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Identifying and Understanding Cerebral Microbleeds

INCREASED MICROBLEEDS IN APPARENTLY HEALTHY PATIENTS. WHAT DOES THIS MEAN?

Increased microbleeds in apparently healthy patients, what does this mean? You are listening to ReachMD XM 157, the channel for medical professionals. Welcome to the clinician's roundtable. I am your host Dr. Maurice Pickard, and joining me today is Dr. Steven Greenberg. Dr. Greenberg is Director of Hemorrhagic Stroke Research, Massachusetts General Hospital, Stroke Research Center.

#### DR. MAURICE PICKARD:

Thank you very much for joining us today.

#### DR. STEVEN GREENBERG:

Thanks for having me.

#### DR. MAURICE PICKARD:

With improved MRIs, we are now finding microbleeding much more than we ever had anticipated. How do you view this?

#### DR. STEVEN GREENBERG:

First, the really striking change in the landscape over the past few years that we already knew these were kind of common, but most estimates have them at sort 5% of asymptomatic elderly, which was a lot, but still not a huge number and with changes really, the MRI methods have gotten better and the populations looked at have been older, so now the most recent numbers have them as high as 20%-30% of elderly and people over 80 even higher than that and so it really focuses the question on either what they mark or what they actually do to the brain, but whatever they are they are certainly not a bare lesion at all any more.

#### DR. MAURICE PICKARD:

Is there is any significance based on where they may be located in the brain?

#### DR. STEVEN GREENBERG:

We think we can make a good guess at the underlying small vessel disease that gives rise to them based on the location and this comes out of years of work, first from neuropathological work and more recently from MRI work that says that of the 2 most common causes,

the 2 most common small vessel diseases that cause microbleeds are hypertensive vasculopathy and cerebral amyloid angiopathy that amyloid from Alzheimer disease that gets deposited in small blood vessels and that hypertensive small vessel disease tends to be in deep gray matter structures, so the basal ganglion, thalamus, and pons and cerebellum where as the amyloid and the blood vessels is more likely to cause bleeds out in the lobar brain region, so right at the gray-white junction near the surface or at the surface of the brain so that anatomic distinction is pretty useful for making an educated guess as to the basis of microbleeds from looking at the distribution on an MRI scan.

**DR. MAURICE PICKARD:**

Would you then say that if you found microbleeds deep in the brain that blood pressure control was not adequately done?

**DR. STEVEN GREENBERG:**

I think that is the most likely inference, not all the data or in yet and there probably is more to the equation than just how the blood pressure was controlled over time. I think we are still getting a handle on that, but in general, it is a good summarize that is a marker of longstanding hypertensive damage to the small blood vessels.

**DR. MAURICE PICKARD:**

The most remarkable work that recently came out was from the Rotterdam Scan Study and I think this is what has caught everybody's attention. Would you comment on how they were able to acquire so much material over a pretty short period of time?

**DR. STEVEN GREENBERG:**

Well, first it illustrates the power of population based study here in the US, studies like the framing and study your cardiovascular health study and then the Rotterdam study surely another terrific example of the power of getting normal asymptomatic patients from the general population in particular ageing individuals reflecting the fact that western societies are all aging so that this becomes a larger and larger demographic throughout western societies and so they match the power of that with really state of art, MRI techniques they did some innovative work on their own to show how using thinner MRI slices and slightly different acquisition parameters could make a big difference in detection of microbleeds probably without making a sacrifice in specificity, so they are probably still seeing what are bona fide microbleeds, but seeing them at a higher rate than people had seen before, so to say these numbers make a goal from being kind of an odd curiosity to being a really common asymptomatic finding in healthy elderly.

**DR. MAURICE PICKARD:**

Before we leave hypertension in particular, some studies have shown that left ventricular mass index can show whether blood pressure is well controlled, how would you combine this particular diagnostic study with if you found microbleeds in a person's brain?

**DR. STEVEN GREENBERG:**

Ya, I think it did really gets back to the point you raised earlier that it suggested that these microbleeds especially in the deep gray matter structures are a good marker of long-standing hypertension in the same way that we think of left ventricular hypertrophy as being a marker of long-standing hypertension so that study that came from a Korean group really makes the argument that of different factors that may be at play and probably is control blood pressure overtime that really is the trigger for these deep gray matter microbleeds.

**DR. MAURICE PICKARD:**

You mentioned that microbleeds may be associated with amyloid angiopathy. What would we do when we find microbleeds on the surface of the brain, we do not have amyloid yet deposit that we can identify, should we be worried or caution our patients or even begin to think about cognitive changes in these particular persons?

**DR. STEVEN GREENBERG:**

It raises a lot of questions, although at bottom the real problem is we do not yet have good treatments for amyloid angiopathy as we do not have really effective disease modifying treatments for Alzheimer disease to which have closely related from a prognostic standpoint, there is no reason to be pessimistic yet in studies of amyloid angiopathy patients, the majority of them are not committed. They probably do have an increased risk overtime, but clearly is not an inevitable byproduct of having amyloid in the blood vessels having dementia does not necessarily go along hand in hand and the other question that comes up from a practical standpoint is whether we should think differently about anticoagulation or anti-thrombotic treatment in these patients and that is really an important area that is under investigation and right now we have conditions are in a position of having to balance the risk and the benefit of treatment particularly in these individuals who are giving some evidence of having hemorrhage prone state.

**DR. MAURICE PICKARD:**

If you are just joining us, you are listening to the clinician's roundtable on ReachMD XM 157, the channel for medical professionals. I am your host and I am speaking with Dr. Steven Greenberg. Dr. Greenberg is Director of Hemorrhagic Stroke Research, Massachusetts General Hospital, Stroke Research Center and we are talking about the new finding, the increased incidence of microbleeds both deep in the gray matter and also on the surface of the brain and what this may mean as far as predicting cognitive changes or hemorrhagic events.

You bring up an interesting point about antithrombotic agents. I thought I had a pretty well clear in my mind what to do about patients who had atrial fibrillation that had no contraindications to anticoagulation. Do you kind the finding of microbleeds in a patient with atrial fibrillation now may change how I treat them?

**DR. STEVEN GREENBERG:**

It is a great question and unfortunately it is a really high stakes decision because the consequences on either side are so high that on one hand we feel we can do great things as you say for preventing thromboembolic stroke in patients with atrial fibrillation that anticoagulation typically with warfarin is a really effective treatment. On the other hand the most important adverse event related to anticoagulation is hemorrhagic stroke and those are also absolutely devastating events even in our era of acute stroke treatment the mortality among patients who have hemorrhage in the brain on warfarin is about 50% really high, so at this point our recommendation is still to proceed with anticoagulation in someone in whom it is indicated. We do not feel that the microbleeds yet are enough reason to avoid it, but there are lots of ways to have turn the dial slightly in one direction or the other that might tip the decision and so it remains very close to a tipping point for us as clinicians and really draws on our ability to look at the full picture and all the potential risks and benefits in an individual.

**DR. MAURICE PICKARD:**

Dr. Greenberg, is it possible that the association of the mutation of collagen-4 gene might help us understand microbleeding more completely?

**DR. STEVEN GREENBERG:**

Not really an intriguing hint at what may be a future area of research in the field that the investigators and the words your are describing found mutations in the collagen 4 gene in some families who have a constellation of small vessel related problems, but including microbleeding, and what it really focuses attention on is not just the processes like hypertension or amyloid angiopathy that can damage blood vessels, but the makeup of the blood vessel itself and that there may be components of the blood vessel wall such as collagen in which abnormalities trigger particular susceptibility to damage and at this point with relevance to the wider problem of microbleeding remains to be determined, but it is really an intriguing clue that we are looking at only a limited part of the picture of what makes a blood vessel likely to go and suffer damage and cause this kind of small area bleeding.

**DR. MAURICE PICKARD:**

In a clinical setting, do you think we might be able to avoid some of the cerebral angiography that we do in patients with cerebrovascular accidents if we find microbleeding, in other words might suggest we are not going to find any aneurysm or we are not going to find an AV malformation.

**DR. STEVEN GREENBERG:**

Ya, It is really a good question, a good practical question, and my feeling is yes you are correct. I do not know if studies that have been able to apply this in a systematic way, but I think in general in clinical decision making it makes a lot of sense to use microbleeds as a marker for a vasculopathy, again such as hypertension or amyloid angiopathy as you said to avoid the risk of angiography in someone were based on the overall MRI appearance you can say that the yield would be very low.

**DR. MAURICE PICKARD:**

Well do you think there is a place then in investigating patients with unexplained cognitive disturbances especially if they have risk factors of vascular nature?

**DR. STEVEN GREENBERG:**

Well it is relatively easy to do if a patient is undergoing MRI scan. Anyway it is relatively easy to add any additional MRI sequence typically known as gradient echo or magnetic susceptibility sequence is done. Even though there are ways to make it more sensitive in research, it is done as a routine clinical sequence requiring only about 3 minutes of scanning time and so it is reasonable to do that to get a full picture of the kinds of small-vessel related lesions that may be contributing to cognitive impairment. Of course, like any finding it raises a question that of how to deal with it in a practical way and with the beginning of that story clearly we are not at the end.

**DR. MAURICE PICKARD:**

Ya, so much of this has to do; now we have the information what you do with it. In my practice we do MRIs for trauma or migraines and you come up with microbleeding or we might later on talk about lacunar infarctions or atrophy. What do you do with this information now that you have done the MRI for a reason that does not have anything to do with cerebrovascular accidents?

**DR. STEVEN GREENBERG:**

It still largely remains to be determined. I think the straight forward answer is to do what you would have done anyway in terms of vascular risk factor control with even more evidence, even more enthusiasm than you would have done otherwise, but really at this point the microbleeding becomes another piece in a puzzle of the kinds of small injuries that we now recognize can add up to be both risk for cognitive impairment and of course also risks for future hemorrhagic stroke and becomes another factor to put into the decision making.

**DR. MAURICE PICKARD:**

Well how do you deal with patients if it can just aggress a little from microbleeding who have lacunar infarctions that you have discovered or even have early cerebral atrophy. What do you tell them, how do you treat them, what do you do with this information?

**DR. STEVEN GREENBERG:**

Well what is very clear is that what we used to think of being asymptomatic lesions and so-called silent infarcts are really not particularly silent at all that there are quite potent risk factors for future cognitive impairment and that is really the work over the last 10 years that has changed a lot of our thinking about what it means when we talk about vascular cognitive impairment. It is not the large symptomatic strokes that we already knew about, but now the focus has come on these small asymptomatic lesions that clearly mark an increased

risk for future cognitive impairment and if nothing else, it certainly puts us in a situation of pulling out all that stops to try to prevent future lesions with the hope that this will reduce risk of future cognitive impairment.

**DR. MAURICE PICKARD:**

We have been talking today with Dr. Steven Greenberg. We have been discussing the increased incidents of microbleeds, one more piece in the puzzle about vascular disease, cognitive changes, and cerebrovascular accidents. I want to thank Dr. Greenberg for being our guest today.

I am Dr. Morris Pickard, I have been your host, and you have been listening to the clinician's roundtable on ReachMD XM 157, the channel for medical professionals. To listen to our on-demand library, visit us at [www.reachmd.com](http://www.reachmd.com). If you have any comments or suggestions, call us at 888-MDXM-157. Thank you for listening.