American Journal of Case Reports

ISSN 1941-5923
© Am J Case Rep, 2016; 17: 864-868
DOI: 10.12659/AJCR.899441

Received: 2016.05.06
Accepted: 2016.08.29
Published: 2016.11.18

Eosinophilic Granulomatosis with Polyangiitis Presenting with Skin Rashes, Eosinophilic Cholecystitis, and Retinal Vasculitis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACE Mingbing Zeng*
BDF Xialin Liu*
ACG Yizhi Liu

Zhongshang Ophthalmic Center, Sun Yat-sen University, Guangzhou, Guangdong, P.R. China

* Mingbing Zeng and Xialin Liu contributed equally to this paper

Corresponding Authors: Mingbing Zeng, e-mail: zengmingbing@126.com, Yizhi Liu e-mail: yizhi_liu@aliyun.com
Conflict of interest: None declared

Source of suport: Supported in part by an unrestricted grant from the Science and Technology Planning Project of Guangdong Province (2013B021800125) and by the Natural Science Fund of Guangdong Province, China (2014A030313013)

Patient: Female, 20

Final Diagnosis: Eosinophilic granulomatosis with polyangiitis

Symptoms: Fever • skin rashes • eosinophilic cholecystitis • retinal vasculitis

Medication: —

Clinical Procedure: —

Specialty: Ophthalmology

Objective: Rare co-existance of disease or pathology

Background: Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome (CSS), is a rare vasculitis of unknown etiology. Most of the patients have a long history of asthma and then develop autoimmune inflammation of small and medium-sized blood vessels, with consequent reduction of blood flow to various organs and tissues. EGPA can cause disorders in multiple systems; the most seriously affected organs are the retina, kidney, brain, cardiovascular system, and skin.

Case Report: The patient was hospitalized for high fever and skin rashes and then developed right upper abdominal pain, decreased visual acuity, coma, and convulsions. Laboratory investigations showed marked eosinophilia (9412/mm^3). Following cholecystectomy, histopathological examination revealed a marked inflammatory cell infiltrate composed mainly of eosinophils. Retinal vasculitis and medium and peripheral vascular closure were confirmed by fundus fluorescence angiography (FFA). The coma and convulsions were controlled successfully by high-dose methylprednisolone. After gradual tapering of the methylprednisolone, the patient's blood count recovered to a normal level, and the other systematic disorders disappeared; however, she was left with irreversible blindness.

Conclusions: EGPA can cause eosinophilic cholecystitis, retinal vasculitis, and neuropathy in the short term and calls for effective treatments in order to avoid binocular blindness.

MeSH Keywords: Cholecystitis • Microscopic Polyangiitis • Retinal Vasculitis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/899441

Background

Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome (CSS), is a rare vasculitis of unknown etiology [1]. Most of the patients have a long history of asthma and then develop autoimmune inflammation of small and medium-sized blood vessels, with consequent reduction of blood flow to various organs and tissues. The complications of EGPA are often caused by dysfunction of the organs that are rich with small and medium vessels, for example, heart, brain, kidney, and retina. This patient did not have a long history of asthma but had acute fever, skin rash, and a positive *Spirometra mansoni* serologic test. Cholecystitis, retinal vasculitis, and central nervous system (CNS) neuropathy have seldom appeared successively over a short duration, as they did in this case.

Case Report

A 20-year-old woman presented with scattered, pinky, patchy skin rashes for three weeks and fever for one week. She did not have a history of asthma, allergic rhinitis, and other upper respiratory tract disease. She denied smoking or use of illegal substances. No other vascular risk factors were noted in the past medical history.

Blood tests showed 27,200 leukocytes/mm^3 (normal: 4000–10,000/mm^3), 16,150 neutrophils/mm^3 (1500–7000/mm^3) and 9412 eosinophils/mm^3 (0–600/mm^3), which were multifold increases; while the lymphocytes and platelets were maintained at normal levels. The serum total IgE was 920,000 U/L (277,000–397,000 U/L), which also was a remarkable increase.

The serologic test was positive for *Spirometra mansoni* IgM and negative for cardiotropic viruses, *Aspergillus*, *Toxoplasma*, *Chlamydia psittaci,* and *Mycoplasma pneumonia*. Because *Spirometra mansoni* infection was suspected, praziquantel 60~70 mg/kg was used for three days, combined with use of dexamethasone 10 mg/day. The patient's fever decreased to a normal level, and the skin lesions disappeared gradually.

Eight days after admission, the patient complained of anorexia and right-upper-quadrant pain, and showed tenderness and Murphy sign. The abdominal computed tomographic scan indicated a thickened gallbladder wall (Figure 1A). Laparoscopic cholecystectomy was performed, and the pathological biopsy specimen revealed a marked infiltrate of inflammatory cells composed mainly of eosinophilia (Figure 1B).

Three days after cholecystectomy, the patient's biocular visual acuity dropped sharply from 20/20 to Count Fingers. The color fundus photographs showed retinal opacification and intraretinal hemorrhages in the macular and peripapillary regions (Figure 2A, 2C). The fundus fluorescence angiography (FFA) showed vasculitis-type leakage and nonperfusion and blocking defect from the posterior pole, and both optic discs stained with fluorescein (Figure 2B, 2D).

Seven days after cholecystectomy, the patient developed coma, convulsions, increased muscle tenderness, and high fever. The cranial MRI did not show any lesions, and cerebrospinal fluid

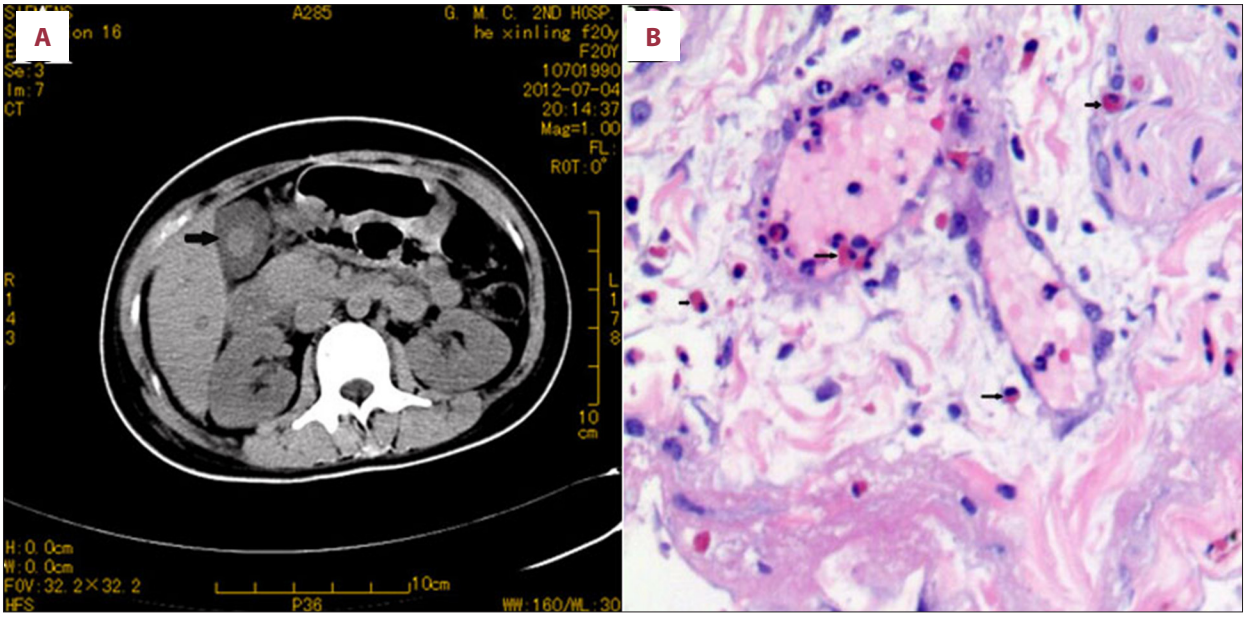

Figure 1. The computed tomographic scan of the abdomen (**A**), showing thickened gallbladder wall (arrow). Gallbladder biopsy specimen (**B**), showing eosinophilic vasculitis involving an arteriole as well as extravascular eosinophils (arrow, HE ×200).

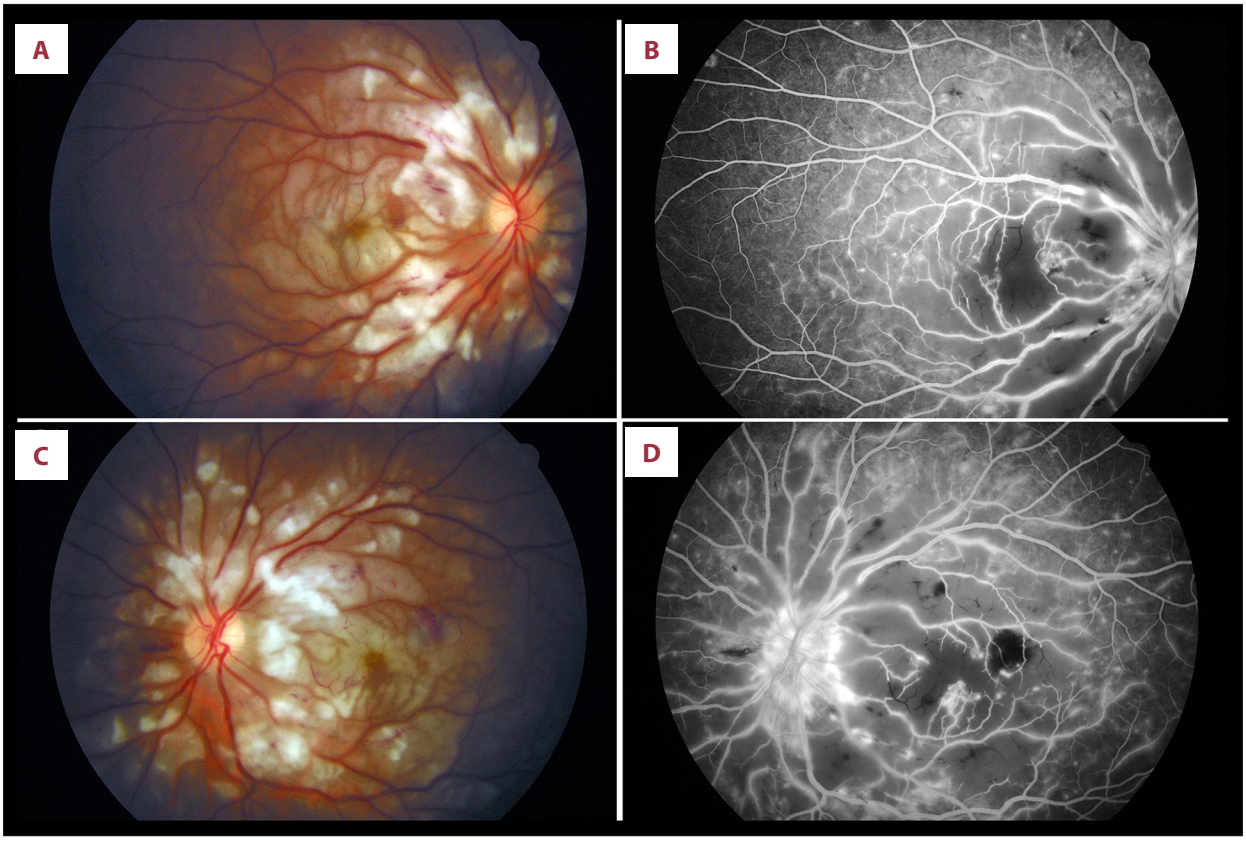

Figure 2. The color fundus photographs of the right (**A**) and left (**C**) eyes, showing retinal opacification and intraretinal hemorrhages in the macular and peripapillary regions. The fluorescein angiogram (recirculation phase) of the right (**B**) and left (**D**) eyes, showing vasculitis-type leakage and nonperfusion and blocking defect from the posterior pole, and both optic discs stained with fluorescein.

(CSF) did not show any positive finding. Lumbar puncture and CSF test showed that the CSF pressure, the biochemical quota, and the enzyme and protein levels were at normal levels. No bacteria and fungi were found on bacterial and fungal culture. The tonic-clonic seizures, with limbs twitching, trismus, and without focal sign, recurred several times a day and were partially controlled by phenobarbital sodium each time. After 2 days, 6-methylprednisolone 1 g daily was used to treat vasculitis, mannitol 50 g twice a day was used to control cerebral edema, and gamma globulin 1 g daily was used for endogenous allergic pathogenic factors for 3 consecutive days; the patient recovered consciousness and the convulsions disappeared.

After intravenous high-dose methylprednisolone administration, the patient received oral prednisolone (from 1 mg/kg/day), which was tapered gradually. After 30 days, the laboratory tests showed that the blood cell count had recovered to normal range. The patient's visual acuity decreased to Light Perception. The color fundus photographs showed retinal and choroidal atrophy and most of the small retinal vessels closing (Figure 3A, 3C). The FFA showed extensive nonperfusion and blocking defect, with only the main retinal artery and vein perfusing (Figure 3B, 3D).

Discussion

Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome (CSS), is characterized by necrotizing eosinophilic vasculitis of medium- to small-sized blood vessels. The American College of Rheumatology in 1990 outlined six criteria for CSS, including moderate to severe asthma bronchiale, eosinophilia (more than 10% in the peripheral blood), pulmonary infiltrates, paranasal sinus abnormality, neuropathy, and eosinophilic vasculitis [2]. In 1994, these criteria were reevaluated, and it was concluded that four of the six criteria sufficed to make a diagnosis of the syndrome [3].

In this case, the diagnosis of EGPA was established based on the hypereosinophilia, retinal vasculitis, craniocerebral lesion, and extravascular eosinophils on biopsy of a specimen after cholecystectomy. To our knowledge, there are no reports of EGPA caused by *Spirometra mansoni*. The positive serologic

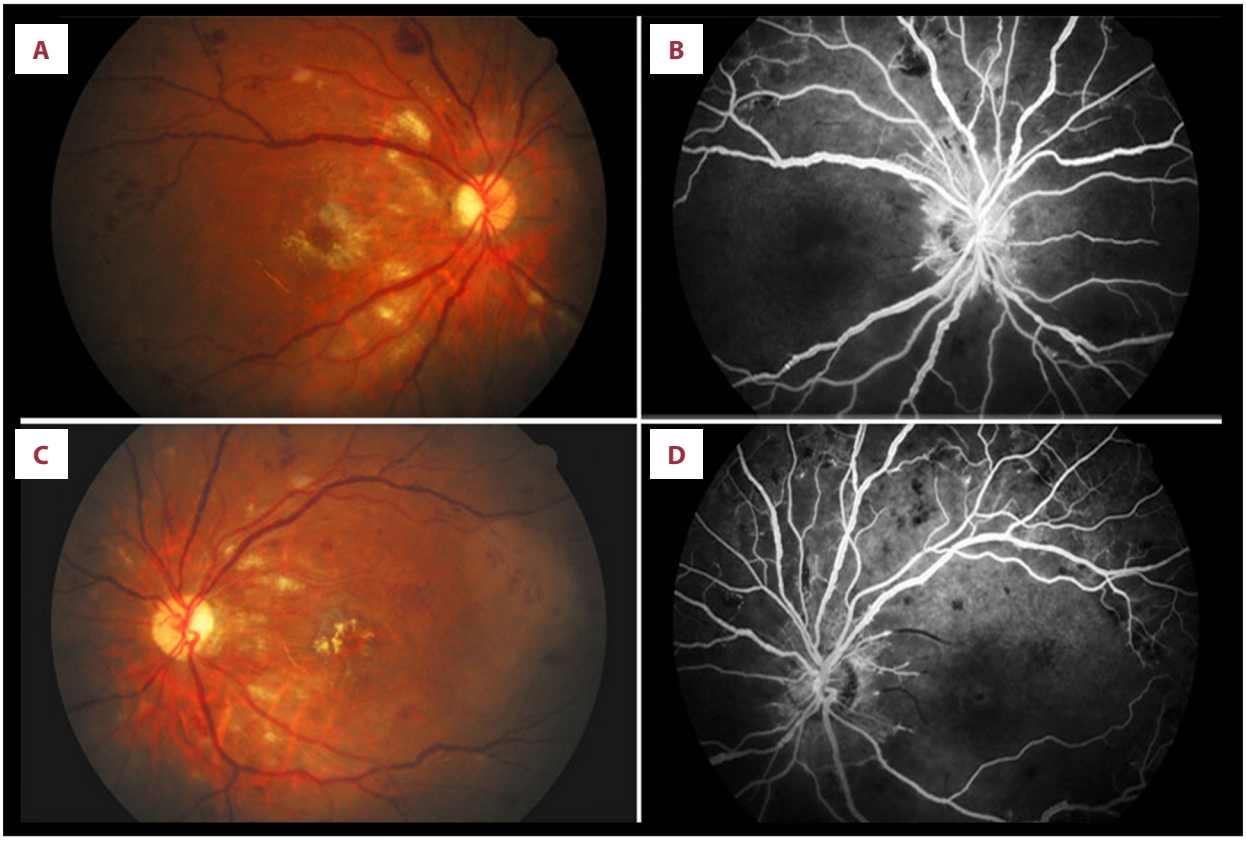

Figure 3. The color fundus photographs of the right (**A**) and left (**C**) eyes, showing retinal and choroidal atrophy and most of the small retinal vessels closed. The fluorescein angiogram (recirculation phase) of the right (**B**) and left (**D**) eyes, showing extensive nonperfusion and blocking defect, and only the main retinal arteries and veins perfusing.

test and effective diagnostic praziquantel treatment showed that positive reactions to parasite antigen were related to the cause of the vasculitis, as in the report by Dr. Kobayashi and colleagues [4]. This diagnosis of EGPA is mostly overlooked because the early symptoms such as purpura, fever, and eosinophilia can also show in parasite infections. This case indicates that the eosinophilia is the main risk factor for EGPA with or without the history of asthma, as Chen et al. indicated that asthma is not the requisite condition for diagnosis of EGPA [5]. Although this case cannot be confirmed as being caused by *Spirometra mansoni* infection without larva isolation, and the *Spirometra mansoni* IgG test also may be more confirmable, it suggests a possibility that the patient's EGPA was caused by parasite infection.

Ocular involvement in EGPA, including ocularitis, corneal ulcerations, retinal infarctions, amaurosis fugax, and ischemic optic neuropathy, is infrequent. Blindness is a rare finding and has been described previously in several cases [6]. Though retinal biopsy was not done, the early retinal vasculitis and the following retinal infarctions were verified by FFA and were consistent with EGPA in this case.

EGPA can cause gastrointestinal pancreatitis, cholecystitis, colitis, and mucosal ulceration, in which the GI manifestations are characterized by abdominal pain, diarrhea, and bleeding [7]. As in this case, the eosinophilic cholecystitis and its diagnosis were confirmed by biopsy after cholecystectomy.

Neurological involvement is extremely common, usually manifesting as peripheral neuropathy [8]. Conversely, the CNS is seldom affected by EGPA, and cerebral ischemic infarctions are the most common reported events [9]. Herein, we report the case of a patient affected by EGPA who presented with convulsions, coma, and CNS symptoms that could not be explained by fever or other imaging-verified CNS lesions. The convulsions and other CNS symptoms could not be controlled by phenobarbital; instead, they were controlled by large doses of methylprednisolone, which is in accordance with the manifestations of EGPA.

The pathophysiology of this syndrome can be divided into three stages: first, a prodromal stage characterized by asthma and allergic manifestations; second, eosinophilic infiltration into tissues, predominantly the lungs and myocardium; and finally, a systemic stage, associated with the development

of necrotizing vasculitis [10]. In this case, involvement of the necrotizing retinal vasculitis and cholecystitis can be described as the third stage of the disease. The disease process from the first stage to the third stage can range from a few weeks to several decades. The patients with a short duration can easily be misdiagnosed and quickly progress into the third stage, causing important organs, such as eyes, heart, brain, or kidneys, irreversible damage.

Most cases can be effectively controlled or cured completely by 0.5 to 1.5 mg/kg/d of methylprednisolone; cases with multiple organ damage involving vasculitis need higher doses. The level of eosinophils and erythrocyte sedimentation can act as indicators of the effectiveness of treatment. The 5-year survival rate has increased to more than 70% because of the use of systemic steroids for vasculitis [11].

In order to prevent irreversible damage of important organs, in addition to high doses of hormone, other effective therapies such as plasma exchange are worth trying to bring inflammation under effective control in the short term [12]. More early or new effective treatments should be applied to prevent permanent irreversible binocular blindness, which occurred in this case.

Conclusions

Eosinophilic granulomatosis with polyangiitis can cause multisystem disorders in a short duration of time. It calls for effective treatments to avoid biocular irreversible blindness caused by retinal vasculitis.

Acknowledgements

We would like to express our very great appreciation to professors Xinwu Zhong and Jianqiang Xing for their valuable and constructive suggestions during the development of this report.

References:

1. Churg J, Strauss L: Allergic granulomatosis, allergic angiitis, and periarteritis nodosa. Am J Pathol, 1951; 27(2): 277–301
2. Masi AT, Hunder GG, Lie JT et al: The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum, 1990; 33(8): 1094–100
3. Jennette JC, Falk RJ, Andrassy K et al: Nomenclature of systemic vasculitis. Proposal of an international consensus conference. Arthritis Rheum, 1994; 37(2): 187–92
4. Kobayashi A, Maeda K, Fu A et al: Allergic granulomatous angiitis in a patient with positive reactions on serological tests for parasite antigens]. Nihon Kyobu Shikkan Gakkai Zasshi, 1996; 34(10): 1130–35 [in Japanese]
5. Chen KR, Ohata Y, Sakurai M et al: Churg-Strauss syndrome: Report of a case without preexisting asthma. J Dermatol, 1992; 19(1): 40–47
6. Sutcliffe N, Morris V, Gomperts B et al: Relationship between the development of blindness in Churg-Strauss Syndriom and anti-myeloperoxidase antibodies. Br J Rheumatol, 1997; 36(2): 273–75
7. Sánchez R, Aparicio JR, Baeza T, Calero Y: Capsule endoscopy diagnosis of intestinal involvement in a patient with Churg-Strauss syndrome. Gastrointest Endosc, 2006; 63(7): 1082–84
8. Koike H, Akiyama K, Saito T et al: Intravenous immunoglobulin for chronic residual peripheral neuropathy in eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome): A multicenter, double-blind trial. J Neurol, 2015; 262(3): 752–59
9. Nakamura M, Yabe I, Yaguchi H et al: Clinical characterization and successful treatment of 6 patients with Churg-Strauss syndrome-associated neuropathy. Clin Neurol Neurosurg, 2009; 111(8): 683–87
10. Pagnoux C, Guilpain P, Guillevin L: Churg-Strauss syndrome. Curr Opin Rheumatol, 2007; 19(1): 25–32
11. Samson M, Puéchal X, Devilliers H et al: Long-term outcomes of 118 patients with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) enrolled in two prospective trials. J Autoimmun, 2013; 43(6): 60–69
12. Fregoni V, Perseghin P, Epis R et al: Churg-Strauss syndrome with peripheral polyneuropathy refractory to steroideal and immunosuppressive therapy successfully treated with plasma exchange. Recenti Prog Med, 1995; 86(9): 353–54