SUCCESSFUL TREATMENT OF SURGICALLY INDUCED NECROTIZING SCLEROKERATITIS (SINS) WITH SYSTEMIC IMMUNOSUPPRESSIVE AGENTS AND AMNIOTIC MEMBRANE GRAFTING

TRATAMIENTO INMUNOSUPRESOR SISTÉMICO Y TRASPLANTE DE MEMBRANA AMNIÓTICA EN ESCLERITIS NECROTIZANTE INDUCIDA POR CIRUGÍA (ENIC)

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ABSTRACT

Clinical case: We report the case of a 74-year-old female who developed a necrotizing sclerokeratitis affecting her left eye after uncomplicated cataract surgery. She had no previous history of systemic autoimmune disease. Histopathology of the lesion revealed necrotic granulomatosis with an increased number of plasma cells.

Discussion: Surgically induced necrotizing sclerokeratitis (SINS) is a serious entity which requires prompt and aggressive therapy to prevent its potential devastating ocular consequences. Conjunctival resection and amniotic membrane grafting may be necessary to temporarily interrupt local immunologic events in severe cases. However, associated systemic immunomodulatory therapy seems to be mandatory (Arch Soc Esp Oftalmol 2009; 84: 577-580).

RESUMEN

Caso clínico: Presentamos el caso de una mujer de 74 años que desarrolló una escleroqueratitis necrotizante en su ojo izquierdo tras cirugía de catarata no complicada. No tenía antecedentes de enfermedad autoinmune sistémica. El análisis histopatológico de la lesión mostró granulomatosis necrotizante con abundantes células plasmáticas.

Discusión: La escleroqueratitis necrotizante inducida por cirugía (ENIC) es una grave afección que requiere tratamiento precoz y agresivo tratando de prevenir sus potencialmente devastadoras consecuencias. La resección conjuntival junto con implante de membrana amniótica pueden ser necesarias para interrumpir temporalmente el proceso inmunológico local. No obstante, es esencial asociar un tratamiento inmunosupresor sistémico.
INTRODUCTION

Surgically induced Necrotizing scleritis (SINS) is a rare local self-immune condition which appears close to previous surgical incisions. It has been related with virtually all kinds of ocular surgeries (1-5). SINS develops after a latency period ranging from a few weeks to several years and could be the first expression of a self-immune vasculitis. It may also indicate the onset of vasculitis in a patient who has been already diagnoses with a self-immune entity (2). Post-surgery infections and the use of specific suture materials have been identified as potentially contributing factors for the development of SINS (3).

CLINICAL CASE

A healthy 74-year old female visits the practice referred by her ophthalmologist for evaluation and treatment of painful red eye with approximately one month of evolution. She had no antecedents of interest excepting a non-complicated cataracts surgery (phacoemulsification) in the same eye four months earlier. The ophthalmological exploration revealed an elevated injury at the level of the superonasal limbus in her left eye (close to the surgical incision) associated to multiple corneal micro-infiltrates as well as vascular ingurgitation in the conjunctiva and deep scleral plexus (fig. 1). Treatment was established with broad range antibiotic eye drops, adding autologous serum eye drops and medroxyprogesterone.

Due to the poor response to treatment, several serological tests were requested (including biochemistry, hemogram, acute phase reactants and self-immunity markers). At the same time, treatment was initiated with systemic corticoids at dosages of 1 mg/kg. In addition, we decided to take a scleroconjunctival sample with prior resection of the adjacent conjunctiva, with subsequent implant of amniotic membrane (inlay technique) joined to the application of biological adhesive (Fibrin Glue®) over the injury area (fig. 2). The biopsy (figs. 3a and 3b) was diagnosed as necrotizing granulomatosis associated to hyperplasia of plasmatic cells without...
traces of vasculitis. The results of the serological tests were normal.

Considering the possibility of SINS, it was decided to initiate treatment with Cyclosporin A (3 mg/kg/day) together with oral corticosteroids (1 mg/kg/day). Notwithstanding the treatment, eight weeks later the inflammation persisted and, due to its severity, it was decided to substitute cyclosporin for Azathioprin (100 mg/day) maintaining the oral corticosteroids.

This therapeutic regime was able to gradually control the inflammatory process (figs. 4a and 4b). Seven months after onset, the patient remains free of symptoms and continues with the treatment.

**DISCUSSION**

The diagnostic of SINS in the instant case was mainly based on the following findings:
1) Ocular surgery antecedents.
2) Absence of clinical or serological signs of systemic self-immune disease.
3) Development of necrotizing scleritis close to the previous surgical injury.

We believe that the surgical treatment, although palliative and temporary, is an important adjuvant for treating these patients. The resection of the conjunctiva adjacent to the injury area has been described as an efficient technique for diminishing the concentration of proteases (such as collagenase), as well as for the temporary interruption of the local inflammatory process, reducing the input of pro-inflammatory cytokines (4). In the instant case, the amniotic membrane contributed to controlling the

Fig. 3: (A) Biopsy of resected tissue (Stain with hematoxilin/eosine, 2X amplification) showing areas of necrotizing granulomatosis, which can be seen better in image (B) with 10X amplification.

Fig. 4: Slit lamp vision at month 1 and month 3 (figures A and B respectively) after the introduction of Azathioprin. Notice the absence of vascular ingurgitation and corneal infiltrates, as well as the residual thinning of the involved sclera.
inflammation in the area of the implant, although the adjacent areas began to be affected as surgery on its own is unable to halt the underlying systemic immunological process. Accordingly, it was decided to begin an immunomodulator treatment in an attempt to achieve optimum control over the disease and prevent recurrences.

It has been postulated that SINS could be related to a localized relative ischemia associated to the surgical wound (1). In approximately 60% of cases it was possible to identify a pathology causing the condition, mostly being a connective tissue disease. However, little is known about the immunological mechanism inducing its appearance. It has been speculated that it could be a T-dependent delayed hypersensitivity reaction against certain unidentified tissue antigens (arising out of the surgical trauma and/or the temporary ischemia) (1). In this regard, some authors (5) have obtained encouraging results utilizing specific T-cell response inhibiting agents such as Tacrolimus. Paradoxically, in our case the patient responded positively to Azathioprine (that inhibits T- and B-dependent immunological responses) and not to Cyclosporine A (T-inhibitor). In fact, the biopsy of our patient tissue exhibited plasmatic cell hyperplasia around the injury area, suggesting a preferential involvement of the B-dependent cellular response. In this sense, although self-antibodies have not been identified, the presence of immunocomplexes has been identified in some cases (1), reinforcing the hypothesis of an involvement of the B-cell response. The fact that SINS may or may not be a defined clinical entity or only the first expression or trigger of a self-immune process in some susceptible individuals is still a controversial topic.

REFERENCES