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A COMPLICATED CASE OF GRANULOMATOSIS WITH POLYANGIITIS

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ABSTRACT

Granulomatosis with polyangiitis, formerly known as Wegener's granulomatosis, is a condition often presenting with granulomatous vasculitis of both the upper and lower respiratory tracts together with glomerulonephritis. Here we present a case of a 17-year-old female patient, who presented with symptoms of pansinusitis with other symptoms gradually following. She was treated with cyclophosphamide which was later switched to rituximab and is now in remission.

Keywords: cyclophosphamide, granulomatosis polyangiitis, pansinusitis, rituximab, vasculitis

INTRODUCTION

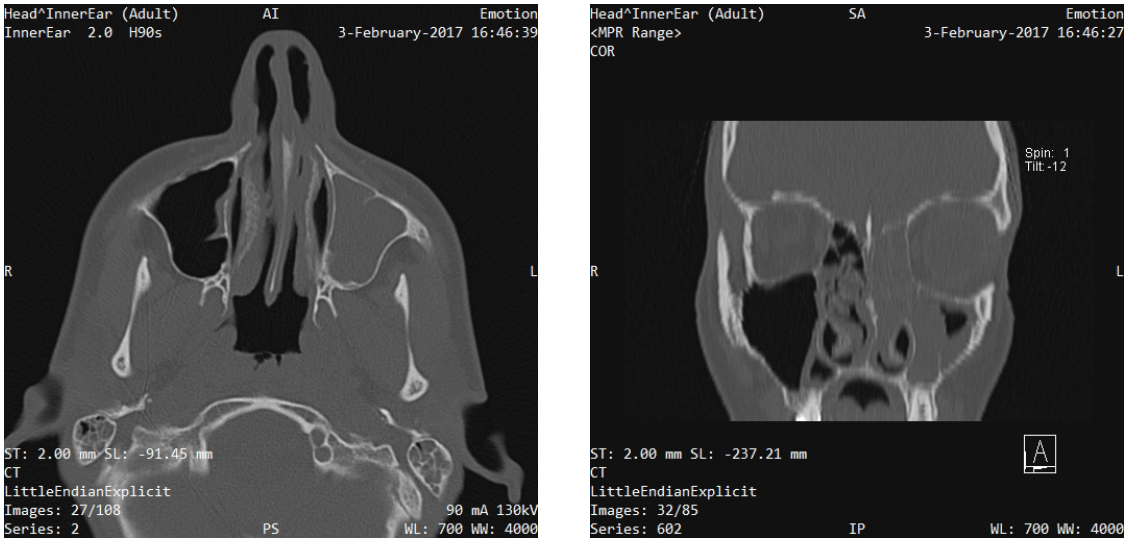
Granulomatosis with polyangiitis is a form of necrotizing vasculitis affecting predominantly small to medium vessels. It commonly presents with granulomatous inflammation, possibly involving the upper and/or lower respiratory tract [1], as well as kidney involvement such as glomerulonephritis [2]. Diagnosing this disease can be challenging as the clinical signs and laboratory results may not be clearly evident early in the course of the disease. Treatment should be started as soon as possible to prevent organ damage or life-threatening complications.

CASE REPORT

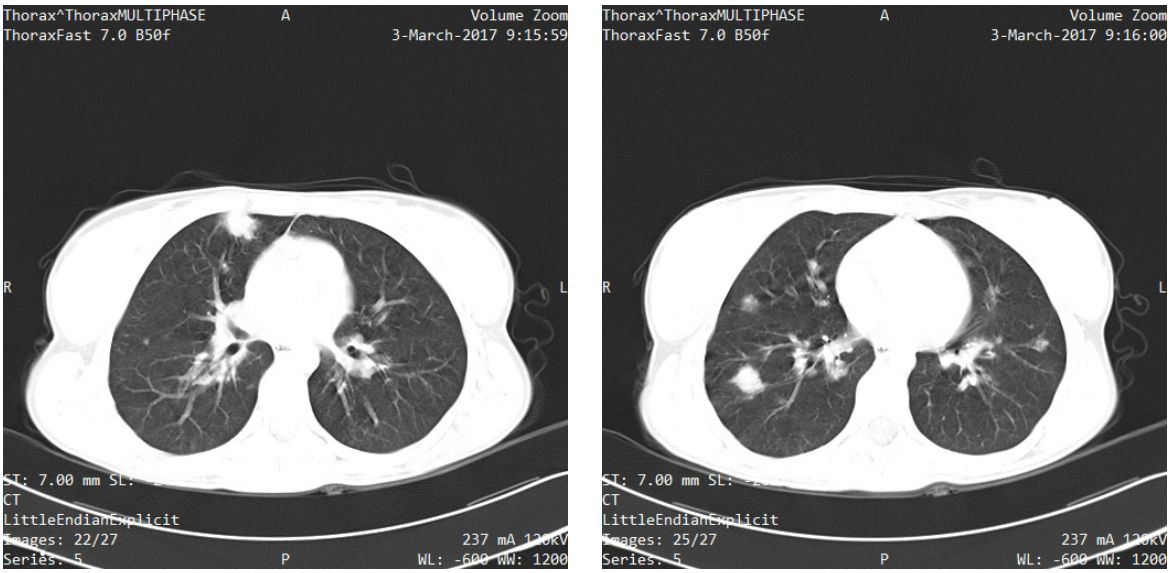
We present the case of a 17-year-old girl with a history of feeling of pressure in her ears who initially was treated with antibiotics. In the following three years she presented with symptoms of pansinusitis and reduced hearing, along with supraorbital headache, weight loss with reduced appetite, abdominal pain, frequent loose stools, elevated body temperature up to 38 degrees Celsius, pain along both of her arms. No arthritis or rash were present on first examination, but there was lividity of her right toes.

Computer tomography of the head and sinuses was performed where it showed findings of pansinusitis (Picture 1), the chest x-ray was unremarkable.

One month later a CT of her lungs was performed (Picture 2) with findings of multifocal zones of consolidation bilaterally, mostly at the lobular level, of which the slightly larger changes are seen on the right upper lobe, subpleural towards the front, as well as a centrally located lesion in the lower lobe on the same side.



Picture 1. Pansinusitis. Inflammatory, polypus changes of the mucosa of the PNS are present that completely obstruct the left OMK with secondary sinusitis of the left maxillary, frontal sinus as well as an anterior group of ethmoid cells on the left. Polypus changes are also seen in the projection of the right OMK, but it is passable, with nodular polypus changes in the bottom of the right maxillary sinus. Chronic inflammatory changes obstruct the ostium of the left sphenoidal sinus with secondary sinusitis. A moderate degree of sinistroconvex deviation of the nasal septum is observed.



Picture 2. *CT chest before treatment*

A follow up CT of the lungs (Picture 3), showed solid nodular changes of different sizes were present bilateral diffusely, of which two to three on the right are presented with central necrosis, a ring-like appearance and a thick irregular wall up to 7mm on the larger change, as well as zones of obliteration of the bronchioles posterobasal subpleural on the right with linear branching nodular changes. Bilateral hilar lymphadenopathy was present.

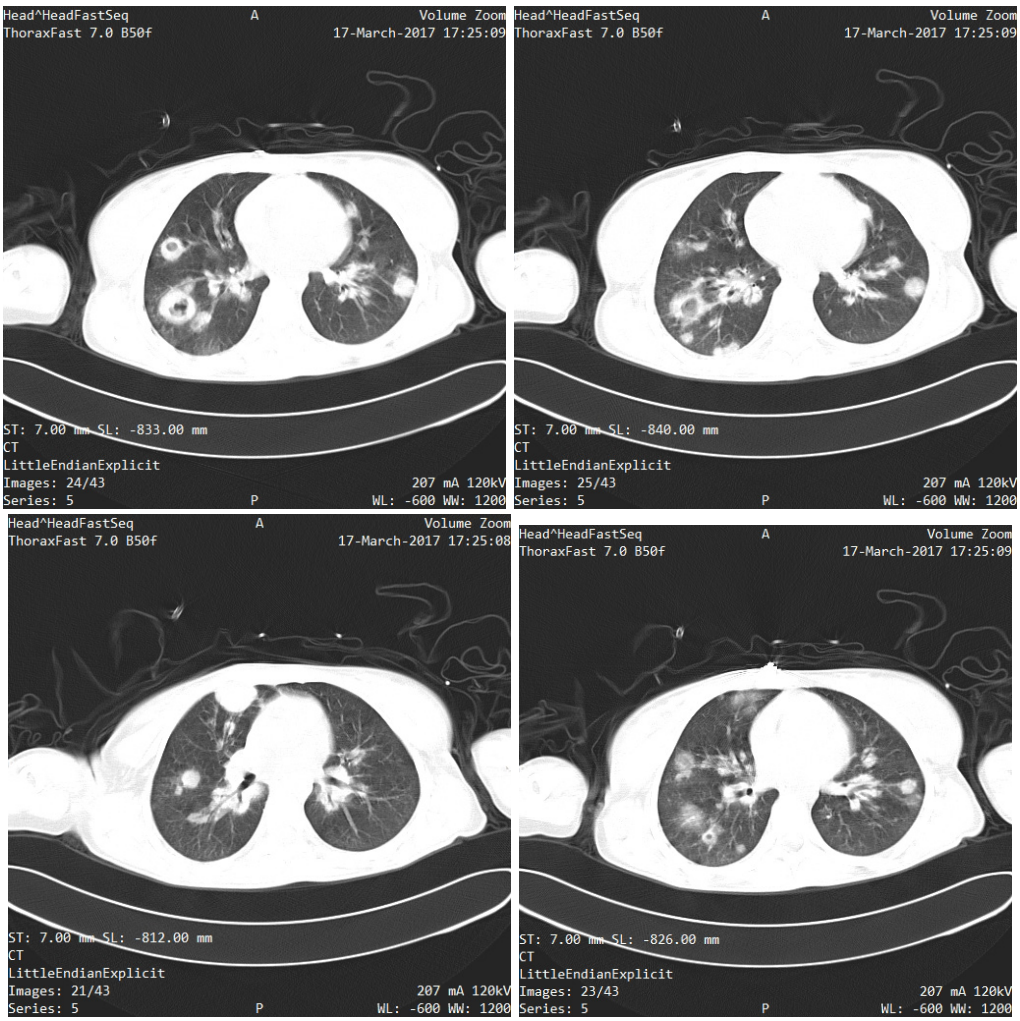
CT angiography of the lower extremities was performed showing defects in the arterial circulation of her right foot. Maxillary sinus changes were biopsied indicating acute vasculitis, polyarteritis with elements of leukocytoclastic vasculitis.

Laboratory tests showed high erythrocyte sedimentation rate (80mm/Hg), a high C-reactive protein of 73mg/L. Significant increase in the level of antibodies, cANCA (PR3:116.04lU/ml; pos:20 lU/ml). Anemia along with secondary thrombocytosis were present, a platelet counts of 1090). 24-hour proteinuria was normal.

Upon meeting the diagnostic criteria for granulomatosis with polyangiitis, treatment was initiated with methylprednisolone intravenous pulses (3 days, 1000mg per day) continued with prednisolone (1mg/kg) with weekly tapering of 5mg and cyclophosphamide (2mg/kg). After achieving remission (table 1) with oral cyclophosphamide, the treatment was continued with methotrexate (15mg weekly) for maintenance.

A year later due to sequelae from a necrotizing process on the toes of the right foot, she was hospitalized at the University Clinic of Thoracic and Vascular Surgery, where amputation of the I, II, III and partial amputation of the IV toe of the right foot was performed.

Three years later she was hospitalized at the University Clinic of Rheumatology-Skopje (table 2) with severe abdominal pain, vomiting and diarrhea. Joint pain had started after the patient ceased her corticosteroid intake on her own (5mg prednisolone daily), thinking that the abdominal pain might be related to it. Dotted small erythematous changes were registered on the lower legs, palms and feet which were deemed to be vasculitic.



Picture 3. *Follow-up chest CT*

Table 1. *Laboratory analysis upon starting methotrexate*

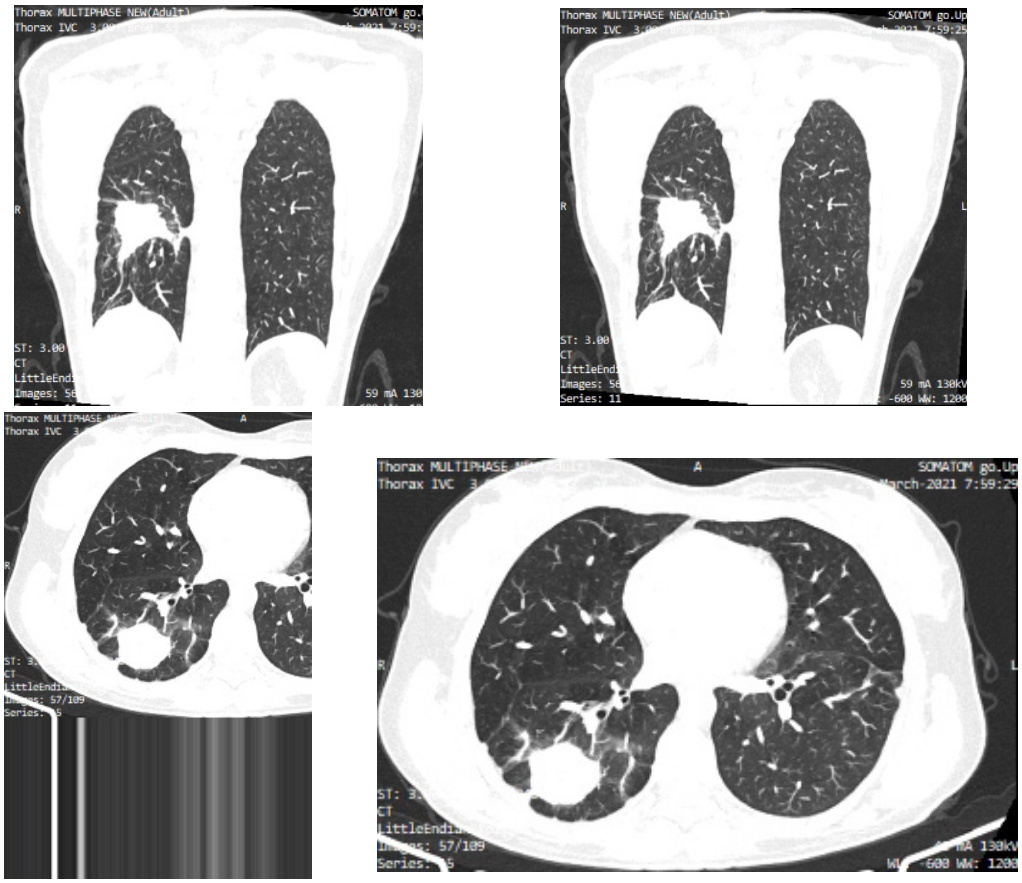
C-reactive protein	2.5mg/L	Erythrocyte sedimentation rate	13mm/h
Hemoglobin	128g/L	Leukocytes	4.35 10^9/L
Thrombocytes	430 10^9/L	Serum Creatinine	57mmol/L
24-hour-proteinuria	0.17g/D	C3, C4	wnl

Anemia, leukocytosis with secondary thrombocytosis were present. An increase in the level of antibodies was also noted cANCA (PR3: 27.8 lU/ml; pos: 20lU/ml). Chest CT showed disease reactivation (Picture 4) with multiple bronchoalveolar infiltrates and cavitating masses bilaterally diffusely without zonal predilection and with irregular margins. Peripheral wedge opacifications were also present.

The treatment for the reactivation of the disease was continued with rituximab, 4 doses of 500mg I.V. administration once a week, in combination with high doses of corticosteroids (60mg) daily, tapering by 5mg every 10 days.

Table 2. Laboratory analysis upon hospitalization at the UC of rheumatology

C-reactive protein	52mg/L	Erythrocyte sedimentation rate	7mm/h
Leukocytes	12 10^9/L	Thrombocytes	925 10^9/L
24-hour-proteinuria	Wnl	D-Dimer	8290



Picture 4. *CT showing Multiple bronchoalveolar infiltrates and solid heterodense masses without zonal predilection and with irregular margins are present bilaterally diffusely. Anteriorly in the upper right lobus, a 2cm solid nodule, a 4cm posterior basal right mass. Left in lateral segment of right lower lobe - 12mm. Central to the changes are zones of lower density*

Table 3. *Laboratory analysis one month after treatment with Rituximab*

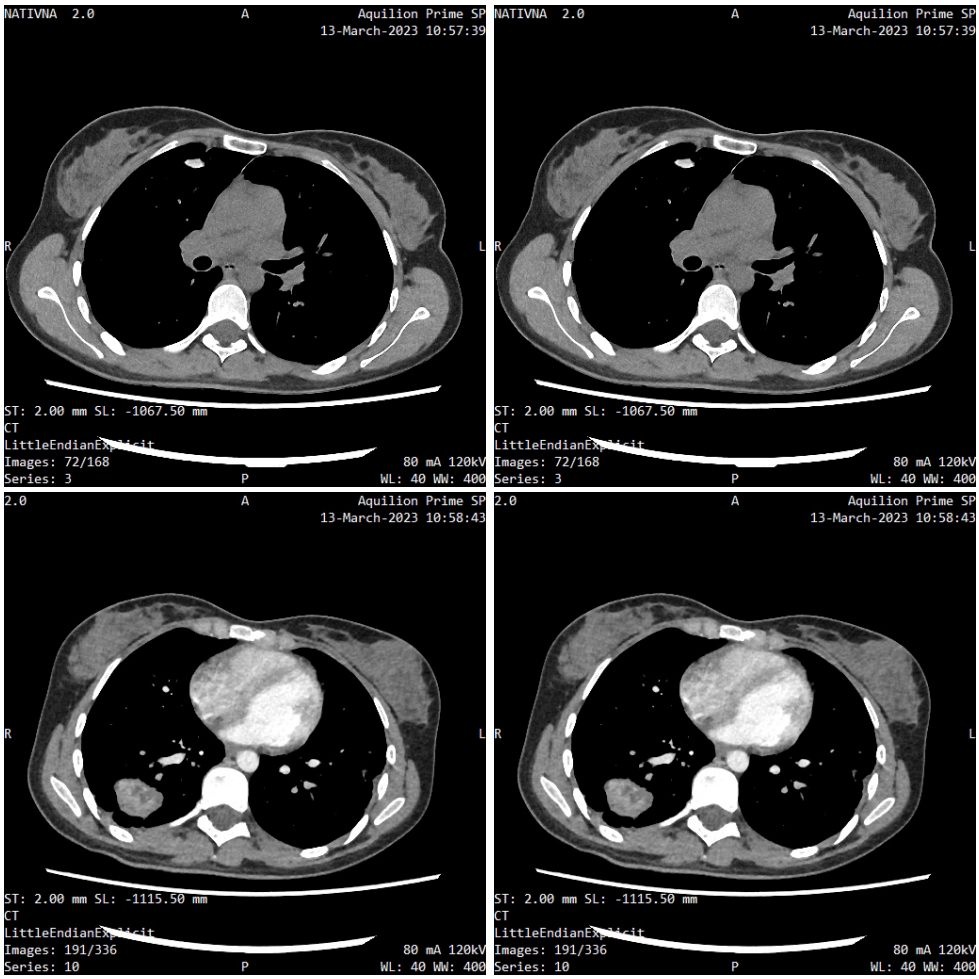
C-reactive protein	1.0mg/L	ESR	15mm/h
Hemoglobin	139g/L	Leukocytes	16.7 10^9/L
Platelets	386	Serum creatinine	44mmol/L
24-hour-proteinuria	0.096	Diuresis	1.6L
C3	Wnl	C4	wnl
ANCA-PR3	Negative (determined 3 months after treatment with Mabthera)		

One month after the application of rituximab, while the patient was still taking high doses of prednisolone orally, bloodwork normalized (table 3) and the patient had no symptoms of the disease. Follow up CTs were done every year showing no active changes (Picture 5).

DISCUSSION

Granulomatosis with polyangiitis is a granulomatous vasculitis of the upper and lower respiratory tract commonly presenting with glomerulonephritis [3]. In our patient the respiratory system involvement was dominant.

The patients long term complaints of pansinusitis and reduced hearing, along with presenting supraorbital pain, weight loss, reduced appetite, abdominal pain, frequent loose stools, fever of 38 degrees Celsius, pain on both her arms and livid erythema changes on the right foot hinted at vasculitis as a possible cause. After the first CT scan which showed pansinusitis, a biopsy with finding of necrotizing vasculitis, lung changes and a significant increase in cANCA, the patient satisfied the criteria for granulomatosis with polyangiitis. The initial treatment with Cyclophosphamide (50mg) and high dose of corticosteroids achieved remission, but methotrexate was unable to sustain long term remission. According to the latest recommendations for maintaining remission in patients with severe granulomatosis with polyangiitis whose disease is in remission after the treatment with cyclophosphamide or rituximab, the treatment with rituximab over methotrexate or azathioprine is conditionally recommended to maintain remission [4]. Rituximab is associated with a lower relapse rate than azathioprine when used to maintain remission after cyclophosphamide-induced remission [4].



Picture 5. *CT after treatment.*

This goal was achieved and is still maintained with rituximab and low dose corticosteroids (5mg daily). Rituximab (500mg i.v.) is administered every 6 months and the patient is in stable remission.

CONCLUSION

Data shows that 85% of patients with vasculitis consulted a doctor within the first three months from the onset of symptoms, but the average time of diagnosis is around 7 months from the onset of the first symptoms [5]. Initially 73% of patients are misdiagnosed. A late diagnosis results in poor outcome and reduced quality of life [5].

Timely diagnosis and treatment of these patient is crucial. Our experience also shows that rituximab is preferable in achieving and especially in the maintenance of remission.

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Резиме

КОМПЛИЦИРАН СЛУЧАЈ НА ГРАНУЛОМАТОЗА СО ПОЛИАНГИИТИС

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Грануломатоза со полиангиитис, порано позната како Вегенерова грануломатоза, е состојба што често се манифестира со грануломатозен васкулитис на горниот и на долниот респираторен тракт, заедно со гломерулонефритис. Овде претставуваме случај на 17-годишна пациентка, која се јавила со симптоми на пансинузитис, со други симптоми што постепено следувале. Таа беше третирана со циклофосфамид, а подоцна беше префрлена на ритуксимаб, и сега е во ремисија.

Клучни зборови: циклофосфамид, грануломатоза со полиангиитис, пансинузит, ритуксимаб, васкулит