Research Article

Neuroimaging Evaluation of Non-Aneurismatic “Top of the Basilar” Syndrome

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Summary

Purpose: We aim to evaluate the clinical and imaging features of “Top of the basilar” syndrome (TOB-S).

Method: We retrospectively evaluated the clinical and imaging features of thirty consecutive TOB-S patients. We analyzed the ischemic parenchymal lesions and vascular disturbances with anatomic correlation by using magnetic resonance imaging (MRI), diffusion-weighted MRI (DWI), computed tomography angiography (CTA), magnetic resonance angiography (MRA), and digital subtraction angiography (DSA).

Results: Thirty patients (14 males and 16 females) with a mean age of 61 years (range: 32–78 years) were diagnosed as TOB-S based on the neuroimaging and clinical findings. Large artery atherosclerosis (LAA) was the common etiology (63.3%), including the subgroups of in situ steno/occlusive, artery to artery embolus (AA), arterial branch (AB) occlusion, and AA+AB combination. The other etiologies were cardioembolism (CE) (16.6%), arterial dissection (AD) (10.0%), vasculitis (6.6%), and undetermined (3.3%). The patients represented 'superficial', 'deep' and 'superficial plus deep' infarcts with segmental, territorial or scattered patterns. The most clinical manifestations were motor deficits, alteration of consciousness, visual/oculomotor disturbance, cerebellar dysfunction, behavioral disorder and speech disorder.

Conclusion: The accurate evaluation of imaging findings in TOB-S is essential for diagnosis and appropriate management. Familiarity with the vascular anatomy, supplying territories, and infarction patterns of the ischemic lesions is crucial.

Key words: Top of the basilar, syndrome, thromboembolus, atherosclerosis, anatomy

Özet

Amaç: Non-anevrizmatik “Baziller Tepe” (BTS) sendromunda nöroradyolojik bulguların değerlendirilmesi.

Metod: BTS tanısı alan otuz hastanın klinik ve görüntüleme bulguları retrospektif olarak incelendi. İskemik parenkimal ve vasküler lezyonlar anatominin korelasyonlarıyla birlikte manyetik rezonans görüntüleme (MRG), diffüzyon ağırlıklı görüntüleme (DAG), bilgisayarlı tomografik anjiografi (BTA) ve dijital subtraksiyon anjiografi (DSA) metodlarıyla incelendi.

Bulgular: Otuz hastaya (14 erkek-16 kadını) ortalaması yaş 61 (32-78 arası) klinik ve nöroradyolojik görüntüleme ile BTS tanısı kondu. Büyük arter aterosklerozu (BAA) en yaygın etyoloji olup (%66.6) in-situ stenokluzyiv, arter-arter (AA) embolisi, arteryal dal (AD) oklüzyonu ve AA+AD kombinasyonları olarak alt gruplara ayrılarak incelendi. Takip eden diğer etyolojiler kardiyoembolizm (KE) (%16.6), arteriyal disseksiyon (%10.0), vaskülit...
ve belirlenemeyen (%3.3) idi. Hastalarda iskemi "süperfisyal", "derin" ve "süperfisyal+derin" lokalizasyonlarda olup segmental, teritoryal ve multipl dağıtık küçük infarkt paternleri şeklinde görüldü. En sık görülen klinik bulgular, motor bozukluklar, bilinç değişiklikleri, vizual/okülomotor bozukluklar, serebellar disfonksiyon ile davranış ve konuşma bozukluklarıydı.

Sonuç: BTS tanı ve tedavisinde etkin nöroradyolojik görüntüleme önemlidir. Bu bölgedeki vasküler anatomı ve besleme alanları ile iskemik infarkt paternlerinin iyi bilinmesi hayatı önem taşır.

Anahtar Kelimeler: Baziller tepe, Sendrom, aterosklerozis, tromboembolus, anatomi

INTRODUCTION
"Top of the basilar" syndrome (TOB-S) denotes a circulation disturbance in rostral part of the basilar artery (BA)(4). The most common causes of TOB-S are atherosclerosis, thromboembolism, vasculitis, aneurysm and trauma(3). The circulation disturbance frequently leads to infarctions in midbrain, pons, thalamus, cerebellum and the medial parts of temporal and occipital lobes(4). Although BA occlusions have been well known for many decades, they had commonly been recognized only on postmortem specimens. In despite of TOB-S needs early diagnosis and immediate treatment, there is still lack of a data concerning the early radiologic clues and clinical signs(4). Therefore, in this study we focused on the neuroimaging findings of non-aneurismatic TOB-S patients and described their anatomo-pathologic correlations for early diagnosis. We evaluated clinical and comprehensive neuroimaging features of the TOB-S cases based on different etiologies using by MRI, DWI, MRA, CTA and DSA.

MATERIAL AND METHODS
Patient Selection
The study population was recruited from the patients underwent MR examination for suspected TOB region stroke between the january 2007 and december 2014. A total of 30 patients (14 males and 16 females) with a mean age of 61 years (range 32–78 years). The diagnosis of TOB-S was made on the basis of the ischemia on the DWI and verified by angiographic evaluation (MRA, CTA or DSA) according to the previously published anatomic studies(3,13)

Imaging
MR examinations were performed on a 1.5- superconducting system (Signa Excite HD; GE Healthcare, Milwaukee, Wisconsin, USA), using a circularly polarized head coil.

CTA examinations were performed with a 16-slice CT scanner (Brilliance 16; Philips Medical Systems, Eindhoven, Netherlands) from the aortic arc to vertex with 1.25 slice thickness at 1.25 interval.

DSA examinations were performed with standard biplane fluoroscopy equipment (ADVANTX LC/LP, GE, Medical systems, Milwaukee, WI, USA). For each inspection, anteroposterior and lateral projections were obtained at 3 frames per second.

All patients underwent MRI and DWI, then following (n=20) CTA, (n=1) MRA, (n=3) DSA examination alone or various combinations, (n=3) CTA+MRA, (n=1) DSA+MRA, (n=1) DSA+CTA, (n=2) DSA+MRA+CTA were performed.

The image evaluation and statistical analysis
Based on the DWI findings, we categorized the anatomical distribution of infarcts into 'superficial' (pial), "deep" (perforating), or "superficial plus deep" territories(13), PCA and SCA territories were considered as the superficial territories. The deep territories are supplied by the TPA, TGA, TTA perforan branches, and PChoA.
Prospective Etiologies of Infarction

Using a modified version of the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification\(^\text{(1)}\), the presumed etiologies of infarction were categorized as follows:

(1) **Large artery atherosclerosis (LAA) etiology**: defined when there was a definite stenosis or occlusion of the PCA, BA or SCA that was considered responsible for the referent ischemic lesion. We divided the LAA into the following groups (Fig 1).

(a) in situ steno-occlusion; when there was an infarct just distal to the steno-occluded site involving a segmental or territorial parenchyma (Fig 1a) (b) artery-to-artery (AA) embolism; when there was a moderate to severe stenosis or occlusion in the proximal segment arteries with infarcts occurring in the remote area not adjacent to the diseased vessel (Fig 1b). Multiple small infarcts in a superficial region defined as superficial scattered pattern. (c) atheromatous branch (AB) occlusion; when the infarcts were on the territory of one or a few perforating branches arising from the stenosed artery that presumably occluded the orifice of perforators (Fig 1c), and (d) AA+AB; when infarcts were located in deep perforator territory adjacent to the stenosed a large artery and also in the remote area.

(2) **Cardioembolism (CE)**

(3) **Vasculitic steno/occlusion**

(4) **Arterial dissection etiology (AD)**

(5) **Undetermined etiology (UE)**

The relationship between infarct pattern on DWI and presumed underlying etiology was analysed using the Pearson correlation test. Probability (P) values equal to or less than 0.05 were considered statistically significant.

**Fig 1**: Schematic drawing and illustrative examples of the various patterns of the TOB region infarction in LAA as assessed by DWI and CTA. A. In situ steno/occlusion; the deep thalamic and whole mid temporo-occipital territory infarction produced by right P1 severe steno-occlusion (arrow). B. AA embolism; atherosclerotic plaques in the BA and bilateral proximal PCA (arrows) probably source of the bilateral multiple small embolic infarcts scattered in occipital lobes. C. AB occlusion; the left proximal P2 stenosis (arrow) and left lateral thalamic infarction probably resulted from occluding the orifice of TGA. D. The illustrative and DW images show the percheron artery infarction in medial thalamus symmetrically.
RESULTS

Patient Characteristic and symptoms

Thirty TOB-S patients were diagnosed and this corresponded to 3.5% of the all admitted ischemic stroke patients during the concerned period.

The most frequent initial symptoms were motor deficit (53.3%), loss of consciousness (46.6%), visual/oculomotor disturbances (43.3%), cerebellar dysfunction (40.0%), behavioral disorder (26.6%) and speech disorder (16.6%).

Prospective Etiologies and Stroke Mechanism

1. LAA (63.3%) (n=19) was the most frequent etiology. In situ steno/occlusive group (n=5), AA embolism (n=9), AB occlusion (n=2), AA plus AB (n=3), 2. CE (16.6%) (n=5), 3. AD (10.0%) (n=3), vasculitic steno/occlusion (6.6%) (n=2), and UE (3.3%) (n=1), (Table 1).

Table 1.

A. Etiologies of TOB-S  

<table>
<thead>
<tr>
<th>Etiology</th>
<th>n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. LAA</td>
<td>19 (63.3%)</td>
</tr>
<tr>
<td>2. CE</td>
<td>5 (16.6%)</td>
</tr>
<tr>
<td>3. Arterial dissection</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>4. Vasculitic steno/occlusion</td>
<td>2 (6.6%)</td>
</tr>
<tr>
<td>5. Undetermined etiology</td>
<td>1 (3.3%)</td>
</tr>
</tbody>
</table>

B. Affected vessels

<table>
<thead>
<tr>
<th>Vessels</th>
<th>Unilateral</th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large arteries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCA</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>SCA</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Basilar tip</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Deep perforans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGA</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>PChoA</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>TPA</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>TTA</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

C. Infarct patterns (on DWI)  

<table>
<thead>
<tr>
<th>Pattern</th>
<th>n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>3 (10.0%)</td>
</tr>
<tr>
<td>Deep</td>
<td>2 (6.6%)</td>
</tr>
<tr>
<td>Superficial plus deep</td>
<td>25 (83.3%)</td>
</tr>
<tr>
<td>Watershead infact + superficial scattered</td>
<td>2 (6.6%)</td>
</tr>
</tbody>
</table>

Distribution of Infarcts Based on DWI Findings

The most affected large artery was unilateral/bilateral PCA (n=23), SCA (n=11) and basilar tip (n=6). Among the deep perforan arteries unilateral/bilateral TGA (n=18) most affected deep perforan vessel and follows, PChoA (n=14), TPA (n=12) and TTA (n=9). The anatomical distributions of PCA territory infarction were the medial occipital area unilateral/bilateral (n = 23), unilateral/bilateral mid-temporal area (n = 11), medial thalamus (n = 8), dorsal thalamus (n = 7), midbrain (n = 6), lateral thalamus (n = 5), anterior thalamus (n = 2).

Isolated superficial territorial infarcts were in (n=3) patients, isolated deep infarcts were in (n=2) patients while (n=23) patients represented superficial plus deep infarct pattern on DWI. Those of the (n=11) patients represented superficial territorial plus deep, (n= 7) superficial scattered plus deep infarct, (n=5) superficial segmental plus deep. Watershed plus superficial scattered patterns and (n= 2) (Table 3). There was a good correlation among the pattern superficial scattered plus deep infarct pattern and CE (p < 0.001).

Angiographic investigations showed the frequency of atherosclerotic plaques in arcus aorta of the (26. 6 %) patients, in vertebral artery (VA) (43. 3 %) and in proximal BA (33. 3 %).

DISCUSSION

TOB-Syndrome was initially defined by Caplan(4) as a circulatory disturbance at the top of BA leading to a group of signs and symptoms related to midbrain, paramedian diencephalic, thalamus, superior pons, cerebellum, medial temporal and occipital lobe dysfunctions(4). The existence of ischemic areas in the territories of PCA, PCoA, SCA and high basilar branch arteries is a common radiologic feature of TOB-S(3, 7).

TOB-S clinical presentation ranges from mild transient symptoms to devastating strokes with high fatality and morbidity. In the current study, the most common initial symptoms were motor deficits, loss of consciousness, visual/oculomotor disturbance, cerebellar dysfunction, behavioral disorder and speech disorder(3,4).

We evaluated TOB region for a better comprehension of this matter. Therefore, we will first discuss the vascular supply around the TOB region and review relevant literature(2). TOB region is composed of five branched junction consisting of the two superior cerebellar arteries (SCA), two posterior cerebral arteries (PCA), and the rostral BA tip itself between the PCA and SCA (Fig 2a).
PCA, supplies the medial part of the temporal lobe (memory) and the occipital lobe (vision) that becomes of even greater importance in persons with an incomplete circle of Willis. PCA has four vascular segments and it has two main territories of vascular supply. The proximal P1 and P2 segments supply the paramedian midbrain, with the medial and posterolateral thalamus by the deep small size perforans whereas the P3 and P4 segments supply the superficial territory of the occipital and medial temporal lobe.

The following small size branches that are originating from TOB region can be distinguished as the small perforans supplying the thalamus and paramedian midbrain (Fig 2b,c).

TTA: Thalamotuberal arteries (polar arteries). They arise from the posterior communicating artery (PCoA), and supply the posterior part of the thalamus. TTA also supply the anterior part of the crus posterior of the capsula interna, TPA: Thalamoperforate arteries (paramedian arteries). They arise from the firs part of the PCA, before merging with the PCoA. They supply the medial part of the thalamus. Rostral BA tip has small size branches (posteromedial central paramedian
arteries) supplies the midbrain and medial thalamus. TGA: Thalamogeniculate arteries. They arise from the PCA after merging with the PCoA and supply the lateral part of the thalamus. PChA: Posterior choroidal arteries, arise from the PCA and supplies the geniculate bodies, pulvinar and the dorsolateral thalamus.

SCA supplies the entire superior aspect of the cerebellar hemisphere, the ipsilateral superior vermis, and the largest part of the deep white matter, including majority of the dentate nucleus. The proximal SCA also has some branches contribute to supply the superior pons, as well as the midbrain and quadrigeminal plate(3).

Since the perfusion gradient between carotid and basilar circulation can allow a pressure equalization in distal part BA stenosis as a result of altered collateral flow through the circle of Willis, atherosclerosis is more severe in proximal BA segment(9,14). In previous studies in which imaging techniques were used for diagnosis of BA occlusion, atherosclerosis was noted in 26–36% of patients, emboli in 30-35%, and dissection in 6-8%, while causes were undetermined in 22–35% of patients(11). We found that intracranial atherosclerosis (ICAS) is the most common etiology in the distal part of the BA and TOB region (65.4%), leading TOB-S.

We identified 19 (63.3%) LAA cases those having a definite stenosis or occlusion that gives rise to TOB-S based on the various potential stroke mechanisms. The degree of atherostenosis in BA, PCA and SCA and the level of occlusion are the main determinants of clinical and neuroradiological features in TOB-S. Two of the five cases (17.2%) in the in situ stenooclusion group represented mild/moderate atherostenosis while three cases had total occlusion. However, all cases of the in situ stenooclusive group even those with total occlusion represented subsegmental, arterial branch or watershed infarctions instead of a territorial ischemia through the presumed mechanism of the chronic hypoperfusion and a compensateur collateral network and retrograde flow through the Willis. In patients with slowly occluding atherosclerotic lesions, the circulation can adapt so that total occlusion causes only small ischemic lesions and transient symptoms.

We found nine cases (30.0%) representing AA embolus; five of those (16.6%) had moderate to severe LAA in the concerned TOB region with infarcts occurring in the remote area not adjacent to the diseased vessel. On the other hand, in four cases (13.3%), the AA embolus was thought to presumably stem from the atherosclerotic plaques in the arcus aorta, cervical and intracranial portions of the VA or proximal BA, since it is widely held that distal BA occlusion is often associated with extracranial vertebral and systemic atherosclerotic disease(9). AA embolus stemming from the TOB region usually affects the distal branches, leading to subsegmental territorial or scattered small infarction, whereas AA embolus stemming from the outside of the TOB region represents more widespread territorial and deep infarcts because the distal BA segment is the most common site where BA demonstrates anatomical narrowing(4,5). Therefore, infarctions may be larger through the extension of the thrombus to the high BA branches ostiums. Depending on the amount of collateral flow from the carotid system over the PoCA, the territory of the PCA can be involved or spared.

There were two patients representing LAA and concomitant isolated AB occlusion. AB occlusion was presumable resulted from a plaque extension over the small penetrating artery ostia based on the in situ LAA. The most affected branch arteries are deep territorial and superior pontin perforans. On the other hand, three patients demonstrated AA leading distal branch infarction and concomitant AB occlusion in the deep territorial area of TOB. Patients
with small vessel disease have a relatively benign outcome in our study.

Five patients (16.6%) were diagnosed with CE and one of them in this group represented brucella septicemia and endocarditis which was complicated with presumed septic CE, resulting in TOB-S. Although septic embolus in the BA is extremely rare in the literature\(^{(15)}\), CE with brucella endocarditis has not been reported yet.

Arterial dissection concerning the TOB region is rare and the majority is confined to the distal BA. Isolated BA dissection (IBAD) has been rarely reported in limited cases and with small patient series\(^{(10)}\). IBAD accounted for roughly 1.0% of all subarachnoid hemorrhage (SAH) events and for no less than 10.5 and 4.5% of posterior circulation and brain supplying artery dissections, respectively. The main clinical presentations were SAH (46%) and posterior circulation brain ischemia (42%); hence, SAH with TOB-S might indicate a distal BA dissection with or without an aneurysm\(^{(10)}\). Three patients in the current study (10.0%), represented spontaneous unruptured distal IBAD. Two cases represented high-grade distal BA dissection with severe stenosis, whereas the other had extensive thrombotic occlusion in mid- and distal BA extending to the proximal BA. One patient represented deep and hemorrhagic superficial infarcts with additional brainstem and ventral pons involvement that lead to locked-in syndrome (LIS) which is a severe condition and an indicator of an advanced stage of the disease, consisting of quadriplegia and lower cranial nerve palsies and preserved consciousness\(^{(2)}\). Since patients with large brain stem infarctions often die before arriving at the hospital, imaging findings of brainstem infarctions with LIS are still scarce. The outcome is generally favorable in stroke patients whereas it is variable in SAH, with a fatality rate of 21.7%\(^{(10)}\). It has been advocated that the unruptured stroke patients should be managed conservatively whereas the treatment decision in patients with ruptured BA dissection or revealed progressive ischemic symptoms should be made on case by case basis including the surgical or endovascular treatment options\(^{(2, 10)}\). All patients had unruptured dissection in our study and revealed partial recanalization after thrombolysis and favorable prognosis.

Two patients (6.60%) were diagnosed as vasculitic stenocclusive TOB-S based on having previously had a rheumatologic etiology. The patients were representing primary sjögren syndrome (pSS) and mixed (rheumatoid arthritis, Behcet and sjögren) rheumatologic disease. Since the mixed rheumatologic patient represented mild to moderate vasculitic stenosis leading to TOB-S, the pSS patient had demonstrated complete mid/distal BA occlusion. Although the vasculitic involvement of BA has been reported to be related to various diseases such as giant cell arteritis, Takayasu arteritis, rheumatoid arthritis, Behcet disease, or associated with aspergillus, candida albicans, or varicella-zoster infections, pSS involvement of the BA has not been reported yet\(^{(8)}\). The pSS is a systemic autoimmune disease with a predominant involvement of exocrine glands leading to sicca symptoms. Systemic vasculitic manifestations of pSS can occur in approximately 5–10% of patients\(^{(6)}\). The patient represented a chronic course, similar to LAA occlusive patients who demonstrated an efficient collateral network which needed to supply the brainstem and midbrain to survive. Vasculitic patients represented at a lower age than those of the other etiologic groups, and showed a favorable prognosis after appropriate medical treatment.

We could not find a strong statistical correlation between the intracranial infarct patterns of presumed TOB-S underlying etiology. The only exception was a good correlation among the superficial scattered
plus deep infarct pattern and CE (p < 0.001). The affected infarction site and the patterns of TOB-S are shown in (Table 1). Superficial territorial concomitant deep perforan infarct was the most common infarct pattern (36.6%), followed by superficial scattered plus deep infarct patterns (23.3%). Three patients represented isolated SCA superficial infarct and two patients represented BA tip deep territorial infarcts only. The uni/bilateral occipital lobe was the most affected superficial, whereas the medial thalamus is the most affected deep territorial site. The thalamic and diencephalic lesion analysis is crucial to the diagnosis of TOB-S and needs to consider deep perforans anatomy around the TOB region. The majority of the cases in our study (76.6.3%) represented thalamic and diencephalic infarction and the most commonly affected site was the medial thalamus, similar to previous reports\(^3\). The thalamic infarcts associated with other territory infarcts ranged from 21% to 61% in previous studies\(^12\). These varying results may be due to the difference in the age of the study population and in the inclusion methods among the studies. The thalamic arterial supply is provided by perforating branches from the PCA, PCoA and BA tip. However, the paramedian arteries have several normal variants which have great variability with respect to number, size and territorial contribution. Unusually bilateral perforating thalamic arteries arise from a single arterial trunk, called the artery of percheron, which arises from the P1 segment of PCA that supplies the paramedian thalami and rostral midbrain bilaterally. Occlusion causes a bilateral paramedian thalamic infarction with or without midbrain infarction\(^7\) (Fig 1d).

**CONCLUSION**

The accurate evaluation of imaging findings in TOB-S is essential for diagnosis and appropriate management. A familiarity with the vascular anatomy, supplying territories, and infarction patterns of the ischemic lesions is crucial.

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