Delayed diagnosis of Granulomatosis with Polyangiitis in a 39-year-old woman with situs inversus totalis: A Case Report

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Compliance with Ethical Standards Data availability statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.**Funding statement:** None.**Conflict of interest disclosure:** None.**Ethics approval statement:** not applicable.**Patient consent statement:** Written informed consent was obtained from all individual participants included in the study.**Permission to reproduce material from other sources:** not applicable.**Clinical trial registration:** not applicable**Author Contributions** Hanie Forouzandeh: Writing – original draft, Data curation, study design, Supervision, Project administration Ahmadreza Rajabi: Writing – original draft, Data curation Abbas Ali Torfeh Esfahani: Supervision, Writing – review & editing, Conceptualization, Project administration Farzin Khorvash: Writing – review & editing, Conceptualization Mansoor Karimifar: Writing – review & editing, Conceptualization**Acknowledgments Conflict of interest** All the authors have declared no competing interests.**Human and Animal Rights** This article does not contain any studies with human participants or animals performed by any of the authors.**Informed consent** Informed consent was obtained from all individual participants included in the study. **Author's contribution** All authors contributed to the study design, data collection, and writing the draft of the study. All read and confirmed the final version of the manuscript.

AbstractSitus inversus totalis (SIT) is a rare congenital condition characterized by the transposition of both abdominal and thoracic organs. Individuals with Situs inversus totalis (SIT) may also have Kartagener syndrome, which is characterized by a triad of situs inversus, bronchiectasis, and recurrent sinusitis. Granulomatosis with polyangiitis (GPA), also known as Wegener's granulomatosis, is a rare condition. GPA involves granulomatous inflammation in tissues and blood vessels, potentially leading to organ damage. To date, no cases of Situs inversus totalis (SIT) individuals with Wegener's granulomatosis have been reported

in the literature. Our study aims to report a case with misleading information in medical history, leading to a delayed diagnosis of Granulomatosis with polyangiitis (GPA). **Keywords:** situs inversus totalis, Kartagener syndrome, Granulomatosis with polyangiitis, Wegener's granulomatosis**key clinical message:** The main clinical point in this article is being aware of all possible differential diagnoses despite all misleading data on the patient's history. It is also very interesting that we have a patient who has a rare congenital condition with a diagnosis of a rare disease.**Introduction**Situs inversus totalis (SIT) is an extremely rare congenital condition characterized by the transposition of both abdominal and thoracic organs. This rare condition occurs in approximately 1:10,000 individuals(1). Even most professional surgeons may encounter only 1 to 2 cases throughout their entire career(2). Typically, these cases are discovered incidentally during medical procedures or imaging tests(3). Sometimes these people have Kartagener Syndrome which is defined by a triad of situs inversus, bronchiectasis, and recurrent sinusitis(1). Granulomatosis with polyangiitis (GPA), also known as Wegener's granulomatosis, is a rare condition with an unknown cause. It affects approximately 3 in every 100,000 people and typically occurs around the age of 45 in both males and females. Granulomatosis with polyangiitis (GPA) is characterized by inflammation in the tissues, known as granulomatous inflammation, as well as inflammation in the blood vessels (vasculitis), which can lead to organ damage. While the sinuses, lungs, and kidneys are the most commonly affected areas, GPA can impact any part of the body(4).

We herein present a patient with situs inversus totalis who has been diagnosed with GPA (Wegener's granulomatosis) at Alzahra Medical & Educational Center \RL of Isfahan.

Case presentation We present a case of a 39–year–old woman with situs inversus totalis and a previous history of Kartagener syndrome and hypothyroidism. She came to the emergency department with intermittent petechiae and purpura in her lower limbs and intermittent high-grade fever and true chills from 3 months ago. She was giving a history of traveling to the Malaria-endemic region. Rashes and fever started right after her trip. She was giving a history of mild weight loss, nausea, and vomiting. Vital signs demonstrated a fever of 38.5°C, blood pressure (BP) 95/60, pulse rate (PR) 100, respiratory rate (RR) 24, and O2sat 88%. In the physical examination, we found a mild crackle in lung auscultation. Rashes were non-blanching. Laboratories were remarkable for leukocytosis of 14.05 with left shifting and thrombocytosis of 535. ESR was 101 and CRP was 88. Serum creatinine was 1.4 at first and then rose to 1.7 in three days. CXR showed evidence of mild infiltration in the lower lobe of the left lung and mild pleural effusion on the left side (Figure1). We tapped the pleural effusion. It had an exudative pattern in analysis. With a suspicion of Malaria, we performed PBS but it didn't confirm Malaria. We requested blood culture, sputum culture, wright test, PPD skin test, Widal test, and viral markers, which all were negative. U/A was remarkable for protein (++), blood (+++), RBC (many, 40% dysmorphic), and granular casts (1-2). Urine culture was negative. The stool exam was normal and the stool culture was negative. Endoscopy was performed for continuous nausea and vomiting and food intolerance, too. It showed erosive gastropathy. We also ruled out endocarditis with a normal echocardiography with no evidence of vegetation. Then we changed our approach from infectious diseases that were related to her travel, to rheumatologic diseases. So, we requested rheumatologic tests, and C-ANCA (Anti PR3) and ANA and RF were positive among them (The results are in Table1). We also performed a Chest M.D.C.T that showed cystic bronchiectasis(Figure2), mild infiltration in the lower lobe of the left lung, and mild pleural effusion on the left side (figure3) and we did a normal Abdominal M.D.C.T Scan.**Differential diagnosis:**Differential diagnoses of fever and rash included infectious diseases like mononucleosis, Meningitis, Endocarditis, Malaria, Dengue fever, Scarlet fever, malignancies like Lymphoma, or autoimmune diseases like Vasculitis, SLE, and Still's.

Treatment plan: At first, we had started antibiotics for her because of our suspicion of infectious diseases but she had a fever for the next 3 days despite antibiotic therapy, then after the positivity of autoimmune tests, we changed our treatment. First, the patient was started on three consecutive pulse doses (1gr) of Methylprednisolone Sodium Succinate then she received 1gr Rituximab, and this dose was repeated fourteen days later. We continued her therapy with a Prednisolone Tab (10mg/three times a day), Azathioprine Tab (daily), and Calcium D Tab (daily). Then a month after the second dose of Rituximab, we increased the dose of Azathioprine Tab to 50mg twice a day and we slowly tapered Prednisolone. This is important to mention

that we chose Rituximab among other common treatments because the patient was of reproductive age and treatments like Cyclophosphamide could lead to infertility. We also added Cotrimoxazole 400/80mg Tab for prevention of Pneumocystis Carinii.**Follow up:**To date when we write this report, the patient's signs and symptoms are improved. Serum creatine decreased to 1.3 and urine analysis turned to normal.

DiscussionAntineutrophil cytoplasmic antibody ANCA-associated vasculitis (AAV) encompasses a group of multisystem disorders that cause inflammation in the small blood vessels. This group includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA)(5)\RL. As described in the classification criteria for granulomatosis with polyangiitis, PR3-ANCA is most frequently linked with granulomatosis with polyangiitis (GPA), but MPO-ANCA is more prevalent in microscopic polyangiitis (MPA)(6)\RL. Advances in the diagnosis and treatment of ANCA-associated vasculitis (AAV) have significantly improved outcomes, changing it from a rapidly fatal disease with an untreated 1-year mortality rate of 80% to a condition that has relapsing and remitting episodes, albeit with ongoing morbidity and mortality in the long term. Pulmonary complications, both acute and chronic, are common in ANCA-associated vasculitis (AAV), affecting 25% to 80% of cases according to references. Lung involvement is increasingly recognized as a key contributor to the persistent morbidity and mortality in ANCA-associated vasculitis (AAV), with early pulmonary manifestations being linked to severe organ damage and poor outcomes in GPA(6)\RL.**Conclusion** Although there are few articles about the association between ANCA-associated vasculitis (AAV) and pulmonary involvements such as bronchiectasis(6), there is no published article about situs inversus individuals with GPA or association between Kartagener syndrome and ANCA-associated vasculitis (AAV). Additionally, our case had a history of traveling to malaria-endemic regions, which misled us in our approach to limb petechiae and fever and it made our case more noteworthy to report. However, further tests led to the diagnosis of ANCA-associated vasculitis (AAV).

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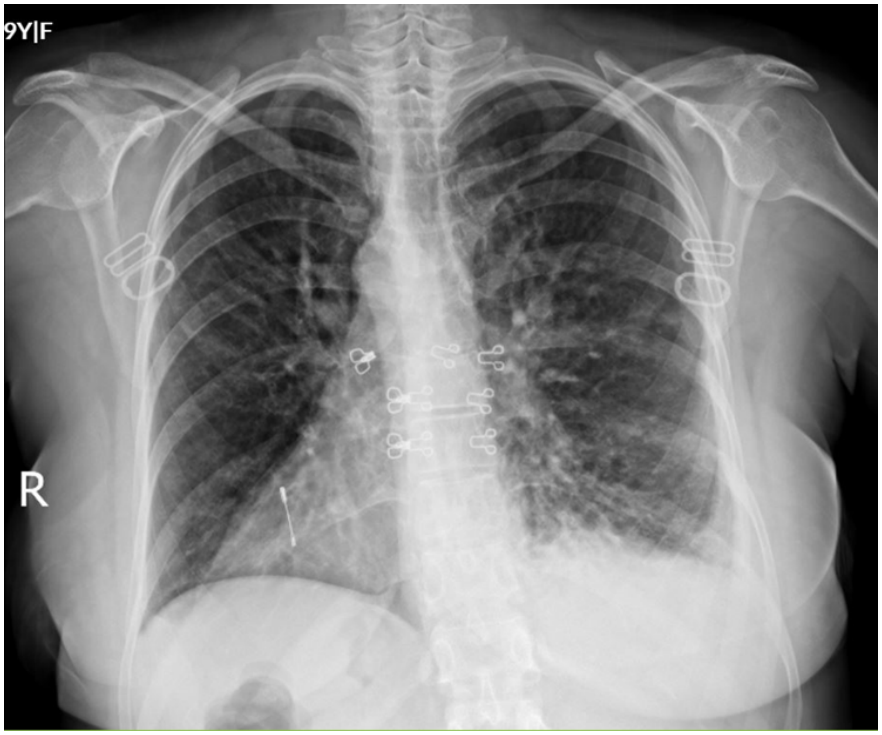
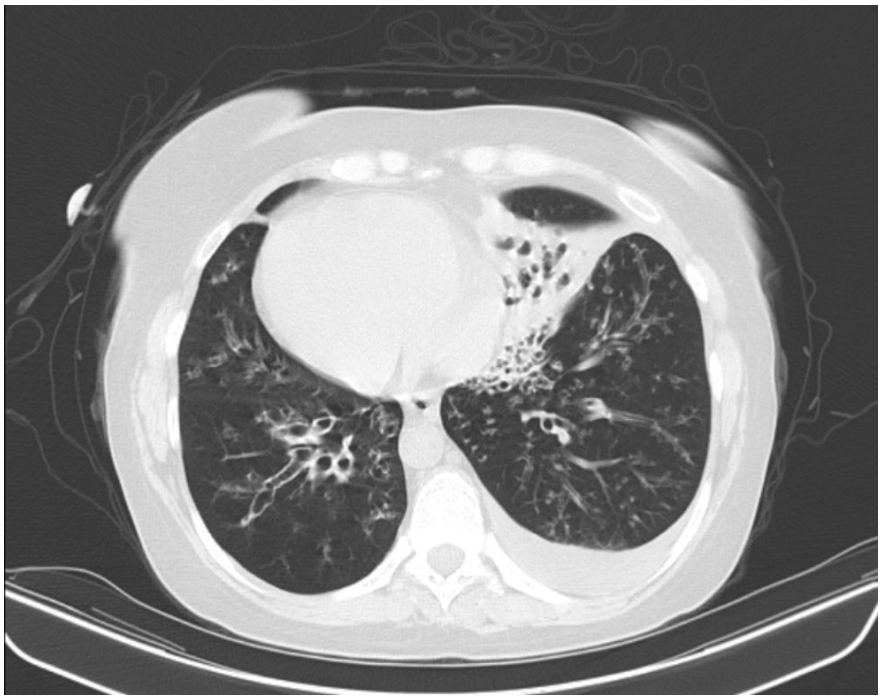
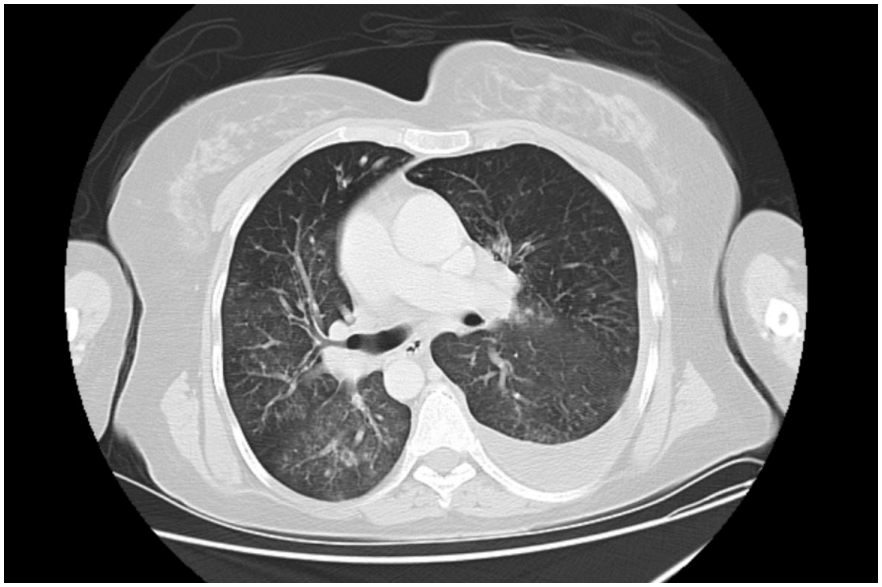
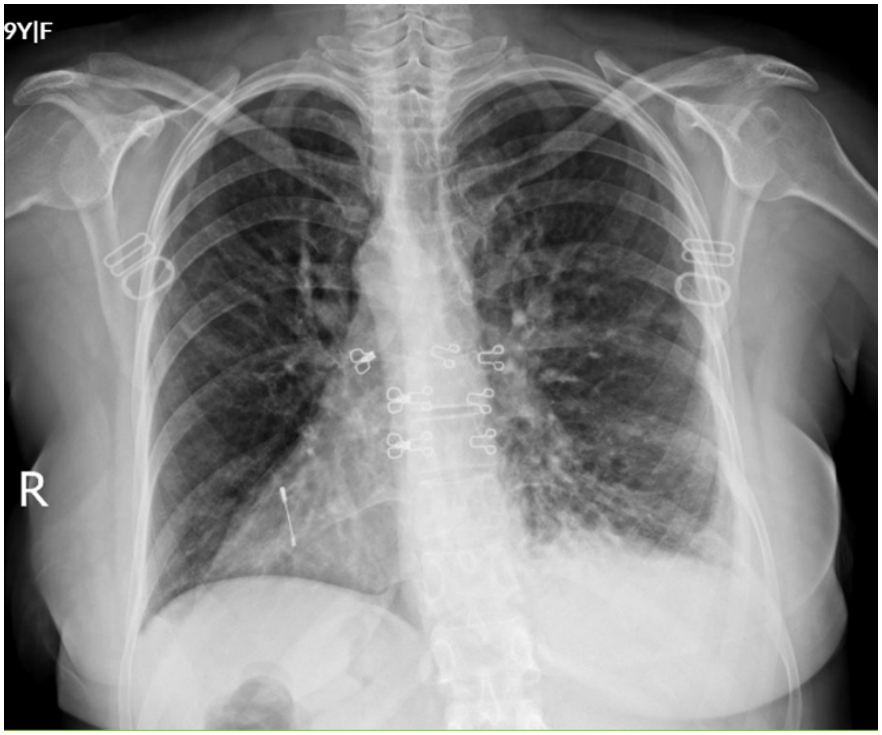
Table1: Results of Autoimmune and Immunology tests

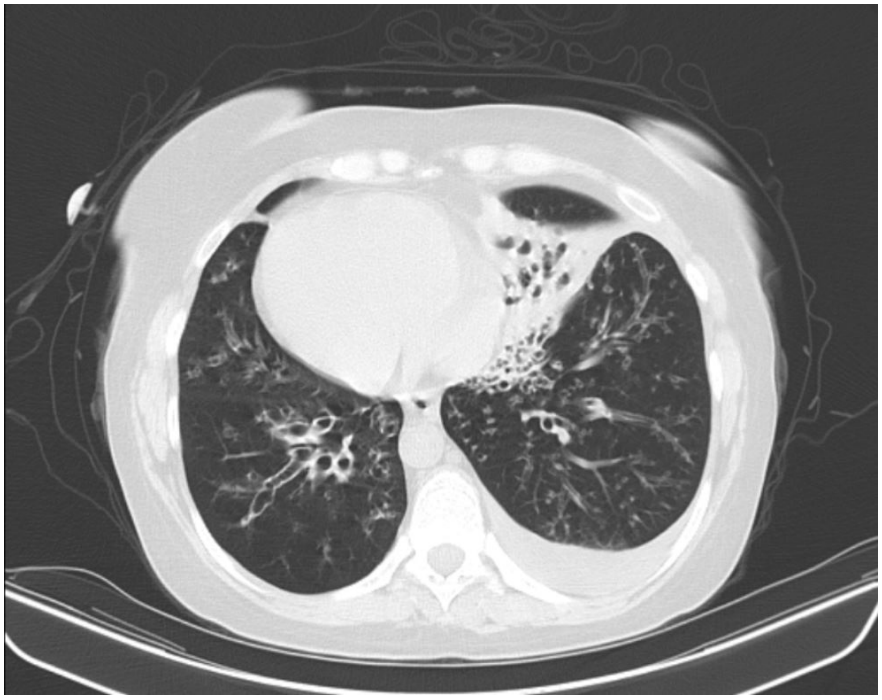
Autoimmune tests	Result Unit	Reference Interval
(F-ANA) Fluorescent ANA. (IgG)	1:160(Positive) titer	Negative: <1:80 Pattern is DFS70 Positive: >1:80
Anti PR3(C-ANCA)Fluorescent	1:40(Positive) titer	Negative: <1:20 Borderline: 1:20 Positive: >1:20
Anti MPO(P-ANCA)Fluorescent	<1:20(Negative) titer	Negative: <1:20 Borderline: 1:20 Positive: >1:20
(RF)Rheumatoid Factor IgG Quantitative	57.6(H) IU/ml	Normal Range: Up to 30
Immunology test		
(CH50)Total Hemolytic Complement	89.2 unit	Normal Range: 70-150

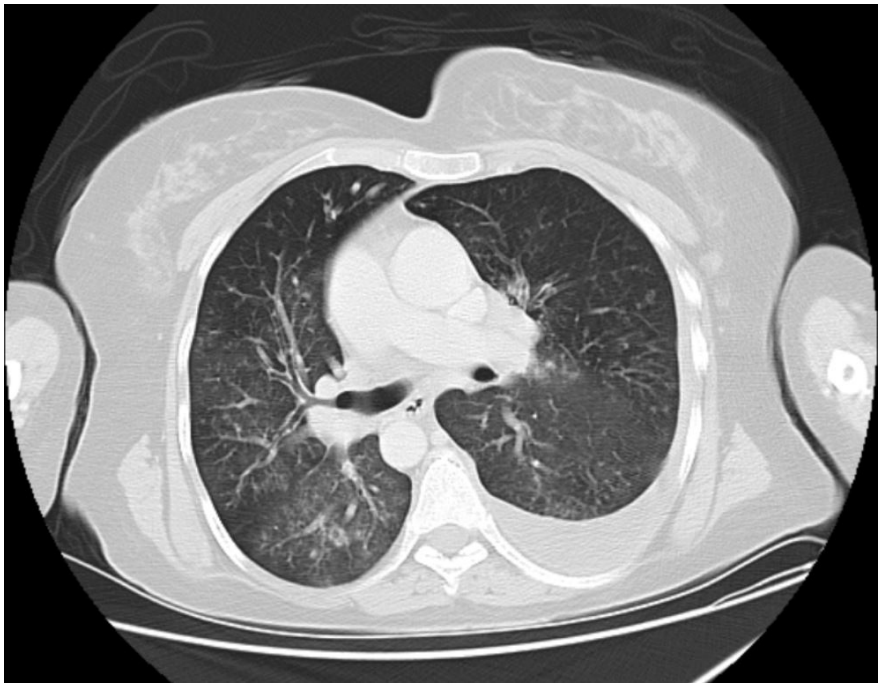












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(RF)Rheumatoid Factor IgG Quantitative	57.6(H)	IU/ml	Normal Range: Up to 30
Immunology test			
(CH50)Total Hemolytic Complement	89.2	unit	Normal Range: 70-150