Thymectomy for myasthenia gravis: The elephant and the blind men

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Each blind man has his own opinion about what an elephant looks like.

Central Message

Open transternal thymectomy has unequivocally been determined to result in improved outcomes in patients with myasthenia gravis, a limited clue in the unsolved puzzle of myasthenia gravis.

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In their recent article, “Thymectomy and myasthenia gravis: A history of surgical passion and scientific excellence,” Sonnett and colleagues¹ critically review the history of thymectomy for myasthenia gravis (MG) from the initial reports by Alfred Blalock to the publication of a randomized, blinded prospective study affirming the role of maximal transsternal thymectomy. This is an important exercise because in doing so the medical community evaluates its assumptions and ethical reasoning regarding a complex problem.

The Eastern parable of the elephant and the blind men (Figure 1) elegantly reveals the methodologic challenges to incompletely understood pathophysiology. The parable illustrates that an accurate description of one part does not guarantee an understanding of the whole. To be intellectually honest we must entertain the thought of the physician as a blind person, MG as the elephant, and blindness as the advancing—but incomplete—understanding of the pathology of MG and its relation to the thymus.

Thus we return to the key assumption Blalock pointed out regarding how thymectomy influences MG.¹ We presume

that acetylcholine receptor autoantibodies are produced in germinal centers of the thymus, and that removing these cells explains the efficacy of thymectomy. But this assumption may be incorrect. Could it be that surgery-related stress instigates an immune response that results in a range of symptomatic improvement in MG? The approach to thymectomy could be significant insofar as more thymic tissue is visualized and removed, or insofar as major surgery itself mounts a heightened local and systemic immune response. This question argues for a sham control arm to the Thymectomy Trial in Non-Thymomatous Myasthenia

FIGURE 1. “And so these men of Indostan disputed loud and long, each in his own opinion exceeding stiff and strong, Though each was partly in the right and all were in the wrong!” —John Godfrey Saxe, American poet (1816-1887), “The Blind Man and the Elephant.”

Gravis Patients Receiving Prednisone Therapy (MGTX), an arm the investigators believed was too unethical to pursue.²

Sonett and colleagues¹ allude to an additional ethical issue addressed by the MGTX. The authors state that the study provides “unequivocal” evidence that extended transsternal thymectomy improves clinical outcomes of patients with MG. The reason this term is appropriate is best understood in light of the aforementioned parable. The most robust counterargument against treating non-thymomatous MG patients with thymectomy would dial the unknowns of the surgeon’s knowledge and the complexity of MG pathophysiology to their hypothetical extremes. This counterargument presumes that a surgeon’s understanding of MG is as limited as the blind man’s sensation and that MG is as complex as one’s tactile experience of an elephant. For thymectomy to withstand the most rigorous ethical questioning possible

regarding its validity as an effective procedure, these conditions must be accepted and empirically tested. The value of finding statistical significance in a randomized, blinded prospective study such as the MGTX is that it is the best evidence short of detailing the full pathophysiology.

The MGTX removes any doubt as to the ethical question of thymectomy as part of the treatment for generalized MG. Not only are further studies to evaluate the surgical approach and efficacy of combination therapies reasonable but also there is an ethical imperative to do so.

References

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