iu/L and SGOT was 101 iu/L.
- The ESR was very high 145 mm/hour, direct Coombs was strongly positive (3+++). Serum LDH was also very high 1900 iu/L (Normal: 200-400 iu/L).

On the 19th of January, 2016 laboratory tests suggested cold autoimmune hemolytic anemia. Hemoglobin was 6.5g/dl; white blood cell count was 10,000/ml with 62 % neutrophils, 24 % lymphocytes, 7% monocytes, and 4% myelocytes.

Red blood cells were generally normochromic with slight anisopokilocytosis, and many macrocytes. There were two nucleated red blood cells per 100 with agglutination of red blood cells. The platelet count was within normal limits.

The urine was dark in color and was positive for urobilinogen and strongly positive for bile pigments (+++). Microscopic urine examination showed 1-3 red blood cells/HPF and 8-12 pus cells/HPF.

On the 20th of January, cold agglutinin test was positive with a titer exceeding 1024.

On the 21st of January, total bilirubin was 26 mg/dl; SGPT was 245 iu/dl.

Treatment included

- Blood transfusion twice; one with AB positive blood (her blood group), and one with O positive blood.
The deterioration in the respiratory symptoms and chest radiographs occurred following discontinuation of steroids which was used to treat the hemolytic anemia caused by anti-tuberculosis medications.

On the 18th of June, 2016, she developed fever, anorexia, cough, abdominal pain, and she had hepatosplenomegaly.

An abdominal ultrasound performed on the 19th of June 2016 showed mild hepatosplenomegaly. The liver was mildly enlarged with normal echo pattern and no focal lesion. The intra-hepatic biliary tree and hepatic veins were normal. The spleen was mildly enlarged (103 mm) with normal parenchyma and normal splenic veins. All other organs including gall bladder, pancreas, kidneys, and bladder were all normal.

General stool examination on the 19th of June showed few red blood cells and the stool was semi-solid with no other abnormality.

Urine test performed on the 27th of June was negative for bile pigments.

Laboratory tests performed on the first of July, showed leukocytosis with absolute eosinophilia. White blood cell count was 14,000/ml with 48% neutrophils, 11% lymphocytes, and 39% eosinophils. Hemoglobin was 11.6/g/dl and the red blood cells were normochromic normocytic with slight anisocytosis. No abnormal cells were seen on blood film. Reticulocyte count was 8%, and platelet count was 256,000/ml. The erythrocyte sedimentation rate was high at 99 mm/hour.

During July, 2016, she was experiencing high grade fever, poor appetite, cough, vomiting and severe abdominal pain.

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also the tail to 2.3 cm. The ultrasound report suggested the possibility of acute pancreatitis. Ultrasound of the abdomen was performed again on the 18th of July, 2016 and the pancreas was enlarged in all parts with hypo-echoic texture, and the possibility of pancreatitis was greatly increased.

On the 24th of July 2016, serum amylase was found to be elevated at 409 iu/L, but it declined to 108 iu/l on the 30th of July in association with disappearance of abdominal pain.

On the 25th of July, a specimen of bone marrow was found negative when tested with real-time PCR for mycobacteria tuberculosis. However, the norm-cellular bone marrow specimen, which was taken on the 27th of July, showed prominent eosinophilia. There were active megakaryocytes with predominance of eosinophilic precursors, and no evidence of neoplastic cells.

On the 28th of July 2016, the treating physicians during that time decided to start two anti-tuberculosis agents, streptomycin and ethambutol as they considered them not associated with hepatitis or hemolytic anemia.

On the 30th of July, laboratory tests performed and showed the following findings:

Hemoglobin was 9.3g /dl, white blood cell count was 5500/ ml with 54% neutrophils and 34% lymphocytes.

Reticulocyte count was 2.5% and platelet count was 302.000/ml.

Total serum bilirubin was 0.9 mg/dl, SGPT was 116 was iu/l, and SGOT was 112 iu/l. Direct coombs test was negative, Urine examination showed normal findings, and was negative for bile pigments.

On the 10th of August, 2016, the treating physicians during that time decided to add INH in small dose and increasing it gradually while monitoring liver enzymes and reticulocyte count.

Treatment with prednisolone was also started. However, liver enzymes were found to be elevated on the on the 27th of August. SGOT was 59 iu/L (Normally less than 50), and SGPT was 90 iu/L (Normally less than 50).

On the 27th of August, 2016, there was more elevation of liver enzymes. SGOT was 121 iu/L (Normally less than 50), and SGPT was 234 iu/L (Normally less than 50).

On the 19th of September 2016, laboratory tests were performed. The Hemoglobin was 14.1 mg and the reticulocyte count was 2%. Platelet count was 165.000/ml.

An ultrasound performed during October 2016 (Figure 4) showed mild acalculous cholecystitis and cholangitis. The gall bladder had normal size, but there was mild thickening of the mucosa, and no stone was present. There was also mild irregular dilatation (4-7 mm) of the common bile duct with mucosal thickening and without obvious distal obstruction. The liver had normal dimensions with coarse echo pattern and mild periportal fibrosis. The pancreas was normal in size and had normal echo pattern.

The diagnosis of the 64th case of pediatric Churg Strauss syndrome in the World and the first case of Churg Strauss syndrome in Iraq was made.

Table 2 shows the main features of the 64th case of Churg Strauss syndrome in the World.

**Discussion**

Hundreds of rare clinical syndromes are known to occur in humans. However, there is often inadequate professional knowledge, experience and awareness of their presentations and their most appropriate management, because of the small number of patients having each one of them. Diagnostic challenges and difficulties, diagnosis delay, and misdiagnoses, inappropriate or unsatisfactory management are well known to be associated with rare syndromes and disorders. It is expected that at least one third of rare syndromes and disorders are misdiagnosed more than once, or the diagnosis is delayed unnecessarily for a variety of reasons. Some rare syndromes often present with a symptom or symptoms of more common illnesses and are associated with variable presentations [1].

Diagnosis of a rare clinical syndrome may depend on whether the consulted physician has seen the rare condition before, and whether he

| Table 2. The main features of the 64th case of pediatric Churg Strauss syndrome in the World |
|----|
| 1 | History of asthmatic attacks. |
| 2 | Unfixed pulmonary infiltrates with fever, night sweats, cough. |
| 3 | Marked eosinophilia. |
| 4 | Histological evidence of extra-vascular eosinophils: Bone marrow biopsy showing prominent eosinophilia. |
| 5 | Mononeuropathy: Sixth cranial nerve palsy. |
| 6 | Pancreatitis presented with abdominal pain, and vomiting. The diagnosis of pancreatitis was based on high serum amylase and ultrasonographic findings of pancreatitis. |
| 7 | Acalculous cholecystitis and cholangitis. |
| 8 | Eye involvement: Keratitis. |
The association of Churg Strauss syndrome with cranial neuropathy is well recognized from Italy reported a case of Churg-Strauss syndrome characterized by the presence of multiple ophthalmological and neuroophthalmological lesions including mononeuritis of the fourth cranial nerve [1].

Vitali, et al. thought that the simultaneous occurrence of multiple ocular features in a patient with Churg-Strauss syndrome suggests that regional vasculitis may be the pathological mechanism underlying the multiple ophthalmological lesions in this disorder [1].

In 2005, Tsuda, et al. from Japan reported a 30-year-old man with Churg Strauss syndrome who had partial oculomotor nerve palsy with restrictions of elevation and adduction, and mydriasis was in the left eye [1].

Cranial magnetic resonance imaging showed an infarction lesion in the territory of the left superior median mesencephalic branch of the posterior cerebral artery. The case was the first case of oculomotor nerve palsy due to midbrain infarction associated with Churg-Strauss syndrome.

In 2008, Naitoh reported the fifth case of Churg-Strauss syndrome associated with oculomotor paralysis. Naitoh emphasized the rarity of cranial nerve paralysis in Churg-Strauss syndrome.

In 2012, Shimada, et al. reported the association of Churg Strauss syndrome with lower cranial neuropathy affecting the glossopharyngeal and vagal nerve palsy and presenting as dysarthria and dysphagia [1].

Ozaki, et al. (2012) from Japan reported a patient with Churg-Strauss syndrome who had eighth cranial nerve (Vestibulocochlear nerve) palsy which is extremely rare in Churg-Strauss syndrome [1].

In 2014, Byun, et al. from Korea described the occurrence of left facial and cochlear neuropathies which were detected in electrodiagnostic studies in a patient with Churg-Strauss syndrome [1].

In addition to the five of the six diagnostic features of Churg Strauss syndrome used by the American College of Rheumatology, the first case of the syndrome in Iraq also had gastrointestinal involvement including non-calculus cholecystitis and pancreatitis which are a well-recognized association in Churg Strauss syndrome.

Cojocaru M, et al. (2011) from Romania emphasized that the systemic autoimmune diseases including Churg Strauss syndrome can involve any part of the gastrointestinal tract, hepatobiliary system and pancreas [1].

The occurrence of non-calculus cholecystitis in Churg Strauss syndrome is well recognized. Imai, et al. from Japan emphasized that acute acalculous cholecystitis can be the initial sign of a systemic vasculitis, specifically Churg Strauss syndrome [1].

In 2003, Nishie, et al. from Japan described a patient with acute cholecystitis and duodenitis associated with Churg-Strauss syndrome [10].

The patient of Nishie, et al. was a 36-year-old male, who had fever, abdominal pain, a transient infiltration in the left lower lung, and marked hypereosinophilia of 17,000/ml. Ultrasonographic and gastroendoscopic examinations revealed acute cholecystitis and duodenitis, respectively [10].

The patient also developed distally dominant mononeuritis multiplex, especially in the upper limbs. Ye L, et al. from China emphasized the rare occurrence of cholecystitis in Churg Strauss syndrome, reported a case and reviewed eleven cases of Churg Strauss syndrome -associated cholecystitis reported in the literature [11].
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