RECURRENT URTICARIA, BLOOD EOSINOPHILIA AND EOSINOPHILIC ASCITES – A NEW VARIENT OF GLEICH'S SYNDROME

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INTRODUCTION

Hypereosinophilia can present a diagnostic problem if initial diagnostic procedures (medical history, physical examination and basic laboratory investigations) fail to reveal the cause. Such patients demand diagnostic intervention in order to rule out neoplastic, lymphoproliferative diseases, chronic inflammatory diseases and idiopathic hypereosinophilic syndrome. If these disorders are ruled out, consideration should be given to rare causes. The Gleich syndrome associates episodic urticaria/ angioedema, hypereosinophilia and elevation of immunoglobulin M [1]. It's a rare cause of nonallergic angioedema and is characterized by lack of organ involvement. It has a benign course and responds to systemic steroids. We describe a patient who presented with the clinical characteristics of this syndrome along with eosinophilic ascites, a feature not reported before with this syndrome.

CASE REPORT

A 30-year-old male presented with recurrent attacks of urticaria for the last two years. He had his first attack in March 2004 and was associated with abdominal pain and cramping. Examination revealed ascities which was tapped and analysis reveald an exudative picture with more than 80% cells being eosinophils. His blood showed a leukocytosis of 22.3 x 103/l with 64% eosinophilis. Haemoglobulin and platelets were within normal limits and no abnormal cells were seen in peripheral blood picture. Investigations, including parasitology, immunological screening for connective tissue disease, chest X-rays and blood chemistries were within normal limits. He did not respond to H1 and H2 histamine receptor blockers so he was started on parenteral steroids He rapidly responded to the treatment with resolution of ascities and disappearance of abdominal pain and resolution of urticaria. There was normalization of his leukocyte count and his absolute eosinophil count fell to 465/cmm. The steroids were tapered off and he was discharged from the hospital symptom free.

Two years latter in March 2006 he was again admitted with complaints of urticaria, and abdominal pain. Examination revealed ascites which was confirmed on ultrasound. His Blood analysis revealed a total white blood count of 10.3x109/l with 12% eosinophils. ESR was 17 mm fall at the end of first hour. Haemoglobulin and platelets were within normal limits and no abnormal cells were seen in peripheral blood picture. On upper GI Endoscopy moderately severe pangastritis was seen. Histopathologically gastric mucosa was congested. No Helicobacterium Pylori or eosinophils were seen. Bone marrow studies showed a hypercellular bone marrow with hyperplastic myelopoeisis showing normal maturation and increased eosinophils / eosinophil precursors. Grade 1 fibrosis was also observed. Cytogenetic analysis did not reveal structural or numerical chromosomal abnormality. Serum immunoglobulin estimation revealed IgA 3.6 g/l (0.8- 4.0 g/l), IgG 14.5 (5.3-16.5 g/l) and IgM 0.53 g/l (0.5-2.0 g/l). Serum LDH level was 1329 U/l (230-460 u/l). Investigations, including parasitology, immunology, chest X-ray, CT scans of the abdomen and pelvis, Upper GI barium studies, echocardiograms and blood

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chemistries were within normal limits. The patient was treated with parenteral and oral steroids. All of his symptoms resolved with normalization of blood counts. The patient was discharged from the hospital with instructions for regular follow up of eosinophil count and to report back if the symptoms recur.

DISCUSSION

Gleich was the first to describe the syndrome in a report of four cases (1 boy aged 4 years, 1 girl of 7 years, 1 boy aged 16 years, and 1 man aged 28 years) who had recurrent episodes of urticaria/angioedema, 10-18 % increase in body weight, fever (3 patients), hypereosinophilia, and high serum levels of IgM [2]. None of the patients developed organ involvement over ten years' surveillance, demonstrating the benign course of the condition. After this initial report, several isolated cases and case series has been described world wide from USA, Europe and Japan with variations in the clinical features and laboratory findings.. The nonepisodic angioedema, with normal levels of IgM was described in Japan [3]. Fever may be absent (4), our patient did not have any fever during the episodes and serum IgM were within normal limits. However IgA an IgG were near the upper limits of normal. The reason could be that the immunoglobulin estimation was done after the episode settled down. Serum LDH levels were raised in our patient as reported in earlier cases [3].

Peritoneum was involved in our patient manifesting as eosinophilic ascites. Eosinophilic ascites may occur as a manifestation of idiopathic hypereosinophilic syndrome [5], as a sole manifestation of idiopathic eosinophilia [6], in association with urticaria without blood eosinophilia [7], and as a manifestation of eosinophilic gastroenteritis with peripheral blood eosinophilia [8]. In our patient it formed a part of Gleich's syndrome. This association has not been reported before. We think that gastritis in our patient was not related as histopathology did not reveal eosinophils.

Bone marrow findings included hyperplastic myelopoeisis with increased eosinophils and eosinophil precursors along with Grade 1 fibrosis. Bone marrow findings have not been described before with Gliesh's syndrome. Although our findings are essentially benign and reactive, the potential for a more sinister outcome in terms of developing hypereosinophilic syndrome or leukemia remains to be ascertained. Cytogenetic studies were normal in our patient.

Our patient had two episodes and both occurred in the start of spring season where as the tendency of the attacks to occur in autumn has been reported before [3].

The etiology is unknown, although certain hypotheses have been proposed including the presence of circulating anti-endothelial cell antibodies suggesting a role in the increased capillary permeability or adhesion of eosinophils to the vascular wall [9]. The immunohistochemical studies permit to explain cytochemical disturbances responsible for the release of cytokines whose initial mechanism is unknown [1].

For the diagnosis of Gleich's syndrome extensive diagnostic evaluations are required to rule out allergic diseases, parasitic infestation, connective tissue disease, or neoplastic disorders.

Gleich's syndrome can be distinguished from primary hypereosinophilic syndrome (PHS) the criteria of which include eosinophilia > 1,500/mm for more than 6 months, and signs or symptoms of organ involvement. Hypereosinophilia persists in PHS, whereas it is transient in Gleich's syndrome. In contrast to primary hypereosinophilia syndrome, this syndrome normally has a good prognosis because there is no organ involvement.

Other conditions related to eosinophilia may be considered in the differential diagnosis. Eosinophilia-myalgia syndrome in patients exposed to L-tryptophan and its metabolites, first described in 1989 is characterized by several symptoms of varying

frequency (myalgia, fatigue, respiratory symptoms, paresthesia, muscle weakness) and by focal or generalized nonspecific cutaneous involvement (maculopapular or sclerodermoid eruptions, urticaria) which distinguish it clearly from Gleich's syndrome. Toxic oil syndrome can be distinguished by the symptoms, which are similar to eosinophilia-myalgia syndrome [10]. Capillary leak syndrome or Clarkson's disease [11] is a clinical condition characterized by episodes of hyper permeability of the capillaries responsible for diffuse edema, with weight gain, transient renal failure, and dysglobulinemia. In general there is no eosinophilia, which distinguishes it from Gleich's syndrome.

There is no specific treatment for Gleich's syndrome. Low-dose of systemic corticosteroids is the best treatment and is required for short duration only during the episodes.

CONCLUSION

Our patient presented clinical features compatible with a diagnosis of Gleich's syndrome. We reported a new association of eosinophilic ascites with Gliesh syndrome. We also reported the bone marrow changes and cytogenetic studies for the first time. Our case, combined with those reported in the literature, suggests that individual cases may differ from each other in clinical findings and laboratory parameters.

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