

Clinical Aspects of the Temporal Arteritis

Francisco Xavier Palheta Neto*, **Kássia Lima Carneiro****, **Orlando Maciel Rodrigues Junior****,
Adilson Góes Rodrigues Junior***, **Celidia Cristina de Souza Jacob*****,
Angélica Cristina Pezzin Palheta****.

* Master's Degree in Otorhinolaryngology at the Federal University of Rio de Janeiro. In course for Doctor's Degree in Neurosciences at the Federal University of Pará. Assistant Professor at the Federal University of Pará and University of the State of Pará. Preceptor of the Medical Residence in Otorhinolaryngology of the University Hospital Bettina Ferro de Souza.

** 3rd year student of the Course of Medicine University of the State of Pará.

*** 2nd year student of the Course of Medicine. Federal University of Pará.

**** Master's Degree in Otorhinolaryngology at the Federal University of Rio de Janeiro. In course for Doctor's Degree in Neurosciences at the Federal University of Pará. (Assistant Professor at the University of the State of Pará. Preceptor of the Medical Residence in Otorhinolaryngology of the University Hospital Bettina Ferro de Souza.)

Institution: Centro de Otorrinolaringologia do Pará - COP.
Belém / PA - Brazil.

Mail address: Francisco Xavier Palheta Neto - Avenida Conselheiro Furtado, 2391, sala 1608 - Bairro: Cremação - Belém / PA - Brazil - Zip code: 66040-100 - Phone numbers: (+55 91) 3249-9977 or 3249-7161 and 9116-0508 - E-mail: franciscopalheta@hotmail.com

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SUMMARY

- Introduction:** The Horton's disease, or temporal arteritis, is the most common autoimmune systemic vasculitis in adults, especially the old-aged.
- Objective:** To review the literature about the several aspects of the Horton's disease, and confirm the otorhinolaryngologic clinical manifestations.
- Method:** The study searched online databases such as EMedicine, Encyclopedia of Medicine, FindArticles, LILACS, MEDLINE, Merck Manuals On-Line Medical Library and Scielo, and applied to the search the terms: Horton's disease, Temporal Arteritis and Giant Cells Arteritis, for articles published between 1996 and 2008.
- Literature's Review:** The disease's clinical manifestations start after 50 years old, and it's more frequent near 72 years old. The intense headache, temporal tumefaction, mandibular claudication and visual loss are the main signals and symptoms. There may occur dysacusis, necrosis of the tongue and odynophagia.
- Considerations:** Lots of aspects of the Horton's disease do not have their due elucidation and, even being a disease that affects many adults, it doesn't have deep investigations in great quantity. A better understanding of this disease will lead to the increment of cure possibilities and reduction of morbidity in the patients, especially in ophthalmologic and otorhinolaryngologic areas.
- Keywords:** Horton's disease, temporal arteritis, giant cells arteritis.

INTRODUCTION

The Horton's disease, also known as giant cells arteritis (GCA), temporal arteritis or cranial arteritis (1) (2), is a chronic granulomatous vasculitis, of unknown etiology, that affects individuals older than 50 years, Caucasian, and specially of the feminine sex.

Its clinical manifestations depend upon the location of the relative or absolute ischemia of the territories irrigated by the affected vessels (3). Clinically, most cases have an insidious beginning, which explains the delay until the diagnosis that many times is observed in this disease (5).

The vision loss for ischemic optical neuropathy is the most feared complication, in addition to cerebral infarct and aortic aneurysm. In the otorhinolaryngologic focus, there may occur neurosensorial hearing loss and lingual necrosis (4) (6).

The diagnosis is eminently clinical and laboratorial, with histopathological confirmation, and its treatment is made with long-term corticotherapy (7).

The mortality for temporal arteritis results mainly from secondary factors and seldom from direct factors, with the aortic rupture. However both mortality and morbidity associated to such vasculitis are higher and higher, specially due to its clinical manifestations, the age of the population affected and the relative therapeutic aggressivity.

Because it is a multisystemic disease of late diagnosis and growing morbimortality, the accomplishment of a literature review is necessary whose objective is to clarify its clinical signs and symptoms, as well and confirm its otorhinolaryngologic manifestations both before the poorly broadcast knowledge of this disease and its relevance.

METHOD

The review was made by means of researches on online databases, which provided articles and information for the production of such bibliographic review, and the sources and references to be accessed at any time for research and improvement, taking into account the scientific literature is constantly being renewed.

The databases examined were EMedicine, Encyclopedia of Medicine, FindArticles, LILACS, MEDLINE, Merck Manuals On-Line Medical Library, and SciELO, by using the searches of the terms "Horton's Disease", "Temporal Arteritis", "Giant Cells Arteritis" for publications issued between 1998 and 2008.

LITERATURE REVIEW

General Features

The Horton's disease is an autoimmune systemic granulomatous chronic vasculitis characterized by the tumefaction of large and medium vessels, specially the aorta and cranial arteries, namely the carotids extracranial branches (3, 4).

It was Initially described in 1890 by HUTCHINSON, who observed it in the shape of a very painful inflammation of the temporal artery in an 80-year-old patient. Some years after, HORTON and collaborators made the clinical and histopathological correlations of the disease and named it temporal arteritis. Later on, the term "Horton's Disease" ended up being consecrated. In 1938, both mono and binocular vision loss was registered for the first time as a complication in the affected patients. In 1960, PAULLEY E HUGHES described many forms of the disease. Since then, more varied types of clinical manifestations, prognostics and complications were observed (2).

Epidemiology

The Horton's Disease is the most prominent vasculitis in adults older than 50 years, with peak of incidence between 70 and 80 years (3), and it's of about 200 cases per 100.000 inhabitants, specially in the old-aged, and the age average of 72 years, with large variation from country to country (4).

Women have from 2 to 6 times more chances to be affected than men (1), probably due to hormonal factors; however we observed that the female sex prevalence is associated with the rheumatic polymialgia and not in its pure form (5). The percentage is also higher in persons with a history of smoking. The disease doesn't have preference for racial type, but is slightly higher in Caucasians, specially Scandinavian descendents, which probably relates to the distribution of the HLA-DR4 antigen among the races.

Etiopathogenesis

Until today the etiopathogenesis has not been fully clarified. It's known it's a reaction depending on T-cells activated by antigen and that the giant cells hurt the inner coat and also damage the vessels elasticity, since they damage the vessels whose wall contains elastic tissue, and suggest that the elastin becomes antigenic in time and

starts an immunomediated inflammatory reaction; however, no anti-elastin antibodies were found (8). Nevertheless, an important feature is the fact the intracranial arteries are saved for they don't have elastic tissue. So we can say the more elastic tissue there is in the artery, the greater the probability to develop Giant Cells Arteritis (7, 8).

The most frequently involved arteries are superficial and vertebral temporal in 100% of the cases; followed of ophthalmic arteries in 76%; posterior ciliary in 75%; external carotid in 45%; internal carotid in 38%, and the cavernous and petrous segment of the internal carotid artery is reached in about 60% of the cases, while the internal carotid artery cervical segment and common carotid artery are involved in less than 25% of the patients; the central area of the retina presents with 26% and its proximal portion is the most affected (60%); the aorta is involved in 14% and in a minor proportion in coronary, mesenteric and femoral arteries in 10% of the cases (8) (9). It's worth remarking that the affection of the orbitary cavity arteries also has a relation with the quantity of elastic tissue the different arteries contain in its walls. While the ophthalmic and ciliary posterior arteries contain a moderate quantity of elastic tissue, the retina central artery doesn't contain much elastin, mainly when it penetrates the optical nerve sheath, and specially after perforating the nerve substance (9).

The inflammatory process typical of giant cells arteritis is generally superposed to the arteriosclerotic changes found in adults and old-aged. The inflammatory lesions are generally distributed in a sparse and uneven manner along the course of the affected vessels. Mostly important among all changes is the granulomatous inflammatory process in several focuses with the presence of lymphocytic, histiocytes and epithelioid cells along the elastic lamina and involving the medium and adventitious layers. Multinuclear giant cells are commonly seen in the vicinity of degenerated muscular cells or sometimes close to the elastic fragmented cell. The adventitious layer inflammation is prominent (8, 9).

However, there are traces that in addition to the immune system, other factors are involved, such as infectious, environmental, racial origin (Caucasian Europeans), degenerative processes relating to aging and genetics, because it's known the patients with Giant Cells Arteritis and its variant Rheumatic Polymyalgia have an increased prevalence of antigens of histocompatibility HLA, DL-4 and CW3 (7, 8).

The involvement of nerves and nervous terminations on the artery wall and surface is what causes spontaneous pain and the artery pulsation (9).

Signs and Symptoms

Generally the constitutional symptoms precede the headache, polymyalgia and ocular and neurological manifestations. The systemic symptoms include fever, adynamia, inapetency, weight loss and unspecific myalgias, mainly in the morning, with rigidity of the neck and the musculature of the pelvic and shoulder girdle (8, 9), as well as night sudoresis and anorexia (5).

The rheumatic polymyalgia with pain and hardening of the neck, dorsum, pelvic and shoulder girdle, as well as the upper and lower ends proximal muscles is common in the GCA. The claudication during the walk may also be observed (9).

Jaw claudication is an GCA's classical symptom. The patient feels pain when he chaws or talk longer and improves with rest and it occurs in cases where there is facial artery involvement. The tongue and deglutition muscles claudication and chewing muscles spasms, named as lockjaw may also occur (8, 9).

The ophthalmic manifestations are numerous, among which we remark non-arteritic anterior ischemic optic neuropathy (NAION), that forms one of the most common and severe disease's sequels, and it was reported in between 7% to 60% of the patients. Other causes for vision loss in GCA include posterior or retrobulbar ischemic optic neuropathy, much less frequent than NAION, ischemic ocular syndrome and obstruction of the central artery of the retina or its branches. Ischemia of the anterior segment of the eye with keratopathy, chemosis, scleritis and episcleritis and unevenness of the pupil shape may also occur. Later findings include cataract, secondary glaucoma, rubeosis iridis and nonreactive pupils (8, 9).

Campimetric defects and cortical blindness, resulting from the vertebral, carotid and hypofisary arteries involvement have also been reported (9).

Ophthalmoplegia is a frequent manifestation of the GCA and, sometimes, when the tropy measures only a few dioptries, the patients complain of diplopia without the ophthalmoparesis to be detected in the clinical exam. The contrary, that is, ophthalmoplegia without diplopia, is very common, and it occurs when the vision is significantly reduced. The ophthalmoplegia may precede other more common manifestations of the disease (9).

Anisocoria occurs rarely in the GCA, since the ciliary ganglion is rich in anastomoses. However the mydriasis associated with ophthalmoplegia has been reported. The Horner's syndrome may develop following the central,

pre-ganglionic or post-ganglionic oculo-sympathicomimetic neurons ischemia (9).

Within the neurologic manifestations, the main complaint is headache which is the GCA's cardinal affection and the most frequent complaint that leads the patient to the doctor. Such headache is from a short time ago, about 15 days to 1 month and is different from other headaches the patient could have had before. It's characterized by an intense, persistent, unilateral or bilateral pain in the temporal region and even an occipital (1), lancinating and pulsating pain (5), with periods of exacerbation, and presents with tumefaction, softening and hypersensitivity in the temporal region in about 25% of the cases (5, 10). Some report pain in any part of the head or diffusely as in the muscular contraction headache (9).

In addition, it may present with a number of other manifestations, such as, depression, mental confusion, dementia, psychosis; infarct or cerebral hemorrhage, transient ischemic episodes; ataxia, trembling, deafness, tinnitus, vertigo (manifestations relating to the facial artery); facial paralysis, syncope, convulsions, meningism, insipid diabetes; transverse myelopathy and peripheral neuropathies (8).

Such other manifestations are not as frequent as headache, but in some cases it may be absent, and there's the presence of other symptoms (Arteritis of Hidden Giant Cells). In this case, the visual loss for anterior ischemic optic neuropathy may be the first manifestation. It's a significant feature, because approximately 32% of the Giant Cells Arteritis may exist without headache (8, 9).

The main otorhinolaryngologic manifestations are dry persistent cough, odinophagy, dysphonia, lingual paresthesia and claudication, buzz, glossitis, lingual ischemia and necrosis and neurosensorial dysacusis, which may range from slight to deafness in case the treatment is not duly performed (3, 7, 11) (12, 13).

Diagnosis

The Giant Cells Arteritis diagnosis is mostly clinical. Recently the *American College of Rheumatology* reviewed the GCA diagnostic criteria. By this format, a patient is deemed to be a carrier of GCA if, at least, three of the five criteria are met. The presence of three or more of these five criteria is associated to a sensitivity of 93.55% and a specificity of 91.2% (9). The criteria are: Age equal or higher than 50 years; local headache and of recent beginning (the temporal arteritis may cause occipital or frontal headache) (9); temporal artery abnormalities; elevated erythrocyte sedimentation rate (higher than 50 mm/h);

abnormal arterial biopsy (with necrotizing arteritis or multinuclear giant cells, for instance) (14, 15).

In the initial phase, the exam may reveal only subtle changes such as soreness upon the artery palpation. With the disease's progression, the artery tends to become ingurgitated, tortuous and salient. The area adjacent to the vessel may be edemaciated. Generally upon palpation the artery becomes thick, hard and nodular and the soreness expands to the circumjacent region. The pulse is commonly diminished or absent in the advanced phases. The retinal examination is normal in an individual with full vision. In cases of ischemic optic neuropathy, in the acute phase, the papilla is edemaciated and with small hemorrhages. In the chronic phase, such changes are replaced for paleness and atrophy (5).

The visual loss is an important finding. About 20% of the patients with GCA and visual loss don't have the disease's systemic symptoms. In the other hand, approximately 25% of the patients with GCA present visual accuracy equal or better than 20/40. The visual loss generally results from the anterior ischemic optic neuropathy. Thus, we should suspect of GCA in patients above 50 years old with this ophthalmologic condition diagnosis, and start the corticotherapy (even with normal ESR) (14).

The most consistent laboratorial abnormality is the increase of the erythrocyte sedimentation rate (ESR), which is above 100mm in the first hour in 41% of the patients, and higher than 31 in 89%. However within the normality range the ESR doesn't prevent the diagnosis. The reactive protein C is also elevated in the GCA. Other possible laboratorial changes include: Slight normocytic normochromic anemia; discreet leucocytosis; liver function abnormalities, more commonly discreet increases of the of alkaline phosphatase and transaminases; elevation of the plasma fibrinogen levels; alpha-2 globulin, complement and gamma-globulin and albumin reduction (5).

The temporal artery biopsy must be carried out in all patients for whom there is suspicion of GCA based on the anamnesis and physical exam, even if the ESR had been normal (5). We must perform temporal artery unilateral biopsy and keep on with the treatment when the biopsy is positive. When the biopsy is negative, but the clinical suspicion is high, we should perform contralateral biopsy. In the patients with intermediate clinical suspicion we should request temporal artery biopsy and ESR. This group is composed by patients with any of the criteria of major specificity or with anterior ischemic optic neuropathy. Moreover, any of the following findings represent an intermediate clinical suspicion: High ESR, recent beginning headache in old-aged patient, or clinical changes of the

temporal artery. If both temporal arteries biopsy is negative, other reasons for ESR increase must be researched (infectious diseases, neoplasms, diabetes or conjunctive tissue diseases, for example). In patients with normal ESR and temporal artery unilateral biopsy without changes, the GCA diagnosis is not much probable. However, up to 30% of the patients with normal ESR presented with suggestive biopsy of GCA; therefore, other changes must be researched (14).

The microscopic exam reveals a panarteritis with perivascular inflammatory infiltrate, intima hypertrophy, medium necrosis associated with granulomatous tissue formation, presence of giant cells and light thrombosis. There is interposition of healthy and other committed areas. Biopsies obtained in initial phases normally reveal a prevalence of inflammatory infiltrate, while in the more advanced phases, we observe more easily the formation of granuloma and giant cells. It's important to note that in about 40% of the arteries studied the multinuclear giant cells are absent (5).

In the context of temporal arteritis, the peripheral nervous system involvement is not much frequent (3). Therefore, to achieve the giant cells arteritis diagnosis, we must try and make blood tests, biopsy, ophthalmologic exam, angiography, ultrasonography and thyroid function. The differential diagnosis includes dental problems, trigeminal neuralgia, sinusitis, otitis, blood vessels or ocular muscles alterations, among many other causes of headache (16).

Treatment

The treatment of patients with temporal arteritis is crucial to avoid vision loss and the therapy should be started based on the clinical suspicion, and not on the biopsy results (17). We use one type of corticosteroid, prednisone. Typically, the treatment begins with 40-60mg orally everyday in adults (16), and may reach 60-100 mg per day (17). The dosage for children is normally of 1mg/kg of weight (1). Another drug that may also be used is methylprednisolone (2). The main objective of the corticotherapy is the prevention of blindness, mainly when one of the eyes has already been affected, or of other severe complications of the disease. Once the steroid dosage is defined, it must be maintained until the symptoms have disappeared and the erythrocyte sedimentation rate is back to normal (14). Therefore, inflammatory reaction proofs must be monitored, such as the VSG decrease and C reactive protein. The GCA has a self-limited course that generally lasts for one to two years, but may last from months to 14 years and the use of corticoids must be suspended between 6 months and 2 years. Special attention and care should be given to their use, because they may cause or aggravate osteoporosis, psychosis and digestive

hemorrhage (18). However the disease progression is not uncommon with the occurrence of anterior ischemic optic neuropathy (NAION) in the second eye of a patient receiving conventional dosages of corticosteroids (14). Special attention should be given to the risk of blindness, although it's not very common, which justifies the aggressive treatment (19). Another medications category that may be implemented is that of immunosuppressors, which suppress key-factors involved in the immunologic reaction; the two choice drugs are azathioprine and methotrexate (1). There isn't not much information about the treatment of patients with GCA, who present with contraindications for the use of corticoids, although some defend the use of metotrexate, or of other immunosuppressive drugs (15). Some have been suggesting the use of aspirin or anticoagulants in the treatment of the temporal arteritis to prevent ischemic lesions, due to reports of thrombocytosis in some patients (18).

Prognosis

The prognosis of this entity is good, when it's well treated. The patients survival is not different from the general population in the same age range (20). With the treatment, most individuals achieve complete remission; however, the vision loss may be irreversible (21). If the aorta artery or some of its affluent vessels are involved, the prognosis may be worse, because such vessels may enlarge and even break up. However, most complications relating to giant cells arteritis are caused more by the therapy with steroid hormones than by the disease itself (22).

FINAL CONSIDERATIONS

The Horton's syndrome is the main vasculitis in adults older than 50 years and may be the cause for severe otorhinolaryngologic complications, such as the lingual necrosis and dysacusis, and mainly for ophthalmologic complications, which include ischemic optic neuropathy. In spite of the advances, we still need to research too much about the syndrome's etiopathogenesis, because some data are still uncertain. Several autoimmune mechanisms are related and they cause the arterial inflammatory process. A stronger knowledge about the beginning, development and diagnosis of the temporal arteritis will contribute for the treatment evolution and possibility of more satisfactory prognoses.

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