Invited comment

Cyclosporine (Sandimmune) and wound healing

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Immunosuppressive medication allows transplantation of organs across histocompatibility barriers. To the established immunosuppressants azathioprine, steroids and antilymphocytic serum has been added, the immunosuppressive peptide cyclosporine (Sandimmune) which has caused a revival of a wide variety of organ transplantation. Both, the organ survival and quality of life of the transplant recipients has improved dramatically with this new immunosuppressant.

Any immunosuppressive therapy, however, is associated with side effects, e.g. bone marrow depression and hepatotoxicity (azathioprine), Cushing syndrome (steroids) and nephrotoxicity (cyclosporine). The side effects can be minimized by careful dose adjustments or by changing the immunosuppressant if the patient shows sensitivity to the treatment of choice [1, 4].

Organ transplantation may be complicated by local bleeding, infection, stenosis of the anastamosed vessels or ureter.

Wound healing has not been a major clinical issue. Experimental studies showed a retardation of tissue repair in animals immunosuppressed with azathioprine or steroids [8]. In the case of cyclosporine immunosuppression the experimental data are somewhat conflicting ranging from normal to impaired wound healing [2, 3, 5, 6, 9, 10]. General immunosuppression may be however associated with reduced reparative capacity [12]. In this issue, Recker et al. demonstrated a retardation of the repair processes in experimental ureterocystoneostomy in rats. Delayed reconstitution of the epithelium with pleomorphic microvilli were shown which were fully reversible. As expected no local stenosis was observed at the ureterocystoneostomata even at the rather high cyclosporine doses. It should be noted that adequate controls e.g. animal treated with alternative immunosuppressants should be included in such experimental studies.

Thus, so far both clinical and experimental data indicate almost normal tissue repair processes at uretercystoneostomies and anastamoses of larger vessels and bronchi under cyclosporine immunosuppression. A major issue, alluded in this study, is the risk of tumour development as well as infectious complications. Present evidence however indicates that the risk of tumour development and of infection is not higher – if not lower – with cyclosporine as compared to conventional immunosuppression [7, 11].

However, well controlled clinical and experimental studies with appropriate controls are certainly welcome in this new field of clinical endeavour.

References

- 1. Beveridge T (1986) Clinical transplantation-overview. Prog Allergy 38:269–292
- Fishel R, Barbul A, Wasserkrug HL, Penberthy LT, Rettura G (1983) Cyclosporine A impairs wound healing in rats. J Surg Res 34:572-575
- Goldberg M, Lima O, Morgan E, Ayabe A, Luk S, Ferdman A, Peters WJ, Cooper JD (1983) J Thorac Cardiovasc Surg 85:821–826
- Mihatsch MJ, Thiel G, Ryffel B (1988) Morphologic diagnosis of cyclosporine nephrotoxicity. Semin Diagn Pathol 5:104–121
- Mirkovitch V, Winistoerfer B (1985) Cicatrisation de plaies ouvertes chez les rats. Helv Chir Acta 52:245-247
- Nemlander A, Ahonen J, Wiktorowicz K, Willebrand E, Hekali R, Lalla M, Haeyry P (1983) Effect of cyclosporine on wound healing. Transplantation 36:1-6
- Penn I (1988) Cancers after Cyclosporine therapy. Transplant Proc 20:276–279
- Pessa ME, Bland KI, Copeland III EM (1987) Current research review. J Surg Res 42:207–217
- 9. Pinsker KL, Veith FJ, Kamholz SL, Emeson EE, Norin A, Montefusco C(1985) Bronchial an astomotic healing in canine lung allotransplants treated with cyclosporine. Tranplantation 40:143-
- Saunders NR, Egan TM, Chamberlain D, Cooper JD (1984) Cyclosporine and bronchial healing in canine lung transplantation. J Thorac Cardiovasc Surg 88:993-999
- 11. Shaffer D, Hammer SM, Monaco AP (1987) Infectious complications with the use of cyclosporine versus azathioprine after cadaveric kidney transplantation. Am J Surg 153:381-386
- Wahl SM, Hunt DA, Allen JB, Wilder RL, Paglia L, Hand AR (1986) Bacterial cell wall-induced hepatic granulomas. J Exp Med 163:884–902

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