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The role of ultrasound biomicroscopy in predicting the result of temporal artery biopsy in temporal arteritis patients: A preliminary study

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PURPOSE. *Temporal artery biopsy is considered the gold standard for the diagnosis of temporal arteritis (TA). However, complications following this procedure may occur. The goal of this study is to evaluate if ultrasound biomicroscope (UBM) findings are useful in predicting the result (positive or negative) of temporal artery biopsy in patients with TA.*
METHODS. *Twenty-six consecutive patients with clinical diagnosis of TA seen at the Department of Ophthalmology, Royal Victoria Hospital, Montreal, Canada, were involved in this study. All patients were submitted to UBM before temporal artery biopsy. Eight patients presented histopathologic findings consistent with the diagnosis of TA. Thus, UBM findings of these patients were compared with those from 18 patients with negative biopsy. On UBM we searched for the presence of a hypoechoic effect surrounding the walls of the temporal arteries, the so-called halo sign, as well as an intra-arterial middle reflexive filling, the so-called intra-arterial filling.*
RESULTS. *The halo sign and/or the intra-arterial filling were found in 8 (100%) of 8 patients with biopsy-proven TA. However, 10 (55.5%) of 18 patients with a negative biopsy presented one or both of these two UBM findings. On the other hand, the absence of these two parameters on the UBM of a patient with TA strongly suggests that the temporal artery biopsy will be negative (negative predictive value=100%).*
CONCLUSIONS. *This preliminary work suggests that UBM may play a role in predicting a negative result of the temporal artery biopsy in patients with TA. In the present series approximately 30% of the patients could be spared this surgical procedure and its possible complications. (Eur J Ophthalmol 2005; 15: 655-9)*

KEY WORDS. *Ultrasound biomicroscopy, UBM, Temporal arteritis, Temporal artery biopsy*

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INTRODUCTION

Temporal arteritis (TA) is a systemic vasculitis of unknown cause. It can result in blindness, stroke, and death (1). The disease affects all races but is most commonly seen in white patients (2). There is a threefold greater incidence in women than in men (2). The diagnosis of TA is based on clinical impression rather than on any particular finding or laboratory test (3). A temporal artery biopsy is important to confirm the diagnosis, since long-term use of corticosteroids is the treatment of choice, and the potential for side effects related to their use is great.

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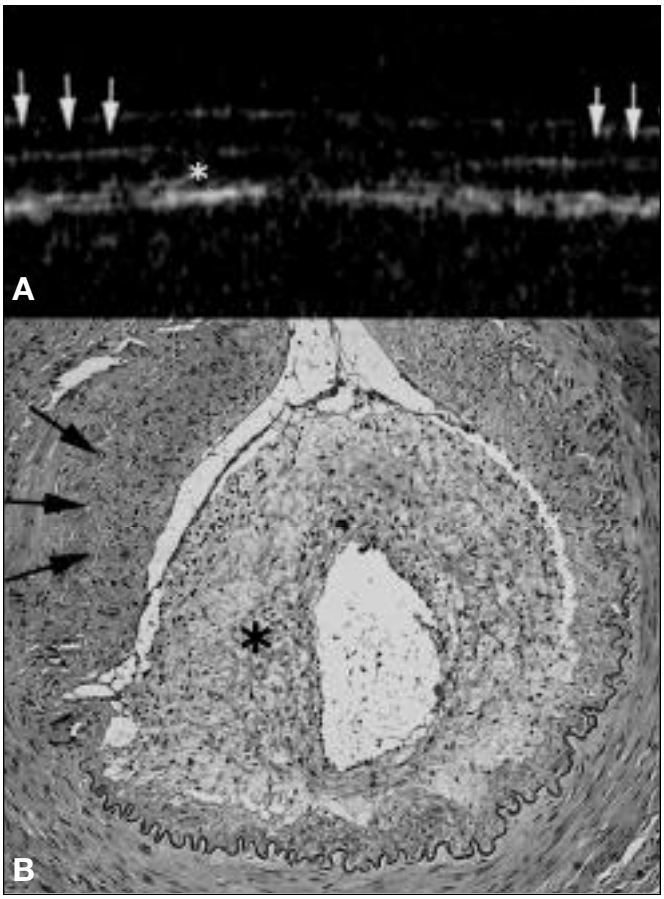

Fig. 1 - A) *Ultrasound biomicroscope (UBM) image disclosing a hypoechoic halo, the so-called halo sign (arrows), seen in the temporal artery of a patient with biopsy-proven temporal arteritis. Observe that the patient also presents the intra-arterial filling sign on UBM (white asterisk).* **B)** *Light microscopy of the same temporal artery revealing a diffuse chronic inflammatory infiltrate spread through the muscular layer.*

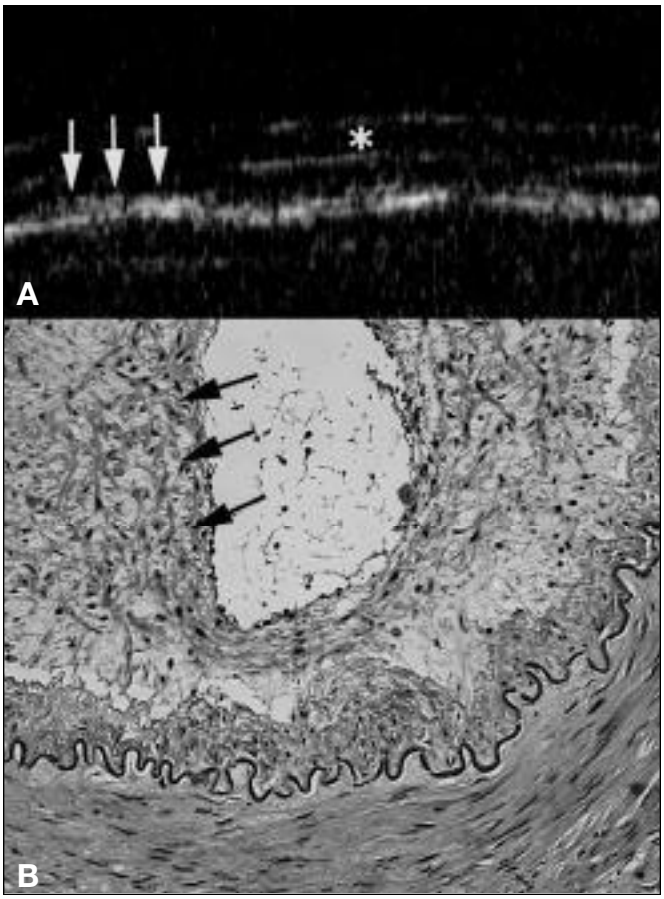

Fig. 2 - A) *Ultrasound biomicroscope (UBM) image showing the middle reflexive filling of the intra-arterial lumen (arrows) observed in the temporal artery of a patient with biopsy-proven temporal arteritis (the so-called intra-arterial filling). The patient also presents the halo sign (white asterisk).* **B)** *Light microscopy of the same temporal artery revealing severely thickened arterial lumen due to intima proliferation (arrows).*

It has been suggested that ultrasound could have a role in the diagnosis and management of TA. High-resolution color-coded duplex sonography has greatly improved the imaging of small lumen arteries and has been introduced in the diagnosis of TA by Schmidt et al (4). In the superficial temporal artery perivascular hypodense areas (halos) and stenoses and occlusions have been found. Wenkel and Michelson and, later, Roters et al found that ultrasound biomicroscope (UBM) allowed a precise evaluation of the temporal arteries due to a high-resolution sonographic image (5, 6). Moreover, they observed a positive correlation between the histopathologic features found in the temporal artery biopsy and the UBM findings.

The present study sought to correlate the UBM findings with the histologic features of the temporal artery biopsy from patients with TA. We also evaluated the role of UBM in predicting the results (positive or negative) of the temporal artery biopsy in these patients.

MATERIALS AND METHODS

All the patients involved in this study provided written informed consent, and the Institutional Review Board of McGill University Health Center approved the study in February 2002.

All the patients had the clinical diagnosis of TA based on the first four of five items of the criteria of the American College of Rheumatology, in which any three of the following features are diagnostic of TA: 1) age greater than or equal to 50 years; 2) new onset of unilateral headache; 3) temporal artery tenderness or decreased pulse; 4) ery-

throcyte sedimentation rate greater than or equal to 50 mm/h; and 5) positive temporal artery biopsy (3).

All patients underwent UBM examination (Humphrey Instruments Inc, Zeiss Group, 50 MHz probe) of one temporal artery territory before biopsy. A unilateral superficial biopsy of the temporal artery was performed in all patients within less than 7 days of the time of the diagnosis of TA.

The temporal artery biopsies in this study were taken by different surgeons with varying lengths of specimens from 18 to 25 mm. All the pathology specimens were treated in a routine fashion and the same pathologist reported on them all. The criterion to determine if the temporal artery biopsy was consistent with the diagnosis of temporal arteritis was based on Heathcote (7). Two groups of patients were recruited: 1) patients with biopsy-proven TA (positive biopsy) and 2) patients with a negative biopsy.

The morphologic aspects of the temporal arteries observed on UBM, such as arterial lumen and wall, were evaluated and compared between both groups. The findings on UBM were correlated to the results of the histologic specimens found in both groups.

RESULTS

The results are summarized in Table I. Twenty-six consecutive patients with the clinical diagnosis of TA were involved in this study. Twenty-one patients were women and five were men. The mean age was 73.1 years (range 57 to 90 years).

All the patients were receiving oral corticosteroid therapy for less than 7 days at the time of the temporal artery biopsy. Eight patients (30.7%) were found to be positive on temporal artery biopsy. Eighteen patients (69.3%) had a negative biopsy. Two conspicuous findings were observed on UBM of our patients: 1) a hypoechoic halo around the arterial lumen, the so-called halo sign (Fig. 1A; and 2) an intra-arterial middle reflexive filling, called intra-arterial filling (Fig. 2A). Both findings had been previously reported (5, 6). The reflectivity of the arterial wall was also evaluated but was found in virtually all patients involved in our study.

Of 8 patients with positive biopsy, 7 (87.5%) presented the halo sign on UBM. The presence of the halo sign

TABLE I - CLINICAL DATA OF THE PATIENTS ENROLLED IN THE STUDY

Patient no.	Sex	Age, yr	UBM findings		UBM final score	TA biopsy result
			Halo sign	Intra-arterial filling		
1	F	76	-	-	0/2	-
2	F	73	-	-	0/2	-
3	F	90	+	+	2/2	+
4	F	85	-	-	0/2	-
5	M	67	-	-	0/2	-
6	F	80	+	+	2/2	+
7	F	59	-	-	0/2	-
8	F	79	+	+	2/2	-
9	F	76	+	+	2/2	-
10	F	66	+	-	1/2	+
11	M	65	+	-	1/2	-
12	F	74	+	+	2/2	-
13	F	66	-	-	0/2	-
14	F	82	-	+	1/2	-
15	F	76	+	-	1/2	+
16	F	67	-	-	0/2	-
17	F	70	-	+	1/2	+
18	F	78	+	-	1/2	-
19	F	57	+	+	2/2	-
20	M	61	+	+	2/2	+
21	F	84	+	+	2/2	-
22	F	77	+	+	2/2	-
23	F	84	+	+	2/2	+
24	M	69	-	-	0/2	-
25	M	81	-	+	1/2	-
26	F	60	+	+	2/2	+

UBM = Ultrasound biomicroscope; TA = Temporal artery

showed a sensitivity of 87.5% to detect patients with a positive biopsy. However, the specificity was 55.5%. The positive predictive value (PPV) and the negative predictive value (NPV) were 46.6% and 90.9%, respectively. Of 18 patients with negative biopsies, only 8 (44.4%) showed the halo sign.

Intra-arterial filling was found in 6 (75%) of 8 patients with biopsy-proven TA. The detection of intra-arterial filling revealed a sensitivity of 75% to detect patients with positive temporal artery biopsy. The specificity was 55.5%. The PPV and the NPV were 42.8% and 83.3%, respectively. Of 18 patients with a negative biopsy, 8 (44.4%) presented this feature.

The presence of the halo sign and/or the intra-arterial filling was found in 8 (100%) of 8 patients with biopsy-proven TA. The presence of the halo sign and/or the intra-arterial filling on UBM showed a sensitivity of 100% to detect patients with a positive temporal artery biopsy. The specificity of these features was 44.4%. The PPV and NPV were 44.4% and 100%, respectively. On the other hand, 10 (55.5%) of 18 patients with a negative biopsy presented one or both of these features on UBM.

Histopathologic findings in all patients with the halo sign on UBM revealed a diffuse chronic inflammatory infiltrate and thickening, which spread throughout the media. Fragmentation of the internal elastic lamina was also observed in these cases (Fig. 1B). Patients with intra-arterial filling on UBM showed fine collagenous tissue in the intimal layer, which caused restriction of the arterial lumen (Fig. 2B).

The eight patients without both the halo sign and the intra-arterial filling on UBM presented histopathologic findings related to arteriosclerosis, as well as mild to moderate intima thickening and calcification.

DISCUSSION

Temporal artery biopsy is the gold standard for diagnosing TA. Prior to exposing the suspected patient to high-dose, long-term corticosteroid or alternative immunosuppressive therapy, many clinicians prefer to obtain histologic confirmation of TA. The average rate of positive biopsies is around 20%, ranging from 11 to 27% (8-11). The biopsy should be performed within 1 week of initiation of steroid therapy, because the rate of abnormal biopsy result falls from 82% in patients who received no steroid treatment to 60% in patients who received up to 1 week of steroid therapy (12). We performed a unilateral temporal artery biopsy in all patients involved in this study. The mean length of the specimen obtained for biopsy in our group was 21.5 mm. In fact, a biopsy length of slightly over 20 mm is recommended because of the presence of skip lesions and a shrinkage factor induced by formalin fixation (13). Some authors recommend taking bilateral biopsies in cases in which the first was negative. However, Danesh-Meyer et al reported that a bilateral simultaneous or sequential temporal artery biopsy improved the diagnostic yield in only 1% of TA cases, whereas in 99% of cases, the two specimens showed the same findings (14). Nevertheless, it is important to point out that a negative biopsy does not rule out TA. As previously mentioned in this article, the diagnosis of TA may be made on a clinical basis (3).

The goal of our study was to evaluate if the information obtained with the UBM would be helpful to select patients with TA for temporal artery biopsy. In fact, temporal artery biopsy is an invasive procedure associated with some morbidity. Despite the fact that the surgical technique and anatomy of superficial temporal artery are both well-described in the literature, some complications have been reported following this procedure, such as incorrect or inadequate tissue sampling, bleeding, hematoma formation, facial nerve injury, scarring, infection, wound dehiscence, and cerebrovascular accident (10, 12, 15, 16). On the other hand, UBM is a noninvasive examination that permits an extensive temporal artery area to be examined.

UBM has already been investigated for the diagnosis of TA. In 1997, Wenkel and Michelson used UBM in patients with TA and found the halo sign in all of their patients with biopsy-proven TA (5). They also described the intra-arterial filling and a condensation and enlargement of the muscularis media. In the same article, the authors found that a morphologic differentiation between a normal and an affected artery was possible (5). Moreover, a positive correlation between histopathologic and clinical findings was seen in all patients. The data obtained from our group also confirmed the positive correlation between the UBM features and the histopathologic examination of the temporal artery.

In 2001, Roters et al found the halo sign on UBM in three of five patients with histologically proved TA (6). This group also described intra-arterial filling, as well as a high reflectivity of the temporal artery wall. They concluded that UBM was helpful in obtaining an indication of the side and segment for biopsy. Since UBM is a method that permits an extensive temporal artery region to be examined, areas without the previously mentioned signs would

be avoided for biopsy. At least theoretically it is possible that this might lead to an increased number of positive biopsies. We found that both the halo sign and intra-arterial filling were easily observed when present on UBM of our patients with TA. However, we did not use the reflectivity of the arterial wall as a parameter to compare both groups, since this feature was observed in virtually all patients involved in the study. In the present study, when the halo sign and/or intra-arterial filling were detected on the UBM of patients with TA, this examination presented a sensitivity of 100% in predicting a positive result of the temporal artery biopsy. However, the specificity in this case was only 44.4%. This indicates that all patients with TA with a positive biopsy would be previously detected by means of UBM. However, 55.6% of patients with a negative biopsy would be included in this group as well (false-positive). Our results suggest that patients with TA who present the halo sign and/or intra-arterial filling on UBM have a PPV of 44.4% to present a positive temporal artery biopsy. In our series the UBM showed a low specificity. However, since all of our patients already had the clinical diagnosis of TA, the false positive results obtained may be due to the fact that the biopsy specimen was collected from an area without lesion. On the other hand, the fact that there were no false negatives among the eight patients with biopsy-proven TA is probably due to the small sample size. We found that the absence of both the halo sign and intra-arterial filling on the UBM of a patient with TA was strongly correlated with the negativity of the temporal artery biopsy (NPV=100 %). Of the 26 patients with TA submitted to temporal artery biopsy, 8 (30.7%) patients could be spared this surgical procedure, since they did not have any of those two features on UBM. To our knowledge, the present article is the first to suggest this negative correlation. The results of this preliminary study are intriguing. However, it is important to point out that we are neither advocating that UBM is a replacement for temporal artery biopsy nor suggesting any change in the current management of patients with TA. Studies with a larger series of patients are warranted to reach definitive conclusions about the usefulness of UBM to screen patients with TA for temporal artery biopsy.

The authors do not have any commercial or proprietary interest in the products used in this study.

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