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Contrast-enhanced T1-weighted 3D Black Blood Imaging and Its Value as Predictor for Temporal Arteritis in A Real World Setting

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ABSTRACT

Giant-cell arteritis (GCA) of the superficial temporal artery presents diagnostic challenges due to its varied clinical manifestations and limitations of available laboratory markers. Imaging plays a crucial role in its diagnosis and monitoring. Contrast-enhanced T1-weighted 3D-Black Blood imaging (T1BB) offers promising potential in non-invasively assessing vascular changes associated with GCA. A retrospective, monocentric observational study involving 250 patients, including 14 with suspected GCA, was conducted using contrast-enhanced T1BB imaging alongside clinical, laboratory, histological and clinical data concerning their predictive value for diagnosing GCA. Inter-rater agreement and imaging accuracy were evaluated. The study revealed poor inter-rater agreement in detecting GCA-related changes using contrast-enhanced T1BB imaging. Sensitivity (10%) and positive predictive value (14%) were notably low, while specificity, negative predictive value, and accuracy were high (>90%). Histologically proven GCA cases often resulted in false negatives on MRI, specifically 9 out of 10 cases. While T1BB imaging demonstrated high specificity and negative predictive value, its low sensitivity and positive predictive value limit its use as a standalone diagnostic tool for GCA and complementary diagnostic methods may be necessary for accurate diagnosis and monitoring of GCA.

Keywords

Vasculitis, Giant-cell arteritis, CNS, Black-blood-imaging, Temporal artery, Vascular imaging.

Introduction

Giant-cell arteritis was first described by Horton in 1937 and characterizes a systemic vasculitis [1]. The vascular inflammation process involves activated T-cells, macrophages, and multinucleated giant cells, which cluster at the internal elastic membrane. The ophthalmic, posterior ciliary, superficial temporal, occipital, and internal maxillary arteries are commonly affected [2]. Due to varying clinical symptoms and limited value of laboratory markers, the diagnostic evaluation of extracranial vasculitis requires an interdisciplinary approach. An early and accurate diagnosis is crucial to prevent long-term damage [3]. With the endeavor to set up a minimally invasive or non-invasive diagnosis for GCA, imaging takes on a key position in the clarification of suspected cases, the monitoring of therapy and the documentation of possible sequel of the disease.

The contrast-enhanced T1-weighted 3D-Black Blood imaging (T1BB) technique has established itself as a valuable tool in the diagnostic work-up of various medical conditions, ranging from inflammatory intracranial diseases to the assessment of brain tumors, metastatic lesions and even cervical dissection. This imaging approach has demonstrated its versatility and clinical significance through its unique attributes and advantages.

One of the key strengths of T1BB imaging lies in its exceptional spatial resolution, which allows for the acquisition of highly detailed images with an incredibly thin slice thickness of less than 1 millimeter. This level of resolution enables radiologists and clinicians to visualize fine anatomical structures and changes with remarkable precision, thereby enhancing the accuracy of diagnosis and assessment. Moreover, the technique's ability to selectively suppress both arterial and venous flow signals is a critical feature. By eliminating these signals, T1BB imaging helps to isolate the region of interest, which is particularly important in cases of intracranial disease, tumor evaluation, and vascular abnormalities. This suppression of flow signals results in a "black blood" appearance, further enhancing the visibility of target structures and lesions against a clear background. In the context of inflammatory conditions like giant-cell arteritis, where changes in blood vessels are of interest, the ability to suppress flow signal can aid in highlighting alterations in vessel wall thickness and contrast enhancement.

Additionally, the suppression of fat signal in T1BB imaging contributes to the technique's diagnostic precision. Fat suppression improves tissue contrast and enables the visualization of abnormalities that might otherwise be obscured by fatty tissue, a feature particularly relevant in cases involving cervical dissection or infiltrative processes within the brain. As a non-invasive imaging modality, T1BB imaging presents advantages over invasive procedures, such as angiography, by providing detailed anatomical information without the need for contrast administration directly into the arterial blood vessels. This is especially advantageous in cases of suspected intracranial inflammation or vascular disorders, where non-invasiveness is a crucial consideration [4-6]. With this technical method, changes of the superficial temporal artery in the context of GCA, i.e. arterial wall thickening and contrast enhancement of the vessel wall should be detectable [7]. In daily clinical routine, however, the detection of such changes is not free from obstacles. For example, due to the small size of the vessel, artefacts caused by movement of the patient can complicate the interpretation of the vessel wall or veins adjacent to the superficial temporal artery can simulate an enhancement of the wall. Accordingly, false-positive findings can affect the diagnostic reliability of imaging. The purpose of this study was to investigate contrast enhancement and thickening of the wall of the superficial temporal artery on T1BB images and its correlation with clinical, laboratory and histological results in a selected patient cohort.

Material and Methods

Study Design

We conducted a retrospective, monocentric observational study at a university based tertiary care hospital. This study investigated the utility of contrast-enhanced T1-weighted 3D Black Blood imaging (T1BB) in detecting changes in the superficial temporal artery associated with giant-cell arteritis (GCA). The study included a selected patient cohort and its design adhered to ethical guidelines and institutional review board approval.

Patient Selection

250 consecutive patients in a single center who received a cranial MRI with contrast-enhanced T1BB between October 2019 and October 2021 were included.

Imaging Protocol

All participants underwent contrast-enhanced MRI using a 3.0 Tesla MR scanner (Philips Achieva, Vienna, Austria), with the following sequences: intracranial time-of-flight angiography (TOF-MRA) with maximum intensity projection reconstructions to visualize the vasculature and a pre- and post contrast-enhanced T1-weighted 3D-Black Blood sequence with multiplanar reformations.

The imaging protocol facilitated high-resolution vessel wall imaging with a slice thickness of less than 1 mm and effectively suppressed arterial, venous, and fat signal.

Contrast Agent Administration

Prior to T1BB imaging, a contrast agent (Gadobutrol 1 mmol/ml, *Gadovist,* Bayer-Germany, EU) was administered intravenously to enhance vascular visualization. The dosage and administration procedure followed standard clinical protocols, i.e. 0,1 ml of Gadovist per kg bodyweight.

Imaging Analysis

Image analysis was performed using DeepUnity Diagnost 1.1. (DH-Healthcare, Bonn, Germany) by two board-certified radiologists as well as a neuroradiology resident. For T1BB images, the presence of contrast enhancement and thickening of the superficial temporal artery wall was assessed. One board certified radiologist and one neuroradiology resident rated the images of each case for presence or absence of pathological vascular wall enhancement. In case of discrepancy, a second board certified radiologist analysed the images and decided, which assessment was correct, thus enabling a majority decision, which served as subjective ground truth.

Clinical and Laboratory Data

Clinical data, including fever, headaches, jaw claudication, visual disturbances, anemia, and polymyalgia rheumatica, as well as laboratory results showing elevated C-reactive protein (CRP) and blood sedimentation speed (BSG), were collected for each participant. Additionally, histological data obtained from biopsies were incorporated into the analysis.

Statistical Analysis

Statistical analysis was carried out using IBM SPSS Statistics (version 29.0.1.0, IBM Armonk, New York, USA) to assess the correlation between imaging findings, clinical data, laboratory results, and histological outcomes. Descriptive statistics, Pearson's correlation coefficient, and regression analysis were employed as appropriate.

Results

We identified 250 patients who received both contrast-enhanced T1BB and TOF-MRA between 10/2019 and 10/2021. Among

these patients, 14 presented with suspected GCA vasculitis. The remaining patients underwent examinations for tumors, inflammatory CNS diseases other than vasculitis, or other conditions. The mean age of the patients was 61 years (SD: 17.37 years). Among those examined, 138 were women (55.2%) and 112 were men (44.8%). Out of the 250 patients, 10 cases showed histologically proven arteritis and met the ACR criteria for the diagnosis of giant cell arteritis.

Rater 1 rated 177 cases as true negative und 6 cases as false negative. There were 63 cases rated as false positive by Rater 1 and only 4 case rated as true positive.

Rater 2 rated 230 cases as true negative und 9 cases as false negative. There were 10 cases rated as false positive by Rater 2 and only 1 case rated as true positive.

Rater 1 and Rater 2 only agreed in 1 case as true positive, however there was agreement in 170 true negative cases.
Cohens Kappa for inter-rater agreement was 0.046 and statistically not significant ($p>0.05$).

After a majority decision about MRI morphological signs of temporal artery vasculitis, only 1 of the 10 histologically proven positive cases was rated as true MRI positive, and 9 were classified as false negatives. Six patients were rated as false positive by the readers, while 234 were classified as true negatives [5].

In summary, as shown in Table 1, there was poor inter-rater agreement. Additionally, MRI readings for predicting histologically proven arteritis showed sensitivity, specificity, positive predictive value, and negative predictive values of 10%, 98%, 14%, and 96%, respectively, with an accuracy of 94%. The specificity, negative predictive value, and accuracy of MRI were excellent, well above 90% each. However, sensitivity and positive predictive value were extremely low.

Table 1:

Statistic	Value	95% CI
Sensitivity	10.00 %	0.25% to 44.50%
Specificity	97.50%	94.64% to 99.08%
Positive Likelihood Ratio	4.00	0.53 to 30.16
Negative Likelihood Ratio	0.92	0.75 to 1.14
Disease Prevalence (*)	4.00%	1.93% to 7.23%
Positive Predictive Value (*)	14.29%	2.16% to 55.69%
Negative Predictive Value (*)	96.30%	95.48% to 96.97%
Accuracy (*)	94.00%	90.30% to 96.60%

Additionally, as shown in Table 2, we correlated the ACR-criteria as ground truth with the MRI findings, revealing a strikingly low sensitivity of 2.56% and a high specificity of 97.16%. The positive predictive value stood at 14.29%, indicating the limited ability of the MRI to accurately predict true positives, while the negative predictive value was 84.36%, suggesting a moderate capacity to rule out false negatives. These findings underscore the challenges in relying solely on the ACR-criteria for diagnosing suspected cases of arteritis, emphasizing the need for complementary diagnostic approaches for more reliable assessments.

Table 2:

Statistic	Value	95% CI
Sensitivity	2.56%	0.06% to 13.48%
Specificity	97.16%	93.91% to 98.95%
Positive Likelihood Ratio	0.90	0.11 to 7.29
Negative Likelihood Ratio	1.00	0.95 to 1.06
Disease Prevalence (*)	15.60%	11.33% to 20.70%
Positive Predictive Value (*)	14.29%	2.02% to 57.38%
Negative Predictive Value (*)	84.36%	83.61% to 85.09%
Accuracy (*)	82.40%	77.10% to 86.91%

Discussion

In this retrospective, monocentric observational study there was poor inter-rater agreement using contrast-enhanced T1BB imaging in the detection of GCA. The findings highlight an important aspect of the diagnostic utility of contrast-enhanced 3D Black-Blood sequences in the context of giant cell arteritis (GCA). Our results in terms of sensitivity and specificity were also in sharp contrast to those of previous publications, which indicated good sensitivity of contrast-enhanced T1BB in diagnosing GCA [7].

One key point to consider in this discussion is the inherent complexity of diagnosing GCA. This condition can manifest with a wide range of clinical presentations and involve various arteries, making accurate diagnosis challenging, even with diagnostic tools like the ACR criteria. The relatively low sensitivity and positive predictive value of the contrast-enhanced 3D Black-Blood sequence in this study could be attributed to the intricacies of GCA's presentation and the limitations of the imaging method itself [7]. It is crucial to recognize that no single imaging technique is infallible in capturing the full spectrum of GCA-related changes, which may involve subtle alterations in vascular morphology and inflammation. However, our results imply that the MRI contrast-enhanced 3D Black-Blood sequence might not be a suitable tool for screening arteritis due to the low sensitivity. It appears that it is also not helpful for confirming suspected arteritis due to its low positive predictive value. One of the reasons, why specificity, negative predictive value and accuracy were relatively high, is the low prevalence of temporal arteritis in our patient population, so that these values need to be interpreted with caution. Thus, MRI contrast-enhanced 3D Black-Blood sequences might produce misleading results and currently cannot be recommended as the sole diagnostic tool for suspected arteritis cases.

Another aspect worth discussing is the potential role of other imaging modalities or diagnostic tools. Combining multiple imaging techniques, such as ultrasonography or positron emission tomography (PET), could potentially enhance diagnostic accuracy by providing complementary information about vascular inflammation and blood flow dynamics. This raises questions about the feasibility of a multimodal approach to GCA diagnosis and whether such an approach might yield improved sensitivity

and positive predictive value compared to individual techniques.

Furthermore, the study's reliance on three raters and majority decision for MRI interpretation may have had an impact on MRI accuracy, especially when considering the poor inter-rater agreement. It is essential to acknowledge the potential impact of variations in interpretation among different raters, which could influence the reported predictive values, sensitivity and specificity. Addressing these challenges may involve refining imaging protocols, standardizing interpretation criteria, and exploring methods to minimize inter-rater discrepancies.

Another point to consider is the time interval between MRI and specimen sampling for histological workup on the one hand, and blood sampling for laboratory testing on the other hand. It seems likely that longer intervals between imaging and sampling could decrease correlation between these findings. We also did not take into account if patients had received treatment for arteritis prior to MRI, especially corticosteroids, which might also influence MRI results. However, this would likely affect the contrast enhancement rather than the thickening of the vessel wall. Lastly, only one of the MRI-positive cases was histologically evaluated. Therefore, we do not know if the MRI findings in the other cases had any histopathological correlation.

Conclusion

In conclusion, while the findings suggest that the sensitivity and positive predictive value of the contrast-enhanced 3D Black-Blood sequence for diagnosing GCA are very low, high specificity and negative predictive values raise hope for possible optimisation of the imaging approach with the aim of increasing sensitivity and positive predictive value. The study underscores the complexities of GCA diagnosis, even with diagnostic tools like the ACR criteria, and emphasizes the need for a comprehensive approach that integrates various imaging modalities, clinical data, and potentially novel biomarkers to achieve more accurate and reliable results. Further investigations could delve into optimizing imaging protocols, refining interpretation criteria, synchronizing imaging and specimen sampling, and exploring the potential benefits of multimodal diagnostic strategies to advance the field's understanding of GCA diagnosis and management.

Contrast-enhanced T1-weighted 3D-Black Blood imaging may prove useful as an additional imaging tool when better correlated with histopathology, but its reliability is limited. Until more accurate imaging parameters and more standardized diagnostic workup are developed, superficial temporal artery biopsy as well as clinical symptoms and lab results should remain the reference standard for diagnostic work-up of suspected GCA cases.

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