

July 25, 2015

Dear 11q Families,

I am writing to inform you of a medical development that we are just now starting to learn about. In the last two years, there have been four children/young adults with Jacobsen syndrome that have suffered a stroke. Prior to that, I knew of two such cases occurring over the previous ~15 years. Knowing that JS people have the Paris-Trousseau bleeding disorder and are at risk for bleeding, I chose not to act based on the two episodes that I knew of, until recent developments came to light. Up until recently, there was one paper published over ten years ago suggesting there was a gene in 11q that could cause an aneurysm (enlargement) of the aorta. At that time and even now, I am not aware of any people with JS that have had an aneurysm of the aorta. However, there have been several much more recent publications in the medical literature suggesting the presence of a gene in 11q (i.e., specifically in the JS region) that could cause aneurysms of blood vessels and lead to a stroke. Given this combination of recent developments, I now believe that we can no longer ignore this situation. Below is an outline of my plan to address this:

1). With your help, we will be attempting to obtain as much information as possible regarding the six known cases of brain hemorrhages that have occurred, as soon as possible, and if there might be any others that I am not aware of. In most, if not all cases, the stroke occurred beyond infancy, and was a spontaneous event. Taken together, this strongly suggests that there was an underlying aneurysm of a blood vessel in the brain that ruptured, which undoubtedly was made worse by the Paris-Trousseau bleeding disorder.

2). Once I have this information, I will consult other physicians to formulate a proactive approach to identify anyone that might be at risk. This would entail a non-invasive imaging study of the brain (probably a special type of MRI in which a contrast agent is injected through an IV). If we consider this to be necessary, we will need to decide at what age (and frequency) this should be done. One concern of course will be to know what to do with the information. (see #3)

3). Identification of anyone who might have a brain aneurysm will require immediate medical follow-up. In at least some cases, an aneurysm of the brain can be treated by an interventional procedure in which the abnormal vascular structure is occluded (e.g., similar to a cardiac catheterization procedure). However, that remains to be seen and it is possible that a surgical approach might be required. I anticipate that I will be consulting a pediatric neurosurgeon to get their input on what might be the best approach. Ultimately, EVERY at-risk person will have to be assessed individually to determine what might be the best therapeutic approach for them. It is also possible that no intervention will be performed, but at the very least close follow-up with serial brain imaging studies will be necessary.

PLEASE understand that this is a very recent development and there is much more that we need to learn, including the actual frequency of these events, the cause, the best way to diagnose the problem, and ultimately the treatment. I am not trying to cause panic, but again I cannot stress enough the importance of

getting more information. Clearly, this appears to be a very serious POTENTIAL problem for which we absolutely need more information, as soon as possible. I will keep you updated over the ensuing weeks to months as we learn more. Thank you, as always, for your help!!!

Sincerely Yours,

Paul Grossfeld, M.D.  
Chief Medical Adviser  
11q Research and Resource Group  
Professor of Pediatrics  
UCSD School of Medicine  
pgrossfeld@ucsd.edu