Systemic and Relapsing Nature of Temporal Arteritis

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Abstract

Aim: The aim of this study was to determine the prevalence of temporal arteritis (TA) and temporal phlebitis (TP) in polymyalgia rheumatica (PMR), to assess the involvement of blood vessels of different caliber, and to verify the relapsing nature of the disease.

Patients and Methods: Surgical biopsy specimens of the temporal artery of 299 patients with PMR were studied. PMR was clinically diagnosed at the National Institute of Rheumatology between 1991 and 2005 according to the criteria of Bird., et al.

TA was diagnosed and characterized histologically based on the cellular infiltration and structural changes of the blood vessels. TA was classified according to Flood., et al. Demographics of different patient cohorts were compared with the Student (Welch) t-probe. The link between blood vessels of different caliber with inflammatory infiltration, and the relationship between TA and TP were analyzed by Pearson's chi-squared (χ²) test.

Results and Conclusions: Segmental or sectoral TA was associated with PMR in 71 (23.75%) of 299 patients. PMR existed without TA in 228 (76.25%) of 299 patients.

In TA the dominant involvement of medium size ateries may be accompanied with vasculitis of smaller vessels, also veins. The close statistical relationships between inflammations in arteries of different size and veins support the assumption that all of these are manifestations of the same disease.

TA, like any type of systemic autoimmune vasculitis, is recurrent pathological process. Sectorial or segmental cellular infiltration in different stages of inflammation and chronic structural changes of the vessel wall exist side by side and indicate the relapsing nature of inflammation.

The early diagnosis of TA in PMR patients is important because of the high risk of loss of vision. An adequate biopsy of the temporal artery requires a length of at least 1.5 - 2 cm, with smaller branches and veins together, and the entire biopsy specimen has to be examined microscopically.

Keywords: Polymyalgia Rheumatica; Temporal Arteritis and Phlebitis; Histology and Stages

Abbreviations

PMR: Polymyalgia Rheumatica; TA: Temporal Arteritis; TP: Temporal Phlebitis; GcA: Giant Cell Arteritis; Calc: Calcification of a Special Globular; DA: Dystrophic Amyloid Deposits; Chr st: Chronic Stage

Citation: Miklós Bély and Ágnes Apáthy. "Systemic and Relapsing Nature of Temporal Arteritis". EC Cardiology 5.3 (2018): 102-117.
Systemic and Relapsing Nature of Temporal Arteritis

Introduction

Temporal arteritis (TA) or giant cell arteritis, cranial arteritis, Horton’s disease, granulomatous arteritis, arteritis of the aged is a systemic immune mediated (autoimmune) vasculitis [1].

There is a close connection between TA and polymyalgia rheumatica (PMR); TA and PMR are essentially different stages of the same disease [2]. Traditionally TA is classified as a large-vessel vasculitis [3], but all calibers of arteries, even veins may be involved [1,3,4].

Aim of the Study

The aim of this study was to determine the prevalence of TA and temporal phlebitis (TP) in PMR, to assess the involvement of blood vessels of different caliber, and to verify the relapsing nature of the disease.

Material and Methods

Surgical biopsy specimens of the temporal artery of 299 patients with PMR were studied at the National Institute of Rheumatology between 1991 and 2005. PMR was clinically diagnosed according to the criteria of Bird., et al [5].

Serial sections (5 microns) were stained with hematoxylin-eosin (HE) [6], lightgreen-orcein [7], Picrosirius red F3BA [8,9], and von Kossa reaction [10]. Amyloid deposits were identified according to Romhányi [11] by a modified (more sensitive) Congo red staining [12] and analysed histochemically according to Bély [13].

The cellular composition of inflammatory infiltration (in selected cases) was confirmed by immunohistochemical techniques using the streptavidin-biotin-complex/horseradish peroxidase method [14].

TA was diagnosed and characterized histologically based on the cellular infiltration and structural changes of the blood vessels. TA was classified according to Flood., et al [1]. Demographics of different patient cohorts were compared with the Student (Welch) t-probe [15]. The link between blood vessels of different caliber with inflammatory infiltration, and the relationship between TA and TP were analyzed by Pearson’s chi-squared ($\chi^2$) test [15].

Glossary of definitions

"Prevalence" concerns the presence of vasculitis in blood vessels of different calibers. Prevalence of vasculitis was characterized based on the inflammatory infiltration and structural changes of blood vessels.

Size of blood vessels in surgical specimens with branches of temporal artery [16]

- Arteriole (a): No internal or external elastic membrane, < 500 micrometers in diameter
- Small artery (A): Only internal elastic membrane present, vessels 500-1000 micrometers in diameter
- Medium size artery (AA): Internal and external elastic membrane are present – vessel > 1000 micrometers in diameter
- Venule (v), small vein (V), medium size vein (VV): Accompanying (a), (A) or (AA)

Histologic patterns of TA according to Flood., et al [1]

- Classic: Characterized by transmural inflammation of T-cells, macrophages (histiocytes) and multinucleated giant cells, with intimal thickening
• **Atypical:** Is an intermediary stage of classic and healed TA, characterized by less dense inflammatory infiltrate predominantly of lymphocytes (with or without macrophages, and without giant cells). The inflammation tends to be most marked in the adventitia, and is accompanied by more or less pronounced structural changes (intimal proliferation, fragmentation or distortion of internal elastic lamina)

• **Healed:** (Chronic stage) is characterized by moderate inflammation. The intima is irregularly thickened (with luminal stenosis or occlusion), and exhibits fibromyxoid change, with or without neovascularization. The internal elastic lamina is multiple, fragmented and discontinuous. Media and adventitia are more or less fibrotic.

**Stages of TA based on the inflammatory infiltration and structural changes of blood vessels of different calibers**

• **"a":** Polymorphonuclear neutrophilic leukocytes are present (with or without eosinophils) - "a" represents acute exacerbation of inflammation (acute stage) in combination with "b" or "c" and occasionally with "d". There is no appropriate class according to Flood., et al[1].

• **"b":** Characterized by intensive transmural inflammatory infiltration (involving complete cross section of the blood vessels, dominated by T-lymphocytes with or without multinucleated giant cells and macrophages (histiocytes), and moderate structural changes of blood vessels (intimal proliferation, distortion of internal elastic lamina) - "b" with multinucleated giant cells corresponding to the "classic" type of TA according to Flood., et al[1].

• **"c":** More or less pronounced inflammatory infiltration is accentuated towards the outer layers of the blood vessel wall (in the media and adventitia), and dominated by T-lymphocytes (without multinucleated giant cells, with or without macrophages): pronounced structural changes (intimal proliferation, stenotic or occluded lumen, multiple, fragmented, discontinuous, distorted internal elastic lamina) - "c" corresponds to the "atypical" form of TA according to Flood., et al[1].

• **"d":** Minimal or missing lymphocytic infiltration (without multinucleated giant cells and macrophages): dominant structural changes of the blood vessels (adventitia and media fibrotic, intima massive, irregularly thickened, with or without fibromyxoid changes and neovascularization, internal elastic lamina is multiple, fragmented and discontinuous) - "d" corresponds to the "healed" stage of TA according to Flood., et al[1].

**Results**

Segmental or sectoral TA was associated with PMR in 71 (23.75%) of 299 patients. PMR existed without TA in 228 (76.25%) of 299 patients.

Demographics of PMR patients with or without TA are summarized in table 1.

<table>
<thead>
<tr>
<th>Sex</th>
<th>N of patients</th>
<th>Average age in years at biopsy</th>
<th>Range (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMR patients</td>
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<td>71.19</td>
<td>88 - 43</td>
</tr>
<tr>
<td>Female</td>
<td>258</td>
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<tr>
<td>Male</td>
<td>49</td>
<td>70.60</td>
<td>86 - 51</td>
</tr>
<tr>
<td>PMR with TA</td>
<td>71</td>
<td>73.25</td>
<td>88 - 53</td>
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<tr>
<td>Female</td>
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<td>73.47</td>
<td>88 - 53</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>71.43</td>
<td>82 - 58</td>
</tr>
<tr>
<td>PMR without TA</td>
<td>228</td>
<td>70.53</td>
<td>88 - 43</td>
</tr>
<tr>
<td>Female</td>
<td>189</td>
<td>70.55</td>
<td>88 - 43</td>
</tr>
<tr>
<td>Male</td>
<td>39</td>
<td>70.44</td>
<td>85 - 51</td>
</tr>
</tbody>
</table>

Table 1: Sex, average age (range) of 299 PMR in patients with (n = 71) and without TA (n = 228).

The average age of PMR patients with TA was significantly higher than the average age of PMR patients without TA (p < 0.0164). Comparing the average age of females with and without TA, the relation between them was the same (p < 0.0159). The difference between the average age of male patients with and without TA was not significant (p < 0.7951).

TA of medium size arteries was present in 52, TA of small arteries in 18, and TA of arterioles in 42 of 299 patients, separately or in combination.

TA of medium size arteries coexisted simultaneously with TA of small arteries in 11, and with TA of arterioles in 33 of 299 patients.

There was a strong positive and significant correlation between TA of medium size and small arteries ($\chi^2 = 25.4821, p < 0.0001$) or arterioles ($\chi^2 = 127.3067, p < 0.0000$). The relationship between TA of small arteries and of arterioles was also significant ($\chi^2 = 53.6878, p < 0.0000$). Inflammation of temporal veins was present simultaneously with TA in 10 of 299 patients. There was a strong positive and significant correlation between TA and TP ($\chi^2 = 21.2063, p < 0.0001$).

According to the classification of Flood., et al. [1] TA was “classic” in 11 (15.49%), “atypical” in 44 (61.97%), and “healed” in 16 (22.54%) of 71 cases.

“Classic” corresponded to TA with multinucleated giant cells, “healed” to chronic stage of TA with minimal (“d”) or missed lymphoid infiltration, and marked chronic structural changes of blood vessels, and “atypical” corresponded to the rest.

The histological characteristics of inflammation and the structural changes of blood vessels with different caliber are summarized in table 2.

**Citation:** Miklós Bély and Ágnes Apáthy. “Systemic and Relapsing Nature of Temporal Arteritis”. *EC Cardiology* 5.3 (2018): 102-117.
Presence of inflammation in blood vessels of different calibers in surgical specimens

<table>
<thead>
<tr>
<th>Artery</th>
<th>Small A</th>
<th>Medium AA</th>
<th>Female</th>
<th>Small V</th>
<th>Medium SV</th>
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<td>Y</td>
<td>Y</td>
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Stages of inflammation and structural changes in blood vessels of different calibers

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<th>Medium AA</th>
<th>Female</th>
<th>Small V</th>
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</table>

Other characteristics

<table>
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<tr>
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<th>Female</th>
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</table>

TA specified according to Flood, et al.

Table 2: Histological characteristics and stage of inflammation in blood vessels of different caliber in PMR patients with TA.

<table>
<thead>
<tr>
<th>Artery</th>
<th>Small A</th>
<th>Medium AA</th>
<th>Female</th>
<th>Small V</th>
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<tr>
<td>Inflammation in arterioles</td>
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<tr>
<td>Inflammation in arterioles</td>
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<td>Inflammation in arterioles</td>
<td>Y</td>
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</table>

Discussion:

Giant cell arteritis (GCA) and temporal arteritis (TA) are systemic inflammatory disorders that primarily affect blood vessels of different calibers. In our study, we observed the presence of inflammation in blood vessels of different calibers in surgical specimens of temporal arteries. The systemic and relapsing nature of these conditions was evident, with different stages of inflammation and structural changes seen in blood vessels of different calibers. The negative and maximal coefficient (-1) exclude correlation between the globular type of calcification and classic atherosclerotic plaques.

Our findings support the concept of a chronic, relapsing disease process in TA, with inflammation and structural changes occurring simultaneously in blood vessels of different calibers. This highlights the importance of comprehensive assessment of blood vessels of different calibers in surgical specimens for a more accurate diagnosis and management of TA.

Future Directions:

Further research is needed to understand the mechanisms underlying the systemic and relapsing nature of TA and GCA. This could include investigating the role of immune cells and inflammatory mediators in the development of inflammation and structural changes in blood vessels of different calibers. Additionally, developing novel therapeutic strategies that target these processes could lead to improved treatment options for these systemic inflammatory disorders.
Acute thromboarteritis of medium size temporal arteries with mixed inflammatory infiltration and moderate structural changes are demonstrated in figures 1a-d.

Figure 1a-d
Main branch of medium size temporal artery with acute thromboarteritis.

(a) Acute luminal occlusion may explain the rapid progression of this patient’s symptoms, HE, x20
(b) Mixed inflammatory infiltration and relatively moderate structural changes, same as (a) HE, x40
(c) Lymphoid infiltration of the medium size main branch is accentuated in the adventitia, and is accompanied by leukocytic infiltration, HE, same as (a) x100
(d) Same as (a) HE, x200

(The original magnification corresponds to the 24x36 mm transparency slide – the correct height: weight ratio is 2:3).

Different stages of inflammation side by side, involving different caliber temporal arteries are demonstrated in figures 2a-h.
Figure 2a-h

(a) Main branch of medium size temporal artery with different stages of inflammation in different segments, HE, x20

(b) Massive structural changes with mixed inflammatory infiltration of lymphocytes and granulocytes (see d), same as (a), HE, x40

(c) Adjacent segment of b, structural changes and inflammatory infiltration are less pronounced, and are dominated by lymphocytes, same as (a), HE, x40

(d) Part of b, with mixed inflammatory infiltration of lymphocytes, giant cells, and granulocytes with focal calcification, same as (a and b), HE, x100

(e) Part of b, with massive intimal proliferation and myxoid changes; inflammatory infiltration is minimal, same as (a and b), HE, x100

(f) Part of c, less pronounced structural changes than in Figure 2b, with moderate cellular infiltration dominated by lymphocytes, same as (a and c), HE, x100

(g) Adjacent small artery with minimal structural changes and moderate sectorial inflammatory infiltration, same as (a and c), HE, x100

(h) Mixed inflammatory infiltration of lymphocytes and neutrophils same as (a and g), HE, x200.

TA and TP involving arteries and veins of different calibers are demonstrated in figures 3a-f.

Citation: Miklós Bély and Ágnes Apáthy. "Systemic and Relapsing Nature of Temporal Arteritis". EC Cardiology 5.3 (2018): 102-117.
**Figure 3a-f**

(a) Main branch of medium size temporal artery and temporal veins of different calibers with different stages of inflammation in different segments, HE, x20

(b) Main branch of medium size temporal artery, same as (a), HE, x20

(c) Main branch of medium size temporal artery, sectorially accentuated transmural inflammatory infiltration, same as (a), HE, x40

(d) Part of Figure (c), lymphocytic infiltration, multinucleated giant cell, and globular calcification, HE, x200

(e) Branch of medium size temporal vein, with sectorially accentuated mixed cellular infiltration, same as (a), HE, x40

(f) Mixed cellular infiltration dominated by lymphocytes, and occasionally with giant cells, same as (a and e), HE, x100.
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Citation: Miklós Bély and Ágnes Apáthy. “Systemic and Relapsing Nature of Temporal Arteritis.” EC Cardiology 5.3 (2018): 102-117.

Figure 4a-b
(a) Main branch, different segment of serially sectioned medium size temporal artery demonstrated on Figure 2a. Transmural sectorially accentuated inflammatory infiltration, with reactive intimal proliferation, myxoid changes, and focal calcification along the internal elastic lamina, von Kossa reaction, x40 Magyary Kossa Gyula allatorvos prof.
(b) Same as (a), von Kossa reaction, x100.

Figures 5 and 6 represent different stages of inflammation and structural changes in branches of temporal arteries.

Figure 5a-l
(a) Branches of temporal arteries, small size temporal arteries and arterioles and veins with different stages of inflammation and structural changes side by side in different segments, HE, x20
(b) Same as (a), HE, x40
(c and d) Small temporal artery, mixed inflammatory infiltration, same as (a and b), HE, (c) x100, (d) x200
(e and f) Small temporal artery, mixed inflammatory infiltration, of neutrophils, eosinophils, macrophages and lymphocytes, same as (c-d), HE, x100, (f) x200
(g and h) Small temporal artery, internal elastic lamina is present and distorted, same as (c-d), combined light green-orcein staining, (g) x100, (h) x200
(i and j) Small temporal artery, fibrotic media, adventitia is compact, same as (c-d), Picrosirius red F3BA specific for collagen, viewed under the light microscope (í) x100, (j) x200
(k and l) Small temporal artery, same as (c-d and i-j), Picrosirius red F3BA viewed under polarized light (k) x100, (l) x200.
Diversity of cellular infiltration is demonstrated in figures 6 and 7.

**Figure 6a-h (Same as Figure 5a-b)**

(a) Granulomatous temporal arteriolitis, inflammatory infiltrate of different cell-type side by side in the same blood vessel, HE, x40

(b) Lymphocytes, macrophages (histiocytes), scattered with neutrophils, same as (a), HE, x100

(c) Same as Figure (a-b), HE, x200

(d) Granulomatous temporal arteriolitis, different segment of the same arteriole, mixed inflammatory infiltrate, same as (a-b), HE, x100

(e and f) Granulomatous temporal arteriolitis, mixed inflammatory infiltrate of lymphocytes, macrophages, giant cells and neutrophils, same as (d), HE, (e) x200, (f) x400

(g and h) Part of Figure 6a, granulomatous arteriolitis, segment dominated by macrophages (histiocytes), HE, (g) x200, (h) x400.

Citation: Miklós Bély and Ágnes Apáthy. "Systemic and Relapsing Nature of Temporal Arteritis". *EC Cardiology* 5.3 (2018): 102-117.
Immunohistochemical characteristics of TA are demonstrated on figures 8-12.
Medium size and temporal artery and arteriole of different calibers with inflammatory infiltration. B-cell reaction in main branch is negative; in arteriole sporadic positivity is present for anti-human CD20 or anti-human CD79α.

(a) Anti-human CD79α [monoclonal antibody N1628; DAKO, Glostrup, Denmark], Streptavidin-biotin-complex/horseradish peroxidase reaction, x40, (b) Same as (a), x100, (c) Same as (a), x200, (d) Same as (a), x400.
Systemic and Relapsing Nature of Temporal Arteritis

Figure 10a-b
Main branch of medium size temporal artery, with cellular infiltration of macrophages. Macrophages and multinucleated giant cells are positive for anti-human CD68.
(a) Anti-human CD68 [monoclonal antibody N1577; DAKO, Glostrup, Denmark], Streptavidin-biotin-complex/horseradish peroxidase reaction, x200, (b) Same as (a), x400.

Figure 11a-b
Main branch of medium size temporal artery, arteriole and venule. In the temporal artery the endothelial cells layer is absent, in the adjacent arteriole and venule it is still present, in some segments the endothelial cell layer is damaged or disappeared. Endothelial cells are positive for anti-human CD31 and CD34.
(a) Anti-human CD31 [monoclonal antibody N1596; DAKO, Glostrup, Denmark], Streptavidin-biotin-complex/horseradish peroxidase reaction, x40, (b) Same as (a), x100.

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Systemic and Relapsing Nature of Temporal Arteritis

Discussion

In our patient cohorts PMR was five times, and TA six times more common in women than in men; PMR with or without TA in agreement with the literature is the disease of the aged, primarily illness of elderly ladies [1-3].

TA is an immune mediated disease of unknown etiology. Viruses and bacteria have been proposed as initiating the T-cell recruitment in the vessel wall [1,17]. The T-cells produce interferon-gamma (INF- γ), and activate the macrophages [18]. Macrophages (histiocytes) and multinucleated giant cells produce pro-inflammatory cytokines such as IL-1, IL-6, and tumor necrosis factor alpha (TNF-α) [18-20].

During inflammation and phagocytosis oxygen free radicals are released. They promote chemotaxis and cause direct cell damage with progressive structural changes of blood vessels (smooth muscle cell apoptosis, endothelial cells necrosis, breakdown of elastic membranes). Endothelial cell damage increases vascular permeability. The immigration of myofibroblasts leads to fibrosis of the vessel walls and fibromuscular intimal proliferation with luminal stenosis.

TA is a systemic disorder with a predilection to involve the extracranial (superficial temporal and occipital) arteries and intracranial branches of the carotid arteries (i.e. the ophthalmic, and posterior ciliary arteries), but other vessels may be involved as well, like the vertebral arteries, the subclavian arteries, the aortic wall, and rarely the femoral or coronary arteries [1].

Our study confirms the systemic nature of TA. All sizes of temporal arteries were involved with different incidence. Dominant involvement of medium size arteries (96.29%) was characteristic in contrast to small arteries (72.0%) or arterioles (95.45%), and veins (83.33%). The close statistical relationships between inflamed arteries of different sizes and veins support the impression that all are manifestations of the same disease.

TA accompanied by inflammation of medium size and smaller veins also indicates the systemic nature because phlebitis without direct contact with arteritis is more likely to be caused by circulating antigens or immune complexes returning on the venous side. The
significant and positive link between inflamed arteries and veins ($\chi^2 = 21.2063, p < 0.0001$) supports the assumed relationship between TA and TP.

TA is characterized by a segmental or sectorial inflammatory infiltrate involving branches of different caliber of the temporal artery. There was an inverse relation between the intensity of inflammatory infiltration and the structural changes of blood vessels. Massive transmural inflammatory infiltration was accompanied by relatively moderate structural changes of the blood vessels. In other words, as the initially intense inflammation subsides the structural damage becomes more pronounced. In the end stage these structural changes become dominant.

Our observations suggest that in TA the gradually decreasing inflammation with increasing structural changes represents a progressive pathological process. The presence of neutrophils in any stage of TA indicates the effect of an active substance or process that is harmful and repetitious, which accounts for the course of the inflammation.

Dominant T-cell infiltration was accompanied with or without macrophages (histiocytes) and multinucleated giant cells. Multinucleated giant cells are considered to be confluent macrophages (syncytial histiocytes) induced by some agents. According to our interpretation the “classic” type is not a stage of TA. Giant cells may be present in all phases of TA, and can be regarded as accompanying phenomena of the disease. Giant cells occur for example around calcified globules or along dystrophic amyloid deposits of internal elastic membranes independently of the stage of the disease.

According to our interpretation TA, like any type of immune mediated or autoimmune vasculitis, is a repetitive and progressive process, and not an one-time phenomenon. Sectorial or segmental cellular infiltration in different stages of inflammation and chronic structural changes of the vessel wall existing side by side indicate the relapsing nature of inflammation.

Non-degradable pathogens in chronic diseases are accompanied by persistent “acute” inflammation with constant presence of neutrophils; in case of repetitive attacks polymorphonuclear leukocytes (incl. eosinophils) are occasionally seen. In our cases neutrophils occurred in combination with more or less pronounced chronic inflammation and progressive structural changes of blood vessels. The histology of TA summarized in table 2 supports this assumption of formal pathogenesis.

Early diagnosis of TA in PMR patients is important because the high risk of loss of vision or even stroke [1-3].

Definitive diagnosis of vasculitis should be made upon biopsy of involved tissue [3,21]. In suspected TA traditionally the surgical biopsy of temporal arteries is suggested [1-3], however visual impairment or stroke is not a direct consequence of TA since the ophthalmic, ciliary or intracranial arteries are not branches of the temporal artery.

An adequate biopsy requires a length of at least 2 - 3 cm, and should be serially sectioned [1], since inflammatory infiltrates can involve a segment or sector of blood vessels.

In our practice 1.5 - 2 cm length is effective (if possible with smaller branches of temporal arteries and temporal veins together), but longitudinal and cross sections of the entire specimen have to be embedded to be serially sectioned. Forty-fifty serial section stained with traditional HE, special stains and immunohistochemical methods are requested. To demonstrate the structural changes of the blood vessels, the lightgreen-orcein combined staining specific for smooth muscle and elastica, and the collagen specific Picrosirius red F3BA are suggested. Amyloid deposits may be diagnosed with the modified Congo red staining, and the calcium phosphate and/or carbonate deposits may be identified with the classic Alizarin Red S staining or von Kossa reaction. For precise analysis of inflammatory infiltration immunohistochemical techniques are needed (in our practice the streptavidin-biotin-complex/horseradish peroxidase method was applied to identify the cell population of TA – see appendix below).
TA is a systemic disorder. Therefore examination of all available surgical or biopsy material is recommended for diagnosis of systemic vasculitis in PMR patients, with or without clinical evidence of visual or neurological impairment. When clinical suspicion of visual or neurological symptoms is raised clinically in case of PMR, a biopsy of the temporal artery is needed.

Corticosteroids suppress the inflammatory response in temporal arteritis and limit the ischemic complications of the disease [1]. Dramatic clinical response of glucocorticoid therapy can be a further support of the diagnosis [2].

Early initiation of therapy has been shown to reduce the risk of blindness and stroke, and there is general agreement that the steroids should be tapered slowly to the lowest dose required to suppress symptoms [2].

Of our 71 patients with TA only 32 (45.07%) had the complete spectrum of inflammation and structural changes of blood vessels, in 39 (54.93%) patients these microscopic changes were only partial which draws attention to the importance of individual treatment.

Conclusions

In TA the dominant involvement of medium size arteries may be accompanied with vasculitis of smaller vessels, also veins. The close statistical relationships between inflammations in arteries of different size and veins support the assumption that all of these are manifestations of the same disease. The significantly positive link between arteries and veins attest to the systemic nature of TA.

TA, like any type of systemic autoimmune vasculitis, is recurrent pathological process. Sectorial or segmental cellular infiltration in different stages of inflammation and chronic structural changes of the vessel wall exist side by side and indicate the relapsing nature of inflammation.

We interpret that decreasing inflammation with increasing chronic structural changes of the blood vessels represents a progressive process which, in combination with acute exacerbations, is characterized by occasional presence of granulocytes.

The early diagnosis of TA in PMR patients is important because of the high risk of loss of vision. An adequate biopsy of the temporal artery requires a length of at least 1.5 - 2 cm, with smaller branches and veins together, and the entire biopsy specimen has to be examined microscopically. A dramatic clinical response to glucocorticoid therapy can be a further support of the diagnosis. Individual therapy is important.

Appendix

Immunohistochemical methods of vasculitis

The cellular infiltration was examined with immunohistochemical techniques using the streptavidin-biotin-complex/horseradish peroxidase method. Endogenous peroxidase activity was inhibited by pretreatment with 3% H$_2$O$_2$-methanol for 20 min at 20°C, and nonspecific protein binding was inhibited by incubation in a solution of Ultra V block (Lab Vision, Suffolk, UK) for 5 minutes at 20°C. The slides were then incubated at 4°C for 12h with the primary antibody anti-human CD31 [monoclonal antibody N1596; DAKO, Glostrup, Denmark], anti-human CD34 diluted [monoclonal antibody M71165; DAKO, Glostrup, Denmark], anti-human LCA (CD45) diluted [monoclonal antibody N1514; DAKO, Glostrup, Denmark], anti-human CD3 [monoclonal antibody RM-9107-R7; Lab Vision, Suffolk, UK], anti-human CD43 [monoclonal antibody N1559; DAKO, Glostrup, Denmark], anti-human CD20 [monoclonal antibody N1502; DAKO, Glostrup, Denmark], anti-human CD79α [monoclonal antibody N1628; DAKO, Glostrup, Denmark], anti-human CD68 [monoclonal antibody N1577; DAKO, Glostrup, Denmark], anti-human SMA [Smooth Muscle Actin, monoclonal antibody IR611; DAKO, Glostrup, Denmark]; followed by incubation with a biotinylated secondary antibody (Anti-Polyvalent and Streptavidin Peroxidase; Lab Vision, Suffolk, UK) for 10 minutes at 20°C. Streptavidin-biotin complexes were visualized with the use of diaminobenzidine [K3466; DAKO, Glostrup, Denmark] and H$_2$O$_2$ to detect peroxidase activity for 15 minutes at 20°C.
Systemic and Relapsing Nature of Temporal Arteritis

Bibliography


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