The Management of Giant Cell Arteritis (GCA) Overlapping with Sjogren Syndrome : A Case Report

Arina Mana Sikana[1], Awalia[2]

[1]Student, [2]Lecturer, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, 60131, Indonesia

Abstract

Giant cell arteritis (GCA) is an autoimmune vasculitis involving large and medium arteries. GCA is rarely associated with autoimmune diseases, such as Sjögren's syndrome. Glucocorticoids (GC) are the cornerstone of the treatment of GCA as they are very effective but are often given for 1 year to avoid relapses. Here we report a rare case of GCA overlapping with Sjögren's syndrome along with the management.

Keywords: *Giant Cell Arteritis, Management, Sjogren Syndrome*

Introduction

GCA is an immune-mediated systemic vasculitis that mainly involves the large and middle arteries, especially the temporal arteries. GCA mainly occurs in people over the age of 50 years old.[1]The lifetime risk of developing GCA is estimated at 1% for women and 0.5% for men.[2]

The symptoms of giant cell arteritis can overlap with its cousin disease polymyalgia rheumatica (PMR). PMR similarly is an autoimmune disease that affects the elderly. Its hallmark symptoms include muscle pain and weakness affecting the large muscle groups especially in the hips and shoulders. Patients with PMR have trouble getting out of a chair and reaching for objects in cupboards. PMR symptoms also include low-grade fever, malaise, poor appetite, and weight loss. When symptoms affect the neck and higher, giant cell arteritis can be at work. Five to 15% of PMR patients will be diagnosed with giant cell arteritis, and 50% of giant cell arteritis patients have PMR symptoms.[3] GCA is rarely associated with autoimmune diseases, such as Sjögren's syndrome.[4]

Corresponding author:
Arina Mana Sikana
E-mail : arinamanasikana010890@gmail.com

Case

A 52 years oldwoman named Mrs. M was admitted by her family to the outpatient clinic of Dr. Soetomo general hospital, Surabaya, with a chief complaint sudden onset headache.

Current Medical History

She complained about having headache since 2 months ago (pain is worse in 2 weeks ago). The headache was like being pressed and localized to the temple. However, it may be occipital or be less defined and precipitated by brushing the hair. The pain feels heavy everyday so it is difficult to sleep. Vertigo absent.

The patient often has anorexia so that the weight goes down. Sometimes nausea but not vomiting. The left eye feels moreblurry than the right eye since 2 months ago. The patient admitted to having both red

eyes since the headache appeared.

The patient had gone to the neurological clinic for headache since 2 month ago and was given therapy methyprednisolone 3x 16 mg and the last month on prednisone treatment 3x 20 mg but the chief complaint did not improve then the patient was referred to a rheumatology clinic RSUD Dr. Soetomo.

Previous medical history

The patient was diagnosed with hepatitis B 13 years ago, had been prescribed tenofovir 1x 300 mg during initial diagnosis. April 2019 was diagnosed sjogren syndrome, had been prescribed methylprednisolone 1x 4 mg, chloroquine 1x 250 mg. may 2019 peptic ulcer and had been prescribed lansoprazole 1x 30 mg.

Familial medical history

There are no family members that experience similar symptomps.

Socioeconomic history

The patient works as a housewife. The patient is married and has 1 child aged 28 years. Her husband works as a farmer.

Physical examination

From vital signs examination, we obtained a general state of weakness with GCS 456. Blood pressure 120/70 mmHg, pulse 78x/minute, irregular rhythm, normal amplitude. Respiratory rate of 20x/minute with 97% SpO2 with free oxygen. Axillary temperature of 36.8 C. Pain scale assessment with Visual Analog Scale obtained a score of 5 (moderate pain). The patient's body weight was 50 kg, body height was 150 cm, with a body mass index of 22 kg/m2 (normal).

There wasa prominence of the temporal artery in the head. On cardiac examination, irregular S1 and S2 were obtained, diastolic murmurs were found in apex. Other examinations were within normal limit.

Additional examinations

From laboratory examinations **(13/12/19)** we found Hb 13.3 g/dL, Hct 25.7%, Leucocytes 6.760/uL, Neutrophil 71.4%, Lympocyte 19.2%, Platelets 135.000. random blood sugar 129 mg/dL, BUN 16 mg/dL, creatinine 0.5 mg/dL, SGOT 41 u/L, SGPT 34 u/L, Albumin 3.5 g/dl, Natrium 145 mmol/l, Potassium 4.4 mmol/L, Chloride 104 mmol/L, CRP 12 mg/L, ESR 54 mm/h.

- VODS > 2/ 60. TO DS 14.6/ 14.6 mmHg
- Anterior segment ODS
- Palpebral oedema -/-, spasm -/-, conjungtiva hiperemis -/-, cornea clear +/+
- Posterior segment ODS
- Fundus reflex +/+, papil NVII strict lines/strict lines, bleeding retina -/-. Exudate -/-, macula reflex +/+.

From brain MRI with contrast **(6/11/19)**: wall thickening and mural contrast enhancement a. temporalis superficialis and a. meningea media right left accompanied by vasculitis picture of a. temporalis superficialis and a. meningea media right and left may represent temporal arteritis

Assestment and management

Based on the history, physical and auxiliary examinations, the patient's assessment is giant cell arteritis, sjogren syndrome, chronic hepatitis b.

Patient is planned for hospitalization. Patient is also planned for temporal artery biopsy. Therapy given to the patient is of NaCl 0.9% infusion 500 cc for 24 hours, Inj. Methylprednisolone 62.5 mg for 24 hours during 3 days, Inj. Cyclophosphamide 500

mgfor 24 hours.

Disease Course

13rd December 2019

Patients complained of headache disappear and arise with VAS 6, sometimes nausea. The vital signs were within normal limit.

Thepatientwasplannedfor Inj. Methylprednisolone 62.5 mg for 24 hours in 3 days. Inj. Tramadol 10 mg for 8 hours. We consult the patient to the neuro surgery for TAB and ophthalmology division.

16th December 2019

The headache disappearedimproved with VAS 4. The patient was planned for inj. Cyclophosphamide 500 mg for 24 hours.

17th December 2019

The patient was discharged and advised to control regularly in rheumatology. The final diagnosis was giant cell arteritis post cyclophosphamide, sjogren syndrome, chronic hepatitis b.

Discussion

GCA and PMR commonly overlap. PMR is observed in 40- 60% of patients with GCA at diagnosis, and 16- 21% of patients with PMR may develop GCA, particularly if left untreated.[5]

The traditional concept of GCA has focused on cranial symptoms such as headache and visual disturbance, but extra-cranial manifestations such as constitutional symptoms, polymyalgia and limb claudication have also long been recognized.These symptoms may coincide with cranial GCA, occur as an independent clinical subset [large-vessel (LV) GCA] or overlap with PMR. Imaging studies have demonstrated that up to one-third of patients with PMR have subclinical LV inflammation at disease outset. Patients with treatment refractory PMR commonly have cranial and/or extracranial arteritis on imaging.[5]

In this case, the patient complained about having headache and the left eye feels more blurry than the right eye since 2 months ago. The patient often has anorexia so that she loses weight. Sometimes nausea but not vomiting. The patient also complained of jaw claudication during the last 2 months.

The most common symptom of GCA is headache, which is present in more than two-thirds of patients. It usually begins early in the course of the disease and may be the presenting symptom. The pain is severe and localized to the temple. However, it may be occipital or be less defined and precipitated by brushing the hair. The nature of the pain varies; some patients describe it as shooting, and others as more like a steady ache. Scalp tenderness is common, particularly around the temporal and occipital arteries, and may disturb sleep. Tender spots, or nodules, or even small skin infarcts may be present for several days. The vessels are thickened, tender, and nodular with absent or reduced pulsation.[6]

The patient complained about having headache since 2 months ago. Headache was like being pressed and localized to the temple. However, it may be occipital or be less defined and precipitated by brushing the hair. The pain feels heavy everyday so it is difficult to sleep.

There is a vessel that is thickened, tender, with reduced pulsation in her head.

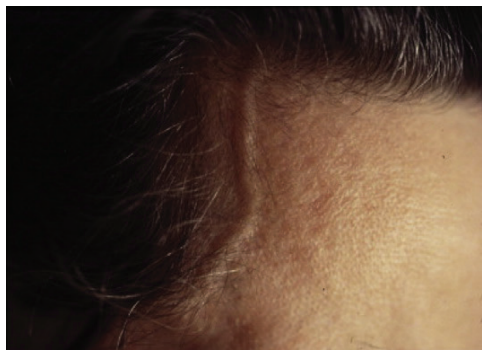

Figure 1. Clinical picture of the patient

Vision symptoms, such as amaurosis fugax, blurred vision, diplopia, and blindness (monocular and binocular) occur in 12%–40% of patients(Arteritis et al., 2003). Sudden, severe, and sequential vision loss is the hallmark of giant cell arteritis. The vision loss is usually discovered upon awakening in the morning. Visual acuity is usually less than 20/200 in greater than 60% of patients who lose vision. The fellow eye usually gets involved within days to weeks of the initial eye. GCA may initially also present with diplopia or eye pain.[3]

In this case, the left eye feelsmore blurry than the right eye since 2 months ago. The patient admitted to having both red eyes since the headache appeared.

Original criteria	Suggested expansion
Age at disease onset ⩾50 years	Age at disease onset ⩾50 years
New onset headache of or new type of localized pain in the head	Any of the following: New onset headache of new type of localized pain in the head, **Visual symptoms, sight loss, PMR, Constitutional symptoms, Jaw and/or tongue claudication**
Abnormality of temporal artery (tenderness to palpation or decreased pulsation unrelated to arteriosclerosis)	Abnormality of temporal **and/or extra-cranial arteries** (tenderness to palpation or decreased pulsation, **bruits of extra-cranial arteries** unrelated to arteriosclerosis)
ESR ⩾50 mm/h	ESR ⩾50 mm/h and/or **CRP levels ⩾10 mg/l**
Abnormal artery biopsy	Abnormal artery biopsy and/or **abnormal imaging result (US, MRI and/or ^{18}F-FDG PET)**[a]

Table 1. Expansion of the 1990 ACR criteria items for the classification of GCA[5]

A patient shall be diagnosed to have GCA if three of the five criteria are present, as long as either temporal artery biopsy and/or imaging results are compatible with a diagnosis of GCA. F-FDG PET: 18-fluorine fluorodeoxyglucose PET/CT.

In this case, there are five criteria, among others

1. Age of disease onset 52 years

2. New onset headache of new type of localized pain in the head, visual symptoms, constitutional symptoms

3. Abnormality of temporal (tenderness to palpation)

4. ESR 54 mm/ hr and CRP levels 12 mg/l

5. Abnormality in MRI: wall thickening and mural contrast enhancement a. temporalis superficialis and a. meningea media right left accompanied by vasculitis picture of a. temporalis superficialis and a. meningea media right and left may represent temporal arteritis

The immunopathological model of GCA can be divided into four phases[8]

Phase 1: loss of tolerance and activation of resident dendritic cells of the adventitia.Phase 2: recruitment, activation and polarization of $CD4^+$ T cells. Phase 3: recruitment of $CD8^+$ T cells and monocytes. Phase 4: vascular remodeling[8]

People with a certain genetic background (such as female sex, northern European descent and other genetic variants) are more susceptible than others. Genetic factors might also influence the phenotype and course of GCA and PMR.[5]

The pathogenesis of GCA is still unclear, and experts believe that it may be caused by a combination of genetic and environmental factors. At present, it is generally believed that the pathogenesis of GCA is dendritic cells (DCs) which in the middle and endometrium layer of the vascular wall are activated, secrete various inflammatory factors and chemokines such as IL6 and IL8, active and recruit $CD4^+$ T cells and macrophages into the vascular wall. Activated $CD4^+$ T cells can polarize to Th1 and Th17 cells, and participate in vascular inflammation. DCs and $CD4^+$ T cells also play a vital role in the pathogenesis of RA

and SS.[1]

In this case, GCA and SS appeared on the basis of PMR and after the aggravation of PMR, which strongly suggested that there may be a common pathogenesis between the three diseases and may promote the occurrence and development of each other.

Acute-phase markers of inflammation are often significantly elevated, and a normocytic normochromic anemia and thrombocytosis may be present, as may elevation of liver transaminase levels with a reduced albumin level. Although the ESR has historically been the acute-phase measure of choice in the diagnosis of GCA, up to a quarter of patients may have a normal value and elevation of the C-reactive protein (CRP) is a better predictor of obtaining a diagnostic TAB (Temporal Artery Biopsy). The combination of an elevated CRP and positive TAB render the highest sensitivity and specificity for the diagnosis of GCA.[9]TAB has been the gold standard test representing definitive pathologic diagnosis.[10]

Both MRI, MR angiography (MRA), and contrast-enhanced CTA provide useful images of mural and luminal changes suggestive of large-vessel vasculitis in GCAthat include circumferential wall swelling, smoothly tapered luminal narrowing of aortic branches and aortic aneurysm formation. MRI and MRA are favored over CTA by most experts. Bright mural enhancement of the temporal artery on contrast-enhanced high-resolution MRI had comparable sensitivity and specificity to temporal artery ultrasound (TAUS) in the diagnosis of GCA.[9]

Current EULAR and British Society of Rheumatology (BSR) recommendations for GCA management suggest immediate treatment of GCA using GCs at a dose of 1 mg/kg (up to a maximum of 60 mg/day) or 40- 60 mg/ day prednisone equivalent, respectively, in order to prevent ischaemic complications, particularly blindness.[11]

Patients presenting early after the onset of visual symptoms may require GC pulse therapy with 0.5- 1 g methylprednisolone for 3- 5 days. EULAR recommends considering MTX in every GCA patient, whereas BSR has reserved this treatment for relapsing patients.[12]

According to the recently published 2015 EULAR- ACR recommendations for PMR, the initial GC dose is 12.5- 25 mg/day prednisone equivalent followed by gradual dose tapering.[13] MTX may be used in patients at risk of relapse and/or GC-related adverse events. BSR recommends an initial GC dose of 15 mg/day for PMR, and the introduction of MTX after the second relapse.[11]

Glucocorticoids (GC) are the cornerstone of the treatment of GCA as they are very effective but are often given for 1 year to avoid relapses. As a result, 86% of patients develop ≥1 GC-related complication(s) after 1 year of follow-up. Therefore, GC-sparing therapeutic strategies are required to improve the management of GCA patients. Methotrexate is often used as a GC sparing agent, but its effect seems moderate and is still debated.[14]

In this case, the patient was given methyprednisolone 1x 4 mg and myfortic addition 2 x 180 mg, chloroquine 1x 250 mg. After a month the complaints still did not get better. So that the patient was admitted to the hospital.

Patients presenting early after the onset of visual symptoms may require GC pulse therapy with 0.5- 1 g methylprednisolone for 3- 5 days. EULAR recommends considering MTX in every GCA patient, whereas BSR has reserved this treatment for relapsing patients. According to the recently published 2015 EULAR ACR recommendations for PMR, the initial GC dose is 12.5- 25 mg/day prednisone equivalent followed by gradual dose tapering.[13]

In this case,the patient was planned for Inj. Methylprednisolone 62.5 mg for 24 hours in 3 days and was planned for inj. Cyclophosphamide 500 mg for 24 hours. One day after cyclophosphamide, headache complaint decreased so that the patient was discharged from the hospital.

Conclusion

A 52 years old woman was admitted by her family to the outpatient clinic of Dr. Soetomo general hospital, Surabaya, with a chief complaint sudden onset headache. The patient was diagnosed withgiant cell arteritis, sjogren syndrome, chronic hepatitis b. TAB has been the gold standard test representing definitive pathologic diagnosis. Glucocorticoids (GC) are the cornerstone of the treatment of GCA as they are very effective but are often given for 1 year to avoid relapses.

Ethical Clearance- Nil

Source of Funding- Nil

Conflict of Interest - Nil

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