

Histologic Analysis of Zafirlukast's Effect on Capsule Formation Around Silicone Implants: Some Considerations

Elisa Grella · Roberto Grella · Francesco D'Andrea

Received: 12 July 2007 / Accepted: 17 July 2007 / Published online: 18 September 2007
© Springer Science+Business Media, LLC 2007

We have read with profound interest the article by Bastos and colleagues entitled Histologic Analysis of Zafirlukast's Effect on Capsule Formation Around Silicone Implants. We have truly enjoyed this study because it focuses on the very important issue of ongoing research toward pharmacologic therapy for the treatment of periprosthetic capsule contracture. The latter has an incidence in the range of 0.5% to 50% [3]. Despite persistent clinical and laboratory investigation, to date, no solution has been developed to solve or prevent this problem.

For several years, many investigators have evaluated the use of antileukotriene drugs, which could be effective in the treatment of periprosthetic capsule contracture. Unfortunately, their use still is not evidence based and has no biochemical or biomolecular support. At the same time, the use of drugs with no specific indication is strongly criticized and discouraged for moral, medical, and legal reasons [6].

Investigations into a molecular basis to justify the use of CysLT antagonists have evaluated the potential modification of cysLTR expression in human contracted capsules [2]. The conclusions of the study by Bastos and colleagues are supported by several clinical studies, which are reviewed in their studies. However, the authors failed to review the animal models proposed to date (rabbits, pigs, rats). Although these animal studies are very accurate, they have disadvantages in terms of reproducibility, standardization, and of course translation to the human setting [1, 4, 5, 7].

In all the experiments, the authors tried to induce contracture through different methods (bacterial contamination, fibrin glue), stressing the fundamental cellular and biochemical difference between the contracted capsule and the physiologic periprosthetic capsule. Unfortunately, Bastos and colleagues used an animal model that, in our opinion, is not accurate with respect to a contracted capsule. Indeed, the authors did not induce capsular contracture in their animal model. With the fundamental differences between contracted and uncontracted capsules in mind, the immunohistochemical and histopathology analysis was carried out on periprosthetic physiologic capsules. Thus, the reduced presence of inflammatory cells and the reduced vascular density in the experimental groups (explained by the intrinsic antiinflammatory activity of zafirlukast) cannot definitely be proof of a therapeutic effect of the drug in reducing or preventing capsular contracture. Moreover, it is unclear why the authors decided to remove the prostheses 90 days after the implantation to analyze the capsules, assuming them to be contracted.

Despite these criticisms, we thank Bastos and colleagues for focusing their attention on a very serious problem in plastic surgery and for proposing a histologic and immunohistochemical analysis of the development of capsular contraction. We hope that many other investigators will undertake the same approach in fighting against this frustrating problem that afflicts patients, plastic surgeons, and manufacturers.

References

1. Adams WP Jr, Haydon MS, Raniere J Jr, Trott S, Marques M, Feliciano M, Robinson JB Jr, Tang L, Brown SA (2006) A rabbit model for capsular contracture: Development and clinical

E. Grella (✉) · R. Grella · F. D'Andrea
Department of Plastic and Reconstructive Surgery, Second
University of Naples, Via de Crecchio 3, Naples 80100, Italy
e-mail: elisa.grella@unina2.it

- implications. *Plast Reconstr Surg* 117:1214–1219, discussion 1220–1221
2. D'Andrea F, Nicoletti GF, Grella E, Grella R, Siniscalco D, Fuccio C, Rossi F, Maione S, De Novellis V (2007) Modification of cysteinyl leukotriene receptor expression in capsular contracture: Preliminary results. *Ann Plast Surg* 58:212–214
 3. Embrey M, Adams EE, Cunningham B, et al. (1999) A review of the literature on the etiology of capsular contracture and a pilot study to determine the outcome of capsular contracture interventions: *Aesth Plast Surg* 23:197–206
 4. Minami E, Koh IH, Ferreira JC, Waitzberg AF, Chifferi V, Rosewick TF, Pereira MD, Saldiva PH, de Figueiredo LF (2006) The composition and behavior of capsules around smooth and textured breast implants in pigs. *Plast Reconstr Surg* 118:874–884
 5. Prantl L, Schreml S, Fichtner-Feigl S, Poppl N, Eisenmann-Klein M, Schwarze H, Fuchtmeier B (2007) Clinical and morphological conditions in capsular contracture formed around silicone breast implants. *Plast Reconstr Surg* 120:275–284
 6. Rohrich RJ, Janis JE, Reisman NR (2003) Use of off-label and nonapproved drugs and devices in plastic surgery: *Plast Reconstr Surg* 112:241–243
 7. Zimmann OA (2007) A rabbit model for capsular contracture: Development and clinical implications. *Plast Reconstr Surg* 119:1955–1956