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Eosinophilic Granulomatosis with Polyangiitis and Spinal Subdural Hematoma: A Case-Based Review of the Literature

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Abstract

Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as a Churg-Strauss syndrome, is a rare systemic vasculitis. Central nervous system (CNS) involvement is described in rare cases. Acute spinal subdural hematoma (SSDH) is an uncommon condition presented with acute severe, radiating pain in the back area, and symptoms of spinal cord compression. The association of these two rare entities has been rarely reported so far.

Case Presentation: A 32-year-old female known case of limited scleroderma for 12 years and EGPA for 6 years with presentation of eosinophilia, high P-ANCA, and skin vasculitis, was admitted to the rheumatology ward of Faghihi hospital related to Shiraz University of Medical Science in Iran (May 2016) due to new necrotizing vasculitis lesions on her hands, dyspnea, bilateral crackles, and eosinophilia. During this hospital admission, while receiving methylprednisolone, low dose aspirin, and prophylactic heparin, she developed severe upper back pain and neck rigidity and in her imaging studies, thoracic spinal subdural hematoma was seen.

Conclusions: This article describes a case of EPGA presented with a non-traumatic acute subdural thoracic hematoma in addition to her classic symptoms along with limited scleroderma. This suggests that non-traumatic spontaneous acute spinal subdural hematomas should be considered in manifestations of EPGA and early recognition could be helpful for appropriate management.

Keywords: Eosinophilic Granulomatosis with Polyangiitis, Spine, Subdural Hematoma

1. Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a rare systemic small vessel vasculitis (1). Asthma, eosinophilia, chronic paranasal sinusitis, nasal polyposis, non-fixed pulmonary infiltrates, and myocarditis are the most common manifestations of EGPA (2). Neurologic involvement mostly involving the peripheral nervous system (PNS) is reported in 59% to 86% of patients, mainly in the form of peripheral neuropathy (3). On the contrary, central nervous system (CNS) involvement is described in less than 10% of cases (3). The most common CNS manifestations are cerebral infarction, diffuse encephalopathy, and rare cases of cerebral hemorrhages (4). Only 4 cases of spinal subarachnoid hemorrhage have been reported so far in association with this disease (5-8).

Acute non-traumatic spontaneous spinal subdural hematoma (SSDH) is an exceedingly uncommon condition. In some reports of subdural hematoma, blood dyscrasias and arteriovenous malformation, have been the predisposing factors (9, 10). Also, anticoagulant therapy (therapeutic doses of warfarin, dabigatran, etc.) and diseases with bleeding tendency, have been reported as risk factors for rapid spinal cord or cauda equina compression due to SSDH (11). Kreppel et al. identified 613 cases during 170 years until year 2003 (12). The classic presentation of SSDH is an acute, severe, radiating pain in the back area and then symptoms of spinal cord compression, sensorimotor deficits, and sphincter disturbance as typical clinical manifestations, which develop minutes to days later (12, 13). Physical findings could be different based on the level of spinal lesion and could be without motor or sensory loss. Spontaneous spinal subdural hematoma is very rare usually with no previous cause (14). This report describes a patient with EGPA and limited scleroderma on low dose aspirin and a prophylactic dose of low molecular weight heparin presented with non-traumatic spontaneous SSDH

that has been very rare till now.

2. Case Presentation

The case was a 32-year-old female, known case of limited systemic sclerosis lasting for 12 years with presentation of sclerodactyly, Raynaud's phenomenon, telangiectasia, active scleroderma pattern of capillaroscopy and mild bilateral lung fibrosis and ground glass radiological features in both lower lungs. After 6 years, EGPA was diagnosed, presented with new onset of asthma, wheezing, eosinophilia (15%), positive p-ANCA, Esr:74, and vasculitic skin lesions with biopsy-proven diagnosis of eosinophilic vasculitis compatible with EGPA, and the patient was admitted to the hospital due to recent necrotizing vasculitis lesions on her hands and increasing dyspnea and lung infiltration. She was on prednisolone 5 mg daily and ongoing cyclophosphamide (CTX) since 1 year ago due to her interstitial lung disease that was detected on her high resolution CT scan (Figure 1A); she received 6 doses of monthly CTX and then every 3 months. The last dose was 3 months ago. Another drug history of the patient was Aspirin 80 mg per day, prednisolone 5 mg per day, amlodipine 2.5 mg per day, and losartan 25 mg per day.

In the physical exam, she had normal vital signs apart from bilateral crackles in the lower 1/3 of lungs and multiple palpable purpuric lesions on her hands, one of which was ulcerated with the necrotizing pattern (Figure 1C). Neurologic exam was completely normal on arrival. She did not have neuropathy in her nerve study and no signs of sinusitis.

Chemistry lab tests including blood sugar, liver function, kidney function, urine analysis, and 24-hour urine protein were in the normal range.

Other clinical and laboratory tests are listed in Table 1.

Skin biopsy of purpuric lesions of the extremities revealed complete epidermal and superficial dermal necrosis with acute inflammatory infiltration in the superficial dermis as well as fibrinoid necrosis of the blood vessels. There was also eosinophilic infiltration in the mid dermis.

The patient's plan was to receive an increasing dose of steroid and rituximab to be effective for her vasculitis and interstitial lung disease. After admission to the rheumatology ward of Faghihi hospital (which is a general hospital related to Shiraz University of Medical Science in Iran with multiple special wards including specialized referral rheumatology ward that our patient was admitted in May 2016), prednisolone was increased to 10 mg per day along with omeprazole 20 mg per day for her reflux complaints, and due to Raynaud's disease amlodipine was increased to 5 mg per day. For her vasculitic skin lesions, 50 mg azathioprine was started twice daily. Since her admission, subcutaneous 40 mg enoxaparin sodium per day was added to her medications as a prophylactic dose. Also, 2 doses of 250 mg IV methyl prednisolone were used for her. On the 6th day of her admission, she developed severe neck rigidity, back pain, and headache, thus enoxaparin sodium and aspirin were discontinued and a cervicothoracic MRI was performed, which revealed linear hypersignality in the

Table 1. Main Clinical and Laboratory Data

Variables	On Arrival	Hematoma	Discharge Day
Physical examination			
weight	63 kg		
Height	159 cm		
Temperature	37.2		
Pulse rate	78/min		
Respiratory rate	16/min		
Blood pressure	110/75		
Lung exam	Bilateral lower 1/2 of lung crackles		
Extremities	Sclerodactyly of both hands and multiple small round protruded purplish necrotizing lesions on both hands		
Capillaroscopy	Late scleroderma pattern		
WBC, per mm^3	12560	14900	13050
Eosinophil, per mm^3	4232	2443	0
ANA, u/mL	6.3 (0 - 10)		
Anti ds DNA, u/mL	1.4 (0 - 18)		
C3, g/L	1.2 (0.89 - 1.87)		
C4, g/L	0.26 (0.16 - 0.38)		
Anti-myeloperoxidase, u/mL	2.2 (< 3.1)		
Anti-proteinase 3, u/mL	0.1 (< 0.4)		
Anti jo1, unit	2 (< 12)		
Anti scl-70, unit	2.4 (< 12)		
Anti RO, unit	2.7 (< 12)		
Anti LA, unit	2.5 (< 12)		
Anti SMITH, unit	2.8 (< 12)		
Anti U1RNP, unit	2.2 (< 12)		
Anti B2 Glycoprotein(IgM), U/mL	2.5 (< 12)		
Anti B2 Glycoprotein(IgG), U/mL	5.9 (< 12)		
RF, IU/mL	Negative		
ESR, mm/hour	37 (0 - 20)		
CRP, mg/L	12 (< 6)		
PT(INR), s		11.5 (1.1)	
PTT, s		31	

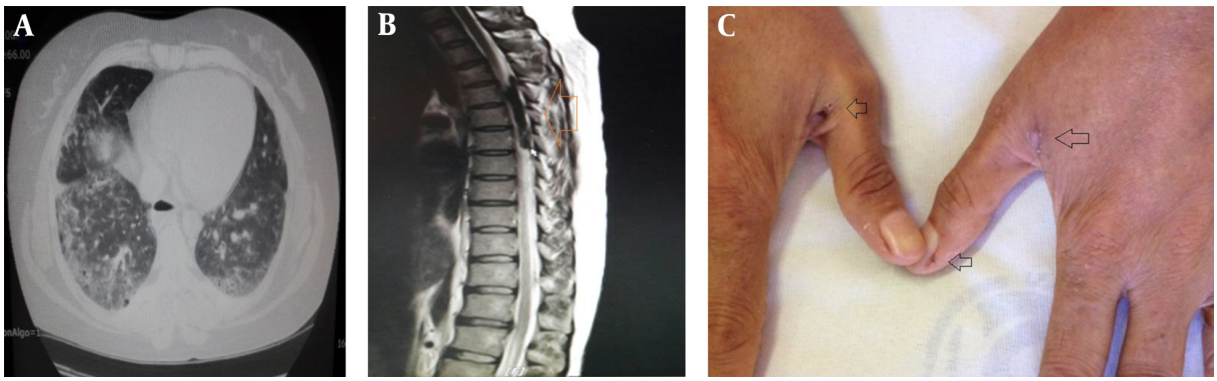

Figure 1. A, Chest high resolution computerized tomography scan showing bilateral lung infiltration and ground glass appearance; B, Thoracic MRI showing upper thoracic subdural hematoma; C, both hands' small necrotizing palpable vasculitic lesions.

central part of the thoracic cord at the level of T3-T4 to T6-T7. There was a sign of associated extramedullary intradural hematoma overlying the right side of the thoracic cord at this level, causing minimal pressure over the thoracic cord. It was about 6.5 cm in length. The diagnosis was a thoracic spinal subdural hematoma (Figure 1B). Due to a headache and neck rigidity, brain MRI was done to rule out intracranial hemorrhage (ICH); it was normal and there was no evidence of mass, hemorrhage or acute ischemic infarction.

A neurosurgical consultation was done for her and since the patient had no neurological symptoms, besides neck rigidity, no surgical therapy was recommended.

After 7 days, when her headache and neck rigidity decreased, 1 gram Rituximab was prescribed and she was discharged with follow-up of a neurosurgeon and rheumatologist. During the follow-up after 3 weeks, her symptoms were completely relieved.

3. Discussion

Eosinophilic granulomatosis with polyangiitis is an eosinophil-rich necrotizing vasculitis of small-to-medium size blood vessels; diagnostic criteria require the presence of any four or more of the following, asthma, eosinophilia greater than 10%, neuropathy, pulmonary infiltrates, paranasal sinus abnormality, or extravascular eosinophils (2). The presentation of non-traumatic acute spinal subdural hematoma is rare and it typically presents with sharp, intense back pain in the region of the hemorrhage (15). Most patients usually present myelopathy, including motor, sensory and autonomic dysfunctions after back pain (12). It is usually related to anticoagulation (in therapeutic doses), blood dyscrasia, spinal arteriovenous malformations, or is idiopathic (10). There has been no association between low-dose aspirin or prophylactic dose of heparin and subdural hematoma except for cases related to post-spinal anesthesia (16, 17). The current case had no history of back trauma.

In scleroderma, there is a case report for the association of renal crisis and subdural hematoma and one case of overlap syndrome and at the same time idiopathic thrombocytopenic purpura (ITP) with very low platelet, which developed spinal hematoma yet with no other associations (18, 19). Although in our case her limited scleroderma manifestations were very mild, her eosinophilic and necrotizing vasculitis was much more prominent.

In reviewing the literature, there were 4 cases of EGPA with the manifestation of subdural hematoma (5-8) (Table 2). All of the patients on presentation had active disease and were on a high dose of steroid treatment.

Central nervous system involvement is very rare in patients with EGPA yet can be presented as ataxia, paraplegia, optic neuritis, hemiplegia-hemiparesis, spasmodic quadriplegia, seizures, meningitis, cerebral infarction, organic psycho-syndrome, other mental changes, stroke, temporal arteritis, leptomeningeal dissemination, memory deficits, and dysarthria (20).

There are case reports of associations of this presentation with lupus. In a previous study on nine reported cases, hematomas were observed in the thoracic spine in 3 cases and in the cervical spine in 4 cases. Six of the 9 reported cases had a high level of disease activity of their systemic lupus. Vasculitis at the bleeding site was pathologically documented in 3 of the 6 active cases. However, there was one case of lupus without disease activity and in the last presented case, hematoma was presented on the ninth day of admission after receiving 3 methylprednisolone pulses and 15000 units of heparin therapy (21). Four cases of granulomatosis with polyangiitis (GPA) were presented with subdural hematoma of the spine as a vasculitis activity pattern of the disease, which mostly responded to cyclophos-

Table 2. Characteristic Findings of Eosinophilic Granulomatosis with Polyangiitis Cases with Subdural Hemorrhage

Ref/ Published Year	Age	Sex	Medications Before SSDH	Clinical Manifestation	ANCA Titer	Eosinophil Count	Treatment	Follow-Up
1/1985	39	Female	Steroids and cyclophosphamide	Severe back pain, paralysis of the left leg from the hip downwards; also weakness of the right leg; vibration sense was totally absent below T12	Not available	Not available	80 mg prednisolone and cyclophosphamide	Was stable for 4 years on a low dose of prednisolone and cyclophosphamide then died with acute subarachnoid hemorrhage
2/2012	40	Female	High dose steroid	Urinary incontinence and an inability to move her legs, complete paraplegia	Low titer p-ANCA	15000	1 g of methylprednisolone intravenously for Three days	Emergency decompression laminectomy was done. After six months, she still had the paraplegia and urinary retention
3/2013	51	Female	No treatment before	Bilateral hand numbness decreased grip strength and hyperreflexia in her lower extremities	Positive (anti-MPO 40 U/mL (normal range 020 U/mL))	Not available	Prednisolone and cyclophosphamide	Recovered well
4/2014	31	Female	Methylprednisolon 1 mg/kg/Day i.v.	A headache and neck stiffness	Positive p-ANCA	13230	Intravenous steroid (methylprednisolone 1 mg/kg/day i.v. For 6 days) and after 5 months rituximab	Recovered well
5/2016 (our case)	32	Female	Aspirin 80, enoxaparin 40/day, prednisolone 10 mg/day	Severe neck rigidity, upper thoracic pain	Negative	4232	Azathioprine, Rituximab, methylprednisolone 500	Recovered well

phamide and a high dose of prednisolone (22).

The patient presented symptoms on the 6th day of admission after receiving two doses of 250 mg methylprednisolone and 5 days of therapy with azathioprine and at the same time aspirin low dose (80 mg) and enoxaparin prophylactic dose 40 mg/day with normal coagulation profiles, and still had eosinophilia, dyspnea, and necrotizing skin lesions on both hands. After this presentation, aspirin and enoxaparin were discontinued and she received 1 gram rituximab and was discharged. On her follow-up, 2 weeks later, her symptoms decreased significantly.

This report presents a patient with EPGA and limited scleroderma manifestations, who was admitted with manifestations of necrotizing vasculitis and eosinophilia along with acute subdural hematoma. Presentation of these two rare manifestations together with 3 previously reported cases before and multiple reports of associations with other vasculitic diseases may indicate the importance of this manifestation as a vasculitic manifestation in EPGA. However, other background causes, such as a low dose of aspirin and a low dose of heparin along with disease activity, should be considered.

3.1. Conclusion

This article describes a case of EPGA, who presented a non-traumatic acute subdural thoracic hematoma in addition to her classic symptoms along with limited scleroderma. This suggests that non-traumatic acute spinal subdural hematomas should be considered in manifestations of EPGA and early recognition could be helpful for appropriate management.

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Footnote

Conflict of Interest: There was no conflict of interest in writing this article.

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