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Horton's disease in elderly women: still an overlooked diagnosis?

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ABSTRACT

Introduction. Horton's disease is the most common form of vasculitis that occurs in patients older than 50 years. Due to its unusual clinical manifestation, the disease is often misdiagnosed and managed inappropriately. Early diagnosis and prompt initiation of treatment are essential to reduce the risk of severe neuro-ophthalmic complications.

Case presentation. We present the case of a 71-year-old woman, with a family history of autoimmune disease, who complains of bilateral shoulder and pelvic girdle pain, low fever, jaw claudication and amaurosis fugax. After the initial tests that have been made in other departments, the patient has been diagnosed with iron deficiency anaemia and treated with iron tablets. Because of the lack of improvement in the clinical manifestations and unresponsive anaemia to oral iron treatment, the patient was admitted to our rheumatology department 5 months later. The anamnestic, clinical and paraclinical tests results along with the presence of the diagnosis criteria, allowed us to establish the Horton's disease diagnosis. The patient immediately received corticosteroid therapy having a prompt clinical and paraclinical response.

Conclusion. Even if sometimes it can be hard to reach the diagnosis, every effort should be made to achieve it. The treatment should be started as soon as the clinical diagnosis has been made to prevent blindness and other potentially irreversible ischemic complications of Horton's disease.

Keywords: Horton's disease, vasculitis, elderly women, temporal arteritis

INTRODUCTION

Horton's disease, also called giant cell arteritis or temporal arteritis, is a vasculitis which affects large, medium and small vessels, particularly superficial temporal arteries. It is the most common form of vasculitis which occurs in patients older than 50 years (1,2). The aetiology remains unknown, but genetic, infectious and autoimmune factors have been incriminated. Age and female sex (female:male = 2:1) are the most important risk factors for temporal arteritis (1). Even if physiopathology remains uncertain, it is based on an immunologic inflammatory response followed by intimal hyperplasia which can narrow the arterial lumen leading to stenosis (1,2).

Clinical manifestations and organ involvement are related to the inflammatory reaction and occlusion of the arteries. The transmural and patchy inflammation makes the histopathological diagnosis hard to establish. Common symptoms include headache, shoulder and pelvic girdle pain, jaw claudication, visual disturbances, fever and prodromal symptoms such as fatigue, myalgia, night sweats and weight loss. These constitutional symptoms may persist for couple of weeks and because of that, the disease is often misdiagnosed and managed inappropriately. Early diagnosis and prompt initiation of treatment are essential to prevent blindness and other potentially irreversible ischemic complications of Horton's disease (3,4).

Moreover, it is an ischemic disease and should be treated as a medical emergency. Temporal arteritis overlapping with polymyalgia rheumatica is one of the most common reasons for long-term corticosteroid therapy prescription (5).

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CASE REPORT

We present the case of a 71-year-old-woman, having a family history of autoimmune disease – one daughter with systemic lupus erythematosus and a personal history of: hypertension, chronic gastritis and hiatal hernia, who complains of bilateral shoulder and pelvic girdle pain and general manifestations: low fever, night sweats, fatigue and unintentional weight loss.

In order to determine the causative factor of her symptoms, she was referred to her family doctor. After the initial common blood tests which have been made, the patient has been diagnosed with iron deficiency anaemia. The family doctor started paraclinical investigations regarding a gastrointestinal pathology. The clinical and paraclinical examinations (upper digestive endoscopy and colonoscopy) highlighted a normal aspect of the colon and internal haemorrhoids, which cannot explain the cause of anaemia. Afterwards, another batch of basic blood tests has been made which has revealed a slight decrease of haemoglobin and serum iron, although the patient received iron supplementation for 3 months.

Next, she was admitted in haematology department where further investigations have been done. In addition, laboratory tests revealed raised inflammatory markers (erythrocyte sedimentation rate (ESR) of 66 mm/h) and high ferritin levels. Due to the lack of improvement in the clinical manifestations, the presence of inflammatory syndrome and unresponsive anaemia to oral iron treatment, the patient was admitted in our rheumatology department 5 months later.

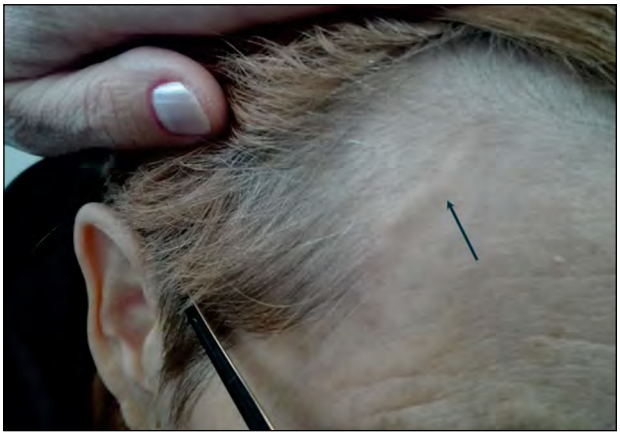

FIGURE 1. *Enlarged right temporal artery*

On admission, the patient complained of important bilateral shoulder and hip girdle pain and morning stiffness which lasts over 5 months, jaw claudication and amaurosis fugax. The clinical examination highlighted an abnormal right superficial temporal artery: enlarged, thickened, tender, with a reduced pulsation (Figure 1). Auscultation of the heart and blood pressure were normal, and the abdomen was painless. Blood tests revealed: normochromic normocytic anaemia, reactive thrombocytosis (490,000/mm^3), increased inflammatory markers (ESR=120 mm/hour and C-reactive protein (CRP) = 14.57 mg/dl), iron deficiency (12.6 µg/dl), high ferritin levels (374 ng/ml). Immunological profile regarding rheumatoid factor (RF) and anti-citrulline protein antibodies (ACPA) was negative. The panel of ANA was in normal limits and p-ANCA and c-ANCA were negative.

Then, we performed a vascular doppler ultrasound that showed the occlusion of the front branch of the right temporal artery and the presence of atherosclerotic lesions at the level of internal carotid arteries (Figure 2). The parietal branch of the right superficial temporal artery and the left temporal artery were normal.

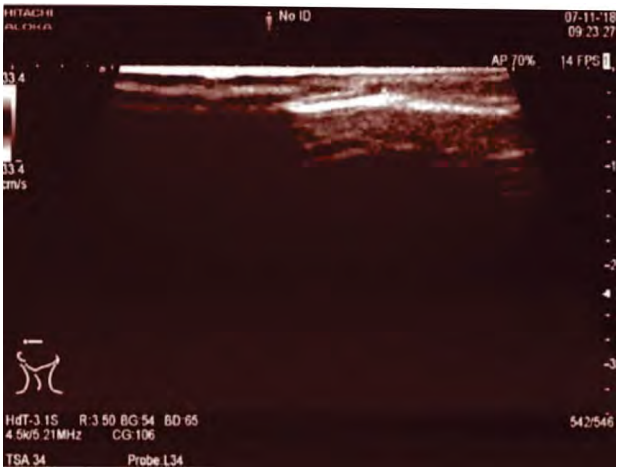

FIGURE 2. *Occlusion of the front branch of the temporal artery*

The angio-computed tomography of the head did not show other lesions, except for bilateral atherosclerotic calcification of the internal carotid arteries. The bilateral temporal artery wall was permeable, and the arteries diameters were within the normal limits (1.3 mm).

The ophthalmological consultation did not show signs of ischemic optic neuropathy.

The temporal artery biopsy was not performed, but the anamnestic, clinical and paraclinical results along with the diagnosis criteria, allowed us to establish the Horton's disease (temporal arteritis) diagnosis. For the diagnosis, we used the 2016 ACR re-

vised criteria for early temporal arteritis: age at onset more than 50 years old, sudden onset of visual disturbances (amaurosis fugax) (1 p), presence of polymyalgia rheumatica (2 p), jaw claudication (1 p), abnormal temporal artery (up to 2 p), unexplained fever and anaemia (1), ESR ≥ 50 mm/h (1 p).

In order to prevent blindness or other potentially irreversible ischemic complications of Horton's disease, the patient immediately received corticosteroid therapy having a prompt clinical and paraclinical response. The clinical symptoms disappeared, the normochromic normocytic anaemia corrected, and the inflammatory markers significantly decreased within 2 weeks of treatment.

Unfortunately, the patient developed side effects to corticosteroid therapy: facial aspect of Cushing syndrome, hyperglycemia and hypercholesterolemia. However, the prognosis of the patient was good, leading to a complete recovery.

DISCUSSIONS

The onset of Horton's disease may be either acute or insidious. The headache in Horton's disease is mostly localized in the temporal area. It is either new, in a patient without a history of headaches, or having a new type, in a patient with chronic headache. 38% of people may not present this initial symptom (6), as was the case with our patient. Usually, the disease has nonspecific symptoms, such as fever, fatigue and weight loss.

About 50% of patients develop transient episodes of visual loss which are mostly unilateral, painless and reversible (6). This can be irreversible if treatment is not promptly initiated. In our case, even if the patient experienced amaurosis fugax, which occurs in 2% of the cases (5,6), there was no evidence of ischemic optic neuropathy. However, ischemic signs, such as jaw claudication, were present (3,4,6).

Laboratory tests show an elevation of inflammatory markers (ESR, CRP). The ESR is usually more than 50 mm/h and in some cases, like our patient, may exceed 100 mm/h. The complete blood cell count reveals mild inflammatory anaemia (which is a normochromic normocytic anaemia). This type of anaemia is characterized by hyposideraemia due to the iron blocking in macrophages and requires etiologic treatment. In our case, the anaemia didn't respond to oral iron tablets for 5 months, but it disappeared 2 weeks after the initiation of corticosteroid therapy. Platelet counts are usually mildly elevated and the rheumatoid factor, complement levels, antinuclear antibodies, and other antibodies are within normal limits 6).

For a certain diagnosis, we need an artery biopsy. According to some studies and to 2016 revised ACR criteria, which proposed a clinical management tool using rACR scores, the temporal artery biopsy is not necessary if rACR ≥ 5 (7,8). In our case, we have a rACR score of 8 points, so this 71-year-old woman has a certain diagnosis of Horton's disease (9,10).

Another important thing is related to recommendations on imaging in temporal arteritis. Ultrasound can complete the clinical diagnosis criteria and make artery biopsy not required (11).

The 2018 EULAR guidelines highlight that the first-line imaging investigation in patients suspected of Horton's disease is temporal artery ultrasound, and if it is not available, it can be used a high-resolution magnetic resonance imaging or a computed tomography. Moreover, in patients having a high clinical suspicion of temporal arteritis and a positive imaging investigation, the diagnosis can be established without biopsy. If there's a low clinical suspicion and a negative imaging investigation, the Horton's disease diagnosis is unlikely. In the case of high suspicion of temporal arteritis, the imaging investigations should not delay the initiation of treatment (11-15).

In our case, the clinical manifestations, paraclinical investigations (including the ultrasound) along with a rACR score of 8 points, allowed us to establish the Horton's disease diagnosis, without an artery biopsy.

From the beginning, the case was challenging due to nonspecific symptoms of the onset. The central element was represented by anaemia, which has not been corrected until the establishment of the etiologic treatment of the disease. Despite improvements in diagnosis methods, Horton's disease carries the risk of severe ischemic complications which can be prevented by an early treatment.

The universally accepted treatment remains corticosteroid therapy. Both American and British guidelines recommend oral corticosteroid treatment by adjusting the doses depending on complications (especially evolving visual disturbances), disease severity, co-morbidities and adverse events. Patients should also receive bone and gastrointestinal protection. Those who experience acute visual changes from temporal arteritis, may need intravenous methylprednisolone daily for three days before oral prednisolone (15,16).

In order to prevent a disease relapse, all patients will require long-term low-dose corticosteroid therapy. The common patient with Horton's disease remains on steroid therapy for at least 2 years and has follow-up visits at weeks 1, 3, 6 and then in months 3, 6, 9, 12 during the first year (16).

Due to the adverse events of the corticosteroid therapy and multiple severe complications of the disease, immunosuppressive therapy prescribed at the presentation can be useful. It could help to obtain a faster withdrawal of steroids, to control the severe manifestations of the disease or to reduce the relapse rate. Methotrexate and Azathioprine are the most common immunosuppressive agents used for their efficient steroid-sparring effect (17-21).

In our case, because of the visual disturbances, we initiated the intravenous methylprednisolone daily for three days. After that, the patient received 40 mg of oral prednisone daily, continued for four weeks. The resolution of symptoms and laboratory abnormalities were seen after 2 weeks of treatment, so this allowed us to reduce the initial oral dose of corticosteroid therapy. In order to prevent a relapse of the disease and for a faster decrease in steroid dose, we associated an immunosuppressive agent (Azathioprine 100 mg daily). Therefore, no relapse has been seen within 6 months of treatment.

CONCLUSIONS

Clinical manifestations of temporal arteritis are nonspecific leading to a delayed diagnosis. Inflammatory anaemia is a frequent condition that can be associated with many different disorders, raising real differential diagnosis problems.

This is just another case which supports the fact that Horton's disease is still an overlooked diagnosis in elderly women. Even if sometimes it can be hard to reach the diagnosis, every effort should be made to achieve it. The treatment should be started as soon as the clinical diagnosis has been made to prevent blindness and other potentially irreversible ischemic complications.

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