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Case Report

Hepatic Involvement in Eosinophilic Granulomatosis with Polyangiitis

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Abstract

We presented a case report of Eosinophilic Granulomatosis with Polyangiitis (EGPA) with hepatic involvement which presented itself as multiple nodules in the liver. This confirmed Hprevious literature results, which have reported hepatic involvement in EGPA. The results of the study showed a 45-year-old female with asthma, presented with polyarthralgia, hypostasis in both hands and skin lesions on the body. Lab tests revealed elevated Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP). The total Leukocyte count was 11900 (/ul) with 22% Eosinophil. Computed Tomography (CT) scan of both lungs and liver showed multiple irregular nodules. In the biopsy of the skin lesions, Eosinophilic Vasculitis was reported. Electromyography and Nerve Conduction Velocity (EMG-NCV) was compatible to C8-T11 radiculopathy and Axonal Sensory Motor Polyneuropathy. According to the tests and biopsies the patient was diagnosed with EGPA. Although EGPA is characterized by asthma, hypereosinophilia and vasculitis, it can be presented with atypical manifestations as well.

Keywords: Churg-Strauss Syndrome; Eosinophilic Granulomatosis with Polyangiitis; Hepatic Involvement; Multiple Nodules

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Introduction

Eosinophilic Granulomatosis with Polyangiitis (EGPA), also known as Churg-Strauss syndrome (CSS), was originally identified in 1951 by two pathologists, Churg and Strauss (1). EGPA is a rare systemic syndrome that is characterized by diffused granulomatous vasculitis accompanied by severe asthma (2). The estimated incidence is 2 to 5 new cases per 1 million adults per year and varies according to the population studied. This condition mainly affects patients in the third to fifth decades of a lifespan and clearly shows no gender or race predominance (3, 4). The diagnostic criteria for EGPA are asthma, a differential white blood cell count showing eosinophilia of more than 10%, multiple mononeuropathy or polyneuropathy, biopsy indicating vascular eosinophilic infiltrate, lungs and paranasal sinuses infiltrates (5).

EGPA is a clinical syndrome and most frequently involves the respiratory system and the peripheral nerves and skin, but there is still a possibility of affecting other organs. The gastrointestinal tract, kidney and heart must be screened for vasculitis involvements, due to their poorer prognosis. Still, it should be taken into consideration that cases of EGPA with hepatic involvement have been rarely reported (6, 7).

In literature review, since 1951, around 6 cases of Eosinophilic Granulomatosis with Polyangiitis with hepatic involvement have been reported. However, there has been no report of patients with multiple nodules in the lungs and liver **(Table 1)**. In this study, the researchers reported a patient with Eosinophilic Granulomatosis, Polyangiitis, hepatic involvement, and furthermore, presenting for the first time generalized vesicular lesions and hypostasis in both hands.

Case presentation

A 45-year-old female with a fever and vesicular skin lesions on the face, neck and both wrists was visited by a primary care physician. She complained of polyarthralgia and general migratory pain in the bones. The initial diagnosis was Herpes Zoster and treatment with Acyclovir was initiated. After she received the related medication, lesions were not fully cured and bone pain persisted.

The patient's symptoms exacerbated, therefore, she revisited the emergency room multiple times and seen by several physicians, however, no improvement in her symptoms was seen. Four months after the initial presentations, due to the progression of the symptoms, she was admitted to our hospital seeking medical help. The patient had severe paresthesia in the hands where she was further investigated for treatment. She was presented with polyarthralgia, a fever, hypostasis in both hands, and skin lesions on the body that appeared as painful, itchy blisters that were negative in microbiological tests. She claimed that she had lost more than 15 kilograms during the last 4 months (**Figure 1 and 2**)

Vital signs including body temperature (37º c), respiratory rate (18 times per minute) and blood pressure (120/80 mmHg) were within the normal range. Upon the physical examination at the time of admission, the findings of cardiac auscultation were normal, but late expiratory wheezing in the right side and diffuse crackles were heard in the lung fields. The head and neck examination showed the conjunctiva to be pale. The musculoskeletal findings reported the Tinel's sign to be positive and the atrophy of thenar muscles was seen (**Figure 3**). No arthritis was reported. In addition, upon examination, pinch strength was not normal. No peripheral edema, organomegaly or gastrointestinal symptoms were observed. No pathological lymph nodes were found except for small nodular palpable lesions in both breasts.

The patient had a past medical history of asthma which was controlled by a Seroflo inhaler (Salmeterol-Combination 250/25) in the past four years. Lab tests revealed an elevated Erythrocyte Sedimentation Rate (ESR) and C Reactive Protein (CRP). Serum tests were negative for anti-nuclear antibody, Anti Double Stranded DNA (anti-dsDNA), rheumatoid factor, anti-cyclic citrullinated peptide and for other viral markers such as Hepatitis B Surface Antigen (HBsAg), Hepatitis C Virus Antibody (HCVAb), Human Immunodeficiency Virus Antibody (HIVAb). Lactate dehydrogenase level was reported normal and tests for Wright, Coombs and 2-mercaptoethanol (2ME) were negative (**Table 2**).

The patient was referred to a rheumatologist for further evaluation. In the complete blood

Table 1. Characteristics of reported patients with Eosinophilic Granulomatosis with Polyangiitis and hepatic complications

No.	First author	Year of publish	Age	Sex	Eosinophilia	Thoracic imaging finding	Histology	ANCA testing	CRP testing	Pulmonary manifestations	Cardiac manifestations	Cutaneous manifestations	Gastrointestinal manifestations	Renal manifestations	Neurological manifestations	Hepatic complications
1	Yuichiro Otani (6)	2003	59	Male	56% (12,936/ul)	Normal	Skin: Organizer thrombi and damaged vessel with proliferating myofibroblastic cells	Negative	5.89 mg/dl	Asthma	Normal	Necrosis of fingers and toes- Crusted ulcers on lower legs- pale digits	Normal	Normal	Sensory nerve neuropathy	Liver infarction
2	Msahiro Suzuki (12)	2005	21	Female	56% (16,408/ul)	Faintly Nodular density in the left lower lung-pneumonia	Colon: Necrotizing vasculitis and eosinophilic infiltration	Negative	2.5 mg/dl	Asthma- sinusitis	Normal	Normal	Abdominal pain (LUQ)- Colon erosions-cholecystitis	Normal	Normal	Liver abscesses
3	Reijo Sironen (11)	2010	64	Male	3.5% (500/ul)	Normal	Appendix and liver: eosinophilic infiltrate and fibrinoid necrosis of vessels	Negative	Elevated	Asthma nasal polyp	Normal	Normal	Abdominal pain (RUQ)- Appendicitis-cholecystitis	Microscopic haematuria and proteinuria-renal insufficiency	Normal	Superficial micronodular lesions
4	Keiji Matsui (13)	2011	64	Female	40% (4420/ul)	Normal	Liver: Eosinophilic infiltration and centrolobular fatty change and macrovascular steatosis	Negative	4.94 mg/dl	Asthma-paranasal sinusitis	Normal	Normal	Diarrhea- anorexia	Normal	Polyneuropathy-weak grip strength and abnormal sensation-paresthesia in distal legs	Liver dysfunction
5	Masaru Harada (7)	2012	56	Female	5.6% (812/ul)	Normal	Liver: fibrinoid necrosis of hepatic artery with granulomatous and eosinophilic infiltration	Negative	12.9 mg/dl	Asthma	Normal	Normal	Cholestasis	Normal	Sensory nerve neuropathy of arms and legs	Cholestatic liver dysfunction-hepatomegaly
6	Jiejing Qian (14)	2014	60	Male	42.7% (7387.1/ul)	Pneumonia – infiltration in right upper and left lower lobe of lungs-pleural thickening	Skin: dermal perivascularity with neutrophils and monocytes infiltrations-fibrinoid degeneration of vessels	Positive (C-ANCA)	-	Asthma	normal	Purpuric rash and nodules on fingers, toes and back	Abdominal pain-nausea and vomiting-intestinal hemorrhage	Kidney hemorrhage	Left limb numbness	Hepatic capsular hematoma

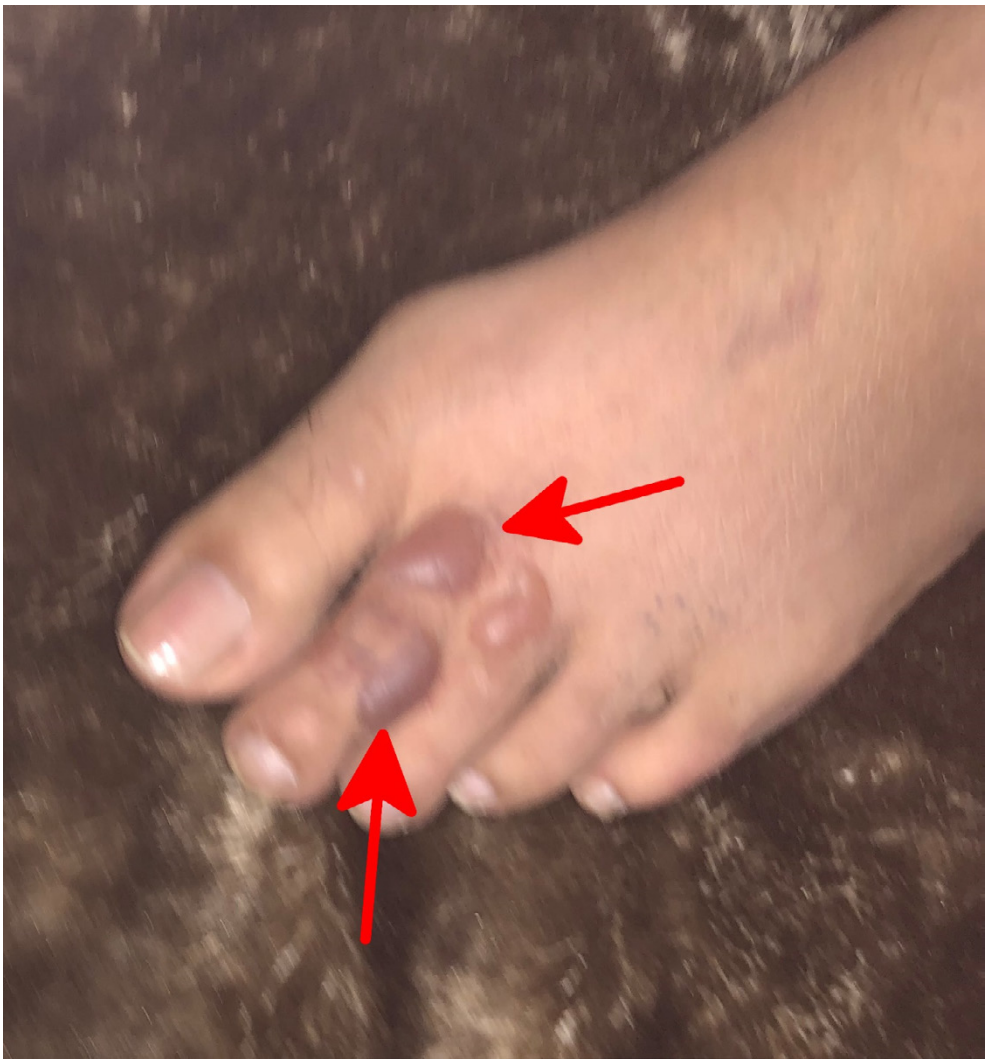

Figure 1. skin lesion on dorsum of the foot

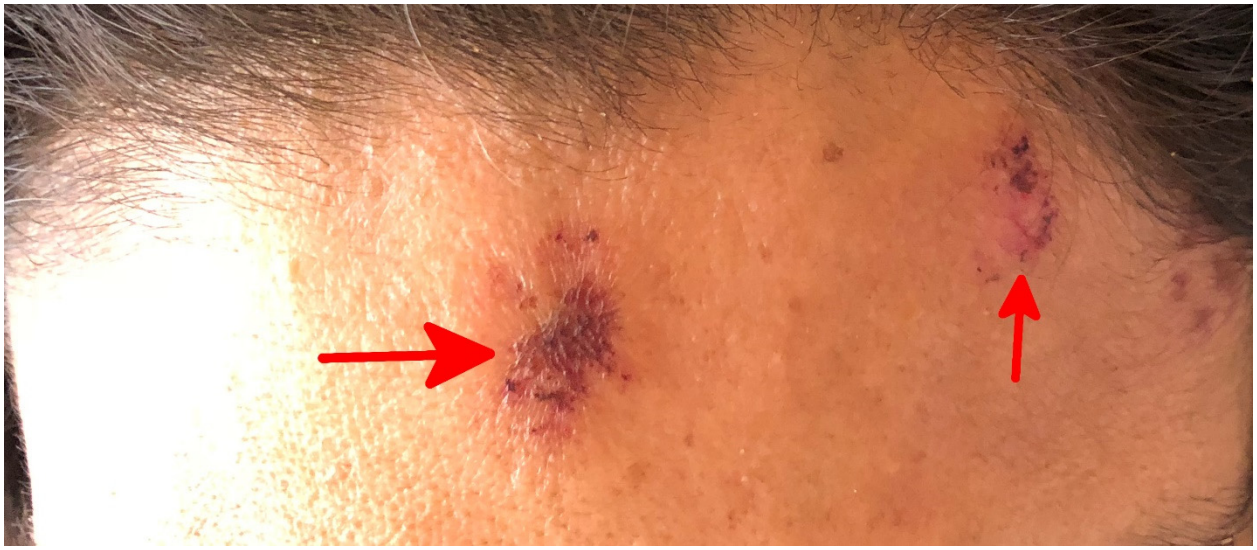

Figure 2. skin lesion on scalp

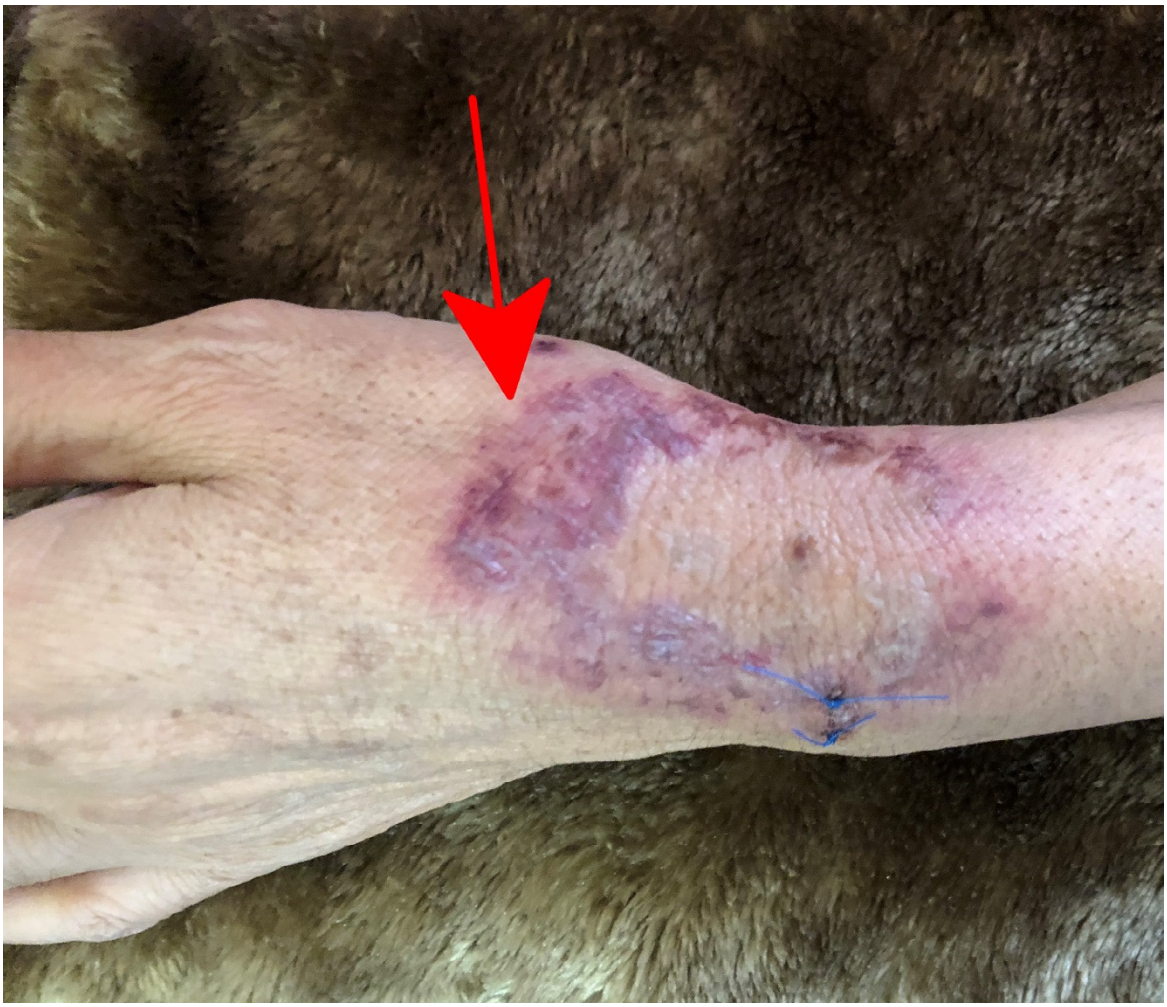

Figure 3. atrophy of thenar muscles in left hand

count (CBC), leukocytes count was 11900 (/ul) with 22% eosinophil and normal Hemoglobin. Antineutrophilic Cytoplasmic Antibody (ANCA), Cytoplasmic ANCA (c-ANCA) and Perinuclear ANCA (p-ANCA) were reported negative.

In the Computed tomography (CT) scan of the chest, multiple irregular nodules were noted in both lungs (**Figure 4**). In abdominal and pelvic images, the following was reported; multiple small hypodense masses in the liver (max. 12mm) (**Figure 5**), a small lesion measuring about 18 mm in the spleen and a few small cysts in the kidney (max. 12mm). Ultrasonography showed kidney stones on both sides. Upper and lower gastrointestinal tract endoscopy appeared normal. Bronchoalveolar Lavage (BAL) was performed and showed negative PCR for fungus, Mycobacterium Tuberculosis and malignancy (serum tumor markers of breast and ovarian cancers).

For malignancy workup, bone marrow aspiration and biopsy were taken that was shown to be normal as well. Moreover, in the biopsy of skin lesions, eosinophilic vasculitis was seen. EMG and NCV were compatible with C8-T11 radiculopathy and axonal sensory-motor polyneuropathy. According to the tests and biopsies, the patient was diagnosed with Eosinophilic Granulomatosis with Polyangiitis. Treatment was started with corticosteroids, gabapentin, and cyclophosphamide and later it was switched to azathioprine due to the undesirable response of former medications. After one month, ESR was shown to decrease to 20, neurological symptoms were reduced and the nodules improved as well.

Discussion

There are three main phases presented in Eosinophilic Granulomatosis with Polyangiitis,

Table 2. Laboratory results in our patient

Tests	Results	Reference range	Tests	Results	Reference range
ESR 1st hr (mm/h)	66	<20	ANA (u/ml)	0.3	<1
CRP	2+	Negative	Anti dsDNA (IU/ml)	11.4	<20
Hemoglobin (gm/dl)	9	12-16	RF	Negative	Negative
Leukocytes (x1000/uL)	11.9	4-11	Anti CCP (u/ml)	1.6	<20
Eosinophil (/uL)	22% (2618)	30-350	ANCA	0.1	<1
Uric acid (mg/dL)	3.7	2.5-6.8	PR3-ANCA	Negative	Negative
Creatinine (mg/dl)	1	0.5-1.5	Anti MPO	Negative	Negative
LDH (U/L)	441	225-500	C3 (mg/dl)	102	66-185
Ca (mg/dl)	9.2	8.1-10.5	C4 (mg/dl)	37	15-52
Vit D (25OH) (ng/ml)	43	30-100	AST (U/L)	100	10-40
ACE (µg/L)	32	Up to 40	ALT (U/L)	150	10-40
Bilirubin Total (mg/dl)	0.8	0.1-1.5	ALP (IU/L)	96	30-120

ESR, Erythrocyte sedimentation rate; CRP, C-Reactive Protein; LDH, Lactate Dehydrogenase; Ca, Calcium; ANA, Anti-Nuclear Antibody; Anti dsDNA, Anti Double Stranded DNA; RF, Rheumatoid Factor; Anti CCP, Anti- Cyclic Citrullinated Peptide; ANCA, Anti- Neutrophil Cytoplasmic Antibodies; PR3-ANCA, Proteinase 3 ANCA; Anti- MPO, Anti Myeloperoxidase; C3 and C4, Complement 3 and 4; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; ACE, Angiotensin-converting enzyme.

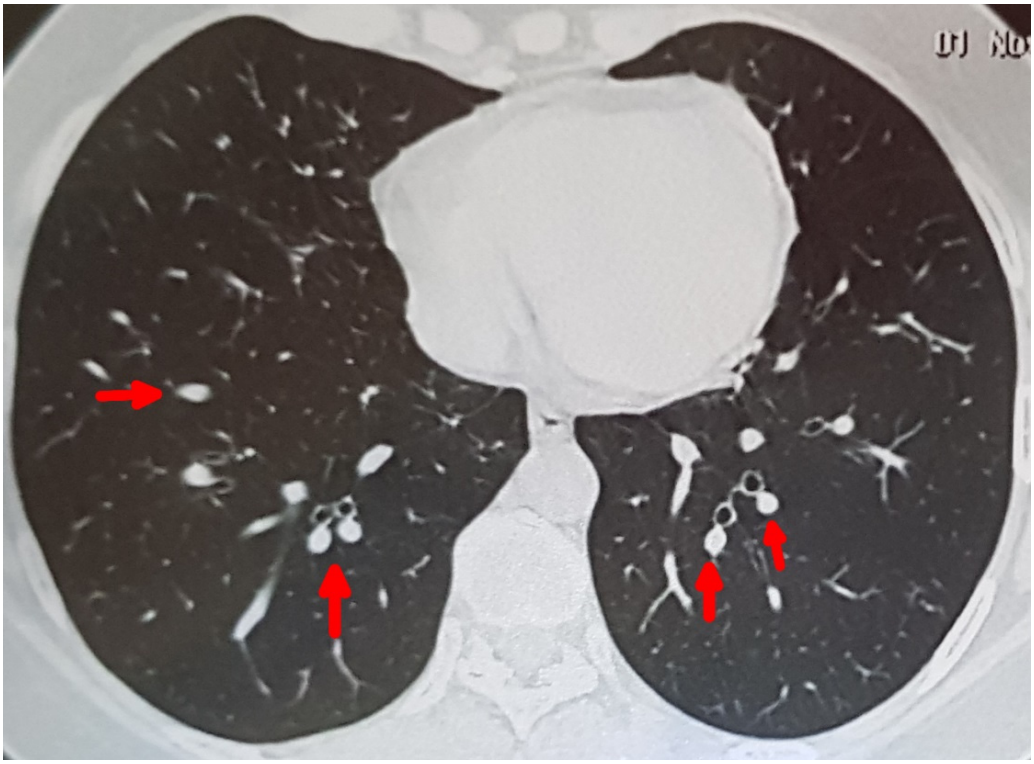

Figure 4. Multiple nodules in CT scan of the lungs

an allergic phase (a history of asthma and rhino-sinusitis), an eosinophilic phase (hallmarked by hypereosinophilia) and a vasculitis phase (manifests as multiple mononeuropathies, purpura and constitutional symptoms) (8).

The present patient was diagnosed with EGPA according to her past medical history of asthma, clinical findings, lab tests showing

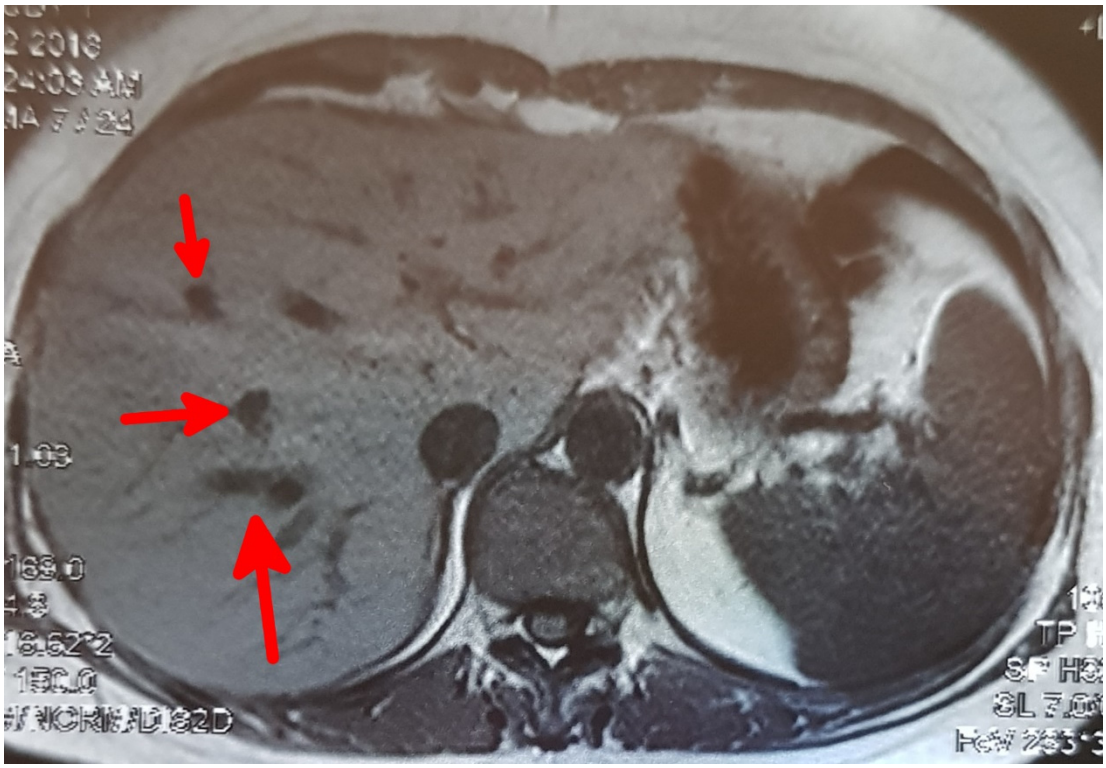

Figure 5. Multiple nodules in the liver

hypereosinophilia and paraclinical evaluations. Manifestations of EGPA in this patient were atypical and rare and common symptoms were not presented. Common clinical manifestations of EGPA include pulmonary and upper airway involvements, like nasal polyps, allergic rhinosinusitis, asthma, eosinophilic infiltrates, and pleural effusion. This clinical picture was presented in our patient as asthma (3). Another distinctive feature of EGPA: peripheral neuropathy presented as multiple mononeuropathies, which occurs in more than 75% of patients, was presented in this case (9). About half of the patients experience skin changes. Hemorrhagic lesions like palpable purpura are the most frequent skin lesions along with dermal or subcutaneous papules and nodules of scalp and limbs (10). This patient had a skin lesion and the biopsy further confirmed the diagnosis of EGPA. Gastrointestinal tract manifestations including abdominal pain, bleeding and intestinal obstruction are common in EGPA patients. However, liver involvement was rarely reported in this case (11). Multiple nodules in the liver were confirmed by liver CT scan.

Conclusion

EGPA can present itself with atypical manifestations without usual clinical patterns. In this situation, a comprehensive history of the patient along with paraclinical evaluations must be accomplished. Furthermore, the diagnosis of EGPA should be considered as a differential diagnosis.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Conflict of interest

The authors declare that they have no conflict of interest.

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