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IgA Nephropathy Improved by a New Modality: MAM14 Immunotherapy: A Case Report in Kuwait

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Abstract

A 45 Year-old- Kuwaiti female with a case of IgA nephropathy (IgA N) was studied from 2002 to 2014 at Mubarak Hospital. The chief complaint was hematuria. In the first year she was given a conventional corticosteroid regimen. Her parameters at this stage are used as controls for the remainder of the study. She was treated with FK506 immunosuppressant capsules in the second year and vaccinated with allogeneic peripheral blood lymphocytes (PBL) in the third year. This study includes the following parameters: serum creatinine, serum albumin, IgA level, and 24-hour urine protein. In the first year the patient was only on corticosteroid, in the second year only FK506, and in the third year was treated only with PBL vaccination. A booster dose of vaccine was administered after approximately 5 years. The patient's significant improvements after PBL vaccination have persisted for 9 years. The mechanism postulated for this kind of immunotherapy is induction of novel therapeutic antigens, including heat shock protein (HSP), that interact with autoreactive T or B cells in the recipient. The result is T regulatory cells (T-reg) claimed to be responsible for shifting T-cell detrimental function to regulatory function, hence preventing the pathological production and deposition of IgA in the kidney. Data accumulated from our lab, but not yet published, demonstrates that MAM14 immunotherapy ameliorates symptoms and signs of certain autoimmune disorders.

Keywords: PBL; MAM14; Immunotherapy; FK 506; IgA nephropathy.

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1. Introduction

IgA Nephropathy (IgA N), also known as Berger disease, is the most common cause of primary (idiopathic) glomerulonephritis in the developed world [1-6]. Slow progression to end stage renal disease occurs in up to 50% of affected patients [7]. Berger disease is a kidney disease that occurs when an antibody called immunoglobulin A lodges in the kidney. This results in local inflammation that, over time, may hamper the ability of the kidney to filter waste, excess water, and electrolytes from blood. Kidney damage may be indicated by blood and protein in urine, high BP, and swollen feet. IgA N usually progresses slowly over many years, but the course of the disease in each person is uncertain. Some people leak blood in their urine without developing problems, some eventually achieve complete remission, and others develop end-stage kidney failure. No cure exists for IgA N, but certain medications can slow its course [8]. In this case report we present a new method to treat IgA N, called MAM14 immunotherapy, using stressed PBL vaccination compared to other immunosuppressant called at one time as FK506(Tacrolimus).

2. Materials and Methods

A 45-year-old female presented complaining of recurrent gross hematuria shortly following any athletic exertion, with proteinuria. Three cohort studies of this patient were conducted. During the first year (2002) this patient was on a conventional corticosteroid regimen only. During the second year (2003) FK506 investigational immunosuppressant capsules from the University of Pittsburgh Medical Center were administered. In 2004 stressed allogeneic lymphocyte vaccination was implemented. The mechanism postulated for MAM14 immunotherapy is that culturing lymphocytes in vitro allow induction of novel, therapeutic antigens , including heat shock proteins . These therapeutic antigens assist the autoreactive T cell to shift to regulatory cell. Regulate the autoimmune attack. Lead to homeostasis and was further explored in 2013 [9].

3. Results

Results are depicted as four Figures.

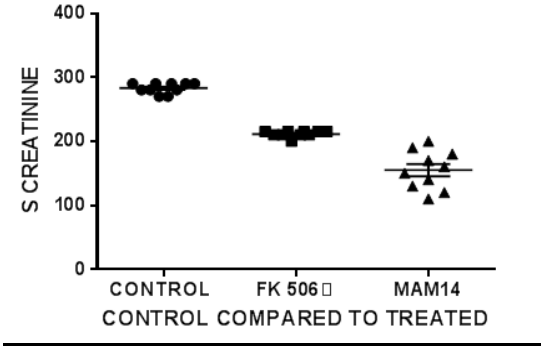

Figure 1: Serum creatinine. Analyzed: One-way ANOVA data, P value < 0.0001.

Figure 1 shows that Serum creatinine improved dramatically using FK506. Also Allogeneic PBL improved serum creatinine significantly. But the difference in this article that is no side effect noted on MAM14

vaccination for 9 years. However, FK506 is a drug with side effects.

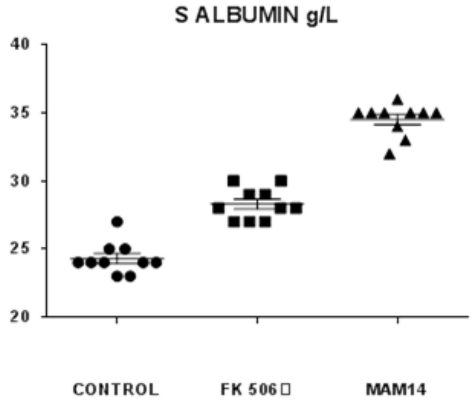

Figure 2: Serum albumin, Analyzed: One-way ANOVA data, P value < 0.0001.

Figure 2 shows that Serum albumin concentration improved with FK506 and PBL vaccination (MAM14) the difference is the safety of MAM14 and long lasting for 9 years.

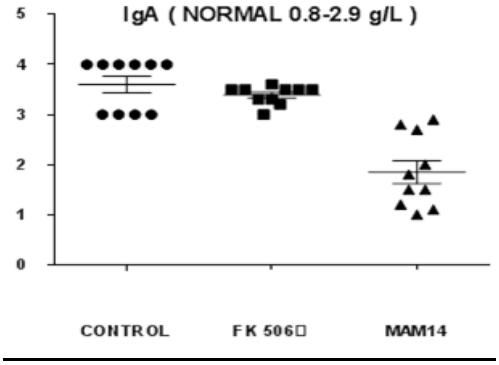

Figure 3: IgA level, Analyzed: One-way ANOVA data, P value < 0.0001.

Figure 3 shows that IgA levels dropped dramatically by FK506 and by PBL vaccination. Normal concentration is 0.8-2.9 g/L

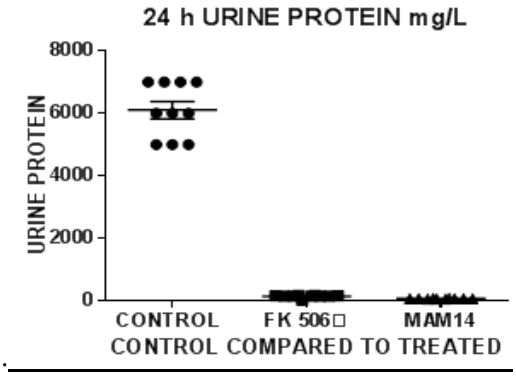

Figure 4: 24 hour urine protein, Analyzed: One-way ANOVA data, P value < 0.0001.

Figure 4 shows that Urine protein was reduced significantly by FK506 for one year and reduced significantly by PBL vaccination for 9 years. The difference is the leukocyte vaccination is safe and FK 506 is a drug with side effects.

The administration of a conventional corticosteroid regimen to this patient resulted in some short-term improvements in the parameters studied. FK506 immunosuppressant caused significant improvements for a short period. MAM14 data showed that after administering the MAM14 immunotherapy protocol remarkable improvements in all parameters tested in this patient (serum creatinine, serum albumin, IgA levels, and 24-hour urine proteins) were sustained from the third year onward for as long as 9 years. A booster dose was given after 5 years.

4. Conclusion

We postulate a mechanism of action in the MAM14 protocol in which culturing donor lymphocytes induces expression of heat shock proteins (9) that interact with activated or autoreactive memory T or B cells in the recipient. The result is a suppressor cell (T-reg) that responds to self-antigens by expression of immunosuppressive cytokines, principally Th2-associated (IL-10 and TGFB), downregulating expression of Th1-associated cytokines (IL-2; IL-12 and IFN-GAMA; and IL-1B, TNF-ALFA, and IL6). The outcome is a suppression of autoimmune attacks on host tissue. T-reg in turn modifies production of IgA through T-B cell interactions. An imbalance of type 1 and type 2 T cell subsets has been proposed as an explanation for the dysregulated IgA responses seen in IgA nephropathy. In addition, there is provisional work suggesting that types 1 and 2 cytokines differentially affect IgA 1 o-glycosylation [8].

The regulatory T cells formerly known as suppressor T cells are a subpopulation of T cells that modulate the immune system, maintain tolerance to self-antigens, and abrogate autoimmune disease. These cells generally suppress or downregulate induction and proliferation of effector T cells. Additional regulatory T cells known as T-reg 17 cells have recently been identified. Mouse models have suggested that modulation of T-regs can positively affect autoimmune disease and cancer, and facilitate organ transplant.

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