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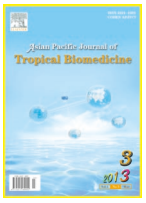

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Effect of mesenchymal stem cells on anti-Thy1,1 induced kidney injury in albino rats

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PEER REVIEW

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Comments

This is a good study in which the authors examined the effectiveness of MSCs treatment in animal model of kidney disease induced by anti-Thy1 antibody. The result is interesting and suggests that glomerulonephritis may be successfully treated with MSCs.
(Details on Page 180)

ABSTRACT

Objective: To evaluate the effect of mesenchymal stem cells (MSCs) in rats with anti-Thy1,1 nephritis. **Methods:** Female albino rats were divided into three groups, control group, anti-Thy1,1 group and treatment with *i.v.* MSCs group. MSCs were derived from bone marrow of male albino rats, Y-chromosome gene was detected by polymerase chain reaction in the kidney. Serum urea and creatinine were estimated for all groups. Kidney of all studied groups was examined histologically and histochemically (total carbohydrates and total proteins). DNA fragmentation and expression of α-SMA were detected. **Results:** Kidney of animals injected with anti-Thy1,1 showed inflammatory leucocytic infiltration, hypertrophied glomeruli, tubular necrosis and congestion in the renal blood vessels. The kidney tissue also showed reduction of carbohydrates and total proteins together with increase in apoptosis and in expression of α-SMA. Moreover, the levels of urea and creatinine were elevated. Treating animals with MSCs revealed that kidney tissue displayed an improvement in the histological and histochemical changes. Apoptosis and α-SMA expression were decreased, and the levels of urea and creatinine decreased. **Conclusions:** The obtained results demonstrated the potential of MSCs to ameliorate the structure and function of the kidney in rats with anti-Thy1,1 nephritis possibly through the release of paracrine growth factor(s).

KEYWORDS
Anti-Thy1,1, Nephritis, Mesenchymal stem cells, α-SMA, Apoptosis

1. Introduction

Glomerulonephritis is a renal disease characterized by inflammation of the glomeruli or small blood vessels in the kidneys. It may present with isolated hematuria and/or proteinuria or as a nephrotic syndrome, acute renal failure, or chronic renal failure. Anti-Thy1,1 antibody is a monoclonal IgG which works against *Thy 1* gene. It is used as standard animal model to produce experimental glomerulonephritis which is popularly known in the field of nephrology as anti-Thy1 glomerulonephritis. Glomerulonephritis induced by a single injection of anti-Thy1 antibody is characterized by an acute and self-resolving disease process, whereas repeated injection of the antibody induces irreversible glomerulosclerosis[1]. Masuda *et al.* studied the pathological process of glomerulonephritis including glomerular capillary damage, and vascular endothelial growth factor (VEGF) after anti-Thy1,1 treatment in rats[2]. They found that VEGF (164) protein levels increased in the damaged glomeruli during 5 to 10 d, and endothelial-cell proliferation increased with capillary repair in the vehicle-injected group. After 2 weeks, anti-VEGF antibody significiantly decreased. At 6 weeks glomerular scleroses developed with mesangial matrix

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accumulation and proteinuria.

Stem cells are biological cells found in all multicellular organisms. Stem cells differ from other kinds of cells in the body. All stem cells—regardless of their source—have three general properties: capable of dividing and renewing themselves for long periods, unspecialized and capable of giving rise to specialized cell types. Bone marrow contains at least two kinds of stem cells, hematopoietic stem cells and stem cells for nonhematopoietic tissues[3], variously referred to as mesenchymal stem cells (MSCs). MSCs are interesting because they are easily isolated from a small aspirate of bone marrow and readily generate single-cell-derived colonies[4]. They can differentiate into different types of cells and for these reasons they are currently being tested for their potential use in cell and gene therapy for a number of diseases[5,6]. Further, MSCs administration could repair injured lung, liver, or heart by reducing inflammation, collagen deposition and remodeling[7].

Kidney injury represents a major clinical problem with high mortality and limited causal treatments. The use of cell therapy has been suggested as a potential modality to improve the course and outcome of kidney injury[8]. When female kidneys were transplanted into male recipients, Y chromosome-bearing cells were found in the transplanted kidney. Yang *et al.* investigated the effect of bone mesenchymal stem cell transplantation on repair of glomerular podocytes and on the nephrin expression in rats with puromycin aminonucleoside-induced nephrosis[9]. Urinary protein and blood cholesterol contents increased in puromycin aminonucleoside-treated animals. The bone mesenchymal stem cell transplantation group had decreased urinary protein and blood cholesterol contents and increased plasma albumin and had increased nephrin mRNA and protein expression compared with the nephrosis model group. Pino and Humes used the stem cell technology for the treatment of acute and chronic renal failure[10]. The stem cell technologies included adult stem cells, embryonic stem cells and induced pluripotent stem cells as cell sources for the treatment of acute and chronic renal failure. The present work was aimed to study the ameliorative effect of MSCs in anti-Thy1 induced nephritis in albino rats.

2. Material and methods

2.1. Rats

Healthy adult male and females albino rats (*Ratus norvegius*) with approximately 2 months old and weight ranging from (150±20) g were used in the present study. The animals were selected randomly and kept in individual special plastic rodent cages in the laboratory under constant condition of temperature of 25 °C with a reverse natural dark-light cycle 12/12 h for at least 1 week before the experimental work. Animals were feed on a standard rodent diet. Water was available *ad libitum*. The use of animals in this study conforms to the guidelines and bioethics of the Egyptian Scientific Research Academy. Animals were divided into three groups:

Group 1: Female rats were served as normal control.

Group 2: Animals were injected via tail vein with anti-Thy1 (Abcam company, US) at a dose level of 1 mg/kg body weight in PBS[11].

Group 3: Animals were injected with anti-Thy1 via tail vein. After 5 d, each animal was intravenously injected with MSCs extracted from male albino rats at a dose of 1×10^6 cells per rat[12].

2.2. Preparation of bone marrow-derived MSC

Bone marrow was harvested by flushing the tibiae and femurs of male albino rats with Dulbecco's modified Eagle's medium (DMEM, GIBCO/BRL) supplemented with 10% (v/v) fetal bovine serum (GIBCO/BRL). Nucleated cells were isolated with a density gradient Ficoll/Paque Pharmacia and resuspended in complete culture medium supplemented with 1% (v/v) penicillin-streptomycin (GIBCO/BRL). Cells were incubated at 37 °C in 5% (v/v) humidified CO_2 for 12-14 d as primary culture or upon formation of large colonies. When large colonies developed (80%-90% confluence), cultures were washed twice with PBS and the cells were trypsinized with 2.5 g/L trypsin in 1 mmol EDTA (GIBCO/BRL) for 5 min at 37 °C. After centrifugation, cells were resuspended with serum-supplemented medium and incubated in a 50 cm^2 culture flask (Falcon). The resulting cultures were referred to as the first-passage cultures. MSCs in culture were characterized by their adhesiveness and fusiform shape[13].

2.3. PCR detection of male-derived MSCs

Genomic DNA was prepared from kidney tissues homogenate of the rats in each group using Wizard Genomic DNA purification kit (Promega, USA). The presence or absence of the sex determination region on the Y chromosome male (*SRY*) gene in recipient female rats was assessed by PCR. Primer sequences for *SRY* gene (forward, 5′-CAT CGA AGG GTT AAA GTG CCA-3′, reverse 5′-ATA GTG TGT AG-GTT GTT GTC C-3′) were obtained from published sequences by Bruckner *et al.* and amplified a product of 104 bp[15]. The PCR conditions were as follow: incubation at 94 °C for 4 min; 35 cycles of incubation at 94 °C for 50 seconds, 60 °C for 30 seconds, and 72 °C for 1 min; with a final incubation at 72 °C for 10 min. PCR products were separated using 2% agarose gel electrophoresis and stained with ethidium bromide. Positive (male albino rat genomic DNA) and negative (female albino rat genomic DNA) controls were included in each assay.

2.4. Extraction of DNA

DNA was extracted according to method of Aljanabi and Martinez[15]. Ten milligram of kidney tissues (0.01 mg) in eppendorf tubes were lysed with 600 μL buffer (50 mmol/L NaCl, 1 mmol/L Na_2EDTA, 5 g/L SDS, pH 8.3) and gently shaked. The mixure was incubated overnight at 37 °C. Then, 20 μL of saturated NaCl was added the sample, shaked and centrifuged at 12 000 r/min for 10 min. The supernatant was transferred to new eppendorf tubes and then DNA precipitated by 600 μL cold isoproprnol. The mix was inverted several times till fine fibres appear. And then centrifuged at 12 000 r/min for 5 min. The supernatant was removed and the pellets were washed with 500 μL 70% (v/v) ethyl alcohol centrifuged at 12 000 r/min for 5 min. After centrifugation the alcohol was decated or tipped out and the tubes plotted on Whatman paper to be dry. The pellets were resuspended in 50 μL or appropriate volume of TE buffer (10 mmol/L Tris, 1 mmol/L EDTA, pH 8). The resuspended

DNA was incubated for 30-60 min with loading mix (RNase + loading buffer) and then loaded into the gel wells.

Electrophoresis was performed for 2 h at 50 V using 1× TBE buffer as running buffer. Gel was photographed using a Polaroid camera. DNA was visualized using a 312 nm UV light under a transilluminator.

2.5. Histological and histochemical examinations

Animals from experimental group were sacrificed immediately after 28 d, and kidney was quickly removed and fixed in 10% (v/v) neutral formalin. Fixed materials were embedded in paraffin wax and sections of 5 μm thickness were cut. Slides were stained with haematoxylin and eosin for histological examination. For histochemical study, specimens were fixed in Carnoy's fluid. Periodic acid Schiff's reaction was used for demonstration of polysaccharides and total proteins was detected using the mercury bromophenol blue method[16].

2.6. Immunohistochemical detection of α-SMA

For immunohistochemical localization of α-SMA, fixed wax sections were stained using the avidin-biotin peroxidase method. Formalin fixed paraffin-embedded tissue sections were deparaffinized and endogenous peroxidase activity was blocked with PBS, 0.3% (v/v) H_2O_2, and 10% (v/v) methanol for 45 min. To prevent nonspecific binding, the sections were incubated for 60 min in PBS containing 3 g/L Triton X-100, 10 g/L BSA, 4% (v/v) goat serum (GS), and 4% (v/v) horse serum (block solution). The sections were then incubated overnight at 4 °C with mouse monoclonal α-SMA primary antibody: Actin, Smooth Ab 1 (1A4) mouse MAb MS-113-PO (1:100; lot: 113P101, Neo Markers Fremont, CA, USA). Thereafter, the sections were incubated for 1 h with biotinylated horse anti-mouse/rabbit IgG secondary antibody (Vector Laboratories). Sections were then incubated with avidin-biotin-conjugated peroxidase for 45 min. Finally, the sections were washed and stained with 3,3-diaminobenzidine tetrahydrochloride (Sigma) containing 0.01% (v/v) H_2O_2 in 0.05 mol/L Tris-buffered saline (pH 7.6) for 3-5 min. After the enzyme reaction, the sections were washed in tap water, counterstained with hematoxylin, then dehydrated in alcohol, cleared in xylene, and mounted in DPX (Merck, Darmstadt, Germany). Area of α-SMA positive staining was assessed in predetermined high power field (40×) of the cortex (10 fields) and then was captured by a digital camera[17].

2.7. Biochemical assays

For biochemical study, sera were obtained by centrifugation of the blood samples and stored at 20 °C until assayed for the biochemical parameters. Creatinine and urea were estimated using the methods of Henry[18], Patton and Crouch[19], respectively.

2.8. Statistical analysis

The results are expressed as mean±SD of different groups. The differences between the mean values were evaluated by ANOVA followed by Student's *t*-test using Minitab 12 computer program (Minitab Inc., State Collage, PA).

3. Results

3.1. PCR analysis of SRY gene

Animals injected with anti-Thy1 and control animals showed negative *SRY* gene. On the other hand, rats treated with anti-Thy1 and given intravenous MSCs showed positive *SRY* gene (Figure 1).

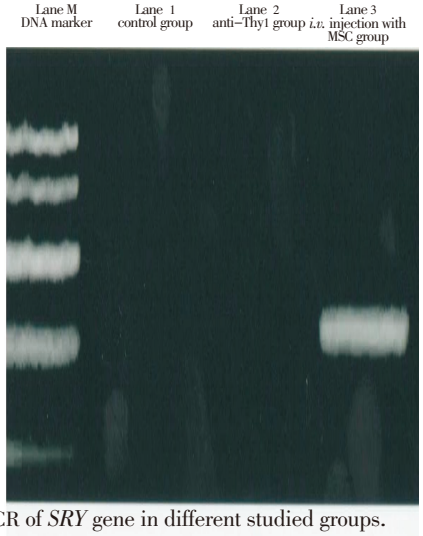

Figure 1. PCR of *SRY* gene in different studied groups.

3.2. DNA fragmentation

Electrophoretic pattern of DNA fragmentation (apoptosis) of kidney tissue appeared as bands in gel and located at 180 bp and its multiply like 360 and 540 bp *etc*. Figure 1 reveals that anti-Thy1 leads to obvious DNA fragmentation and apoptotic bands. On the other hand, treatment with anti-Thy1 and MSCs decreased the amount of fragmented DNA (Figure 2).

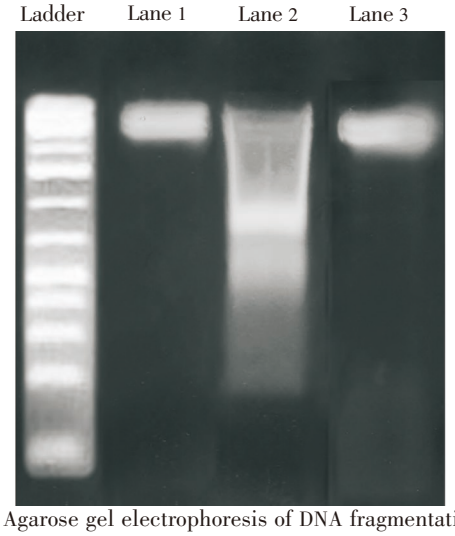

Figure 2. Agarose gel electrophoresis of DNA fragmentation in rat kidney.

Lane 1: Control; Lane 2: Anti-Thy1 group; Lane 3: Treated group by *i.v.* MSC.

3.3. Biochemical results

The levels of urea and creatinine were significantly elevated in animals treated with anti-Thy1 compared with the normal animals. Animals treated with MSCs induced a significant decrease in urea and creatinine levels compared

with anti-Thy1 treated animals (Table 1).

Table 1

Comparison of serum urea and creatinine in experimental groups.

Parameters (mg/dL)	Treatment		
	Control	Anti-Thy1	Anti-Thy1+MSCs
Urea	42.10±4.20	68.80±6.80	44.30±5.10
Creatinine	0.20±0.08	1.02±0.06	0.34±0.04

3.4. Histological observations

Figure 3a shows that kidney cortex of control rat consisted of renal corpuscles and tubules. Renal corpuscles consisted of Bowman′capsule with urinary space between double membrane. Also, a tuft of glumerular capillaries was enclosed in Bowman′s capsule. Renal tubules were of two types, proximal and distal tubules. Proximal tubules were lined with low columnar epithelium and had narrow lumen. Distal tubules possessed wide lumen and were lined by cuboidal epithelial. Animals injected with anti-Thy1 displayed many histopathological features: renal blood vessels appeared elongated and congested (Figure 3b). Intertubular leucocytic infiltration was evident (Figure 3c). The renal tubules were degenerated and lost its normal appearance. Their epithelial linning showed cytoplasmic vacuolation with pyknotic nuclei. The glomeruli were hypertrophoid with pyknotic nuclei (Figure 3d). Some sorts of adhesion were noted between the glomerular tuft and Bowman′s corpuscle. Animal treated with MSCs showed somewhat healthy appearance as the kidney tissue displayed some improvements in the histological changes. The inflammatory cells were reduced and hypertrophoid glomeruli were absent. Bowman′s corpuscle generally appeared in circular shape (Figure 3e).

3.5. Histochemical observations

In control rat, total carbohydrates existed in brush borders of tubular epithelial cells and in the glomeruli (Figure 4a). Examination of kidney section after anti-Thy1 injection revealed a marked reduction of carbohydrates content in the tubular epithelial cells (Figure 4b). Animals treated with MSCs induced a noticeable increase in carbohydrates in renal corpuscles and tubules (Figure 4c).

The protein materials in the cells of renal tubules of control rat were displayed in the cytoplasm in the form of small bluish irregular particles. The nuclear envelope, chromatin materials and nucleoli were positively stained (Figure 5a). Examination of kidney sections of animals injected with anti-Thy1 showed a marked decrease in total proteins, degenerated in renal tubules and most of them appeared devoid of proteins (Figure 5b). A moderated number of total proteins were observed in glomeruli and renal tubules of animals treated with MSCs (Figure 5c).

3.6. Expression of α-SMA

The α-SMA was expressed in the smooth muscle cells of renal arterioles but was rarely evident in the renal interstitium of control animals (Figure 6a). An increase in expression of α-SMA positive interstitial fibroblastic cells was recorded in the kidneys of anti-Thy1 animals (Figure 6b). Treatment with *i.v.* MSCs reduced interstitial expression of α-SMA (Figure 6c). Quantification of α-SMA expression in renal tissue revealed that the percentage of α-SMA positive staining area significantly ($P<0.05$) decreased in animals given MSCs group compared with anti-Thy1 group.

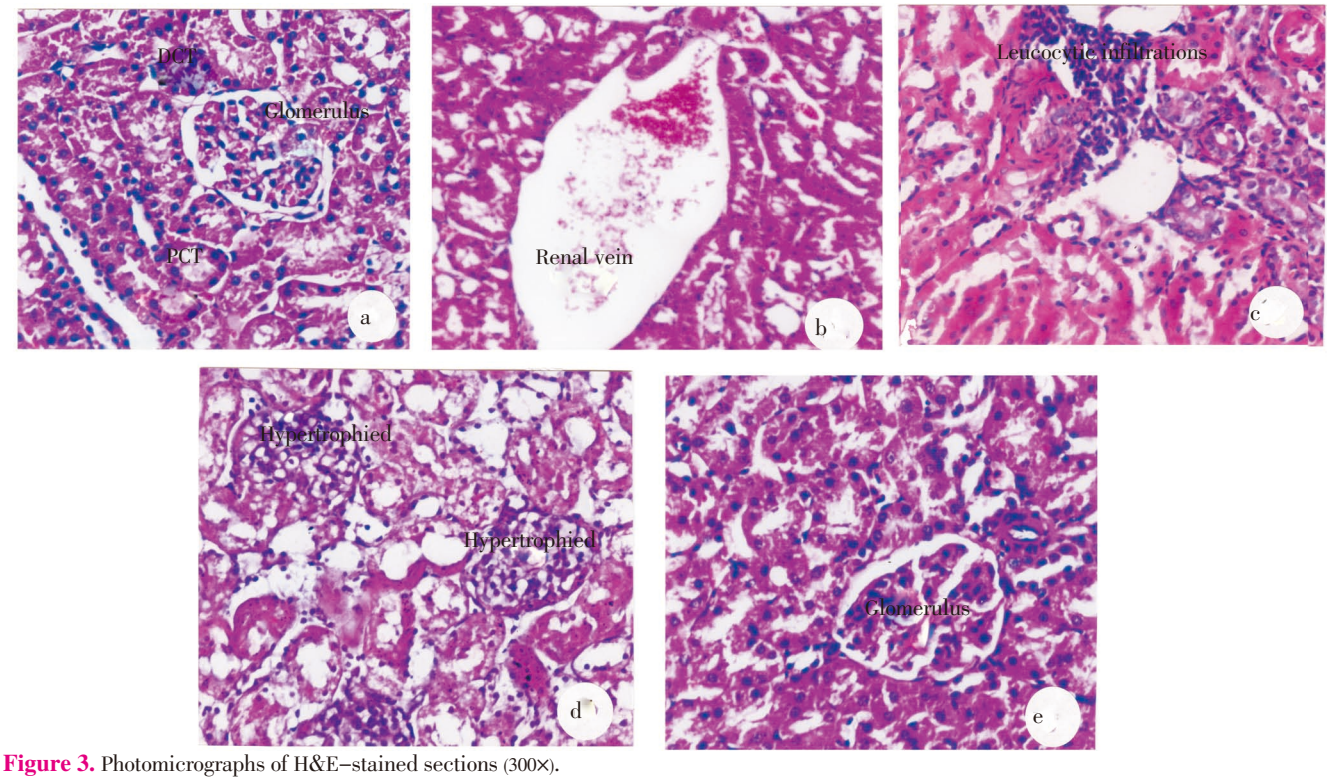

Figure 3. Photomicrographs of H&E-stained sections (300×).

(a) Kidney cortex of a control rat showing glomerulus, distal and proximal collecting tubules; (b) and (c) Kidney cortex of anti-Thy1-treated rats showing congested renal vein and leucocytic infiltrations; (d) Kidney cortex of a rat treated with anti-Thy1 showing hypertrophied glomeruli and degenerated renal tubules; (e) kidney of a rat treated with anti-Thy1 and MSCs showing normal glomerulus and renal tubules.

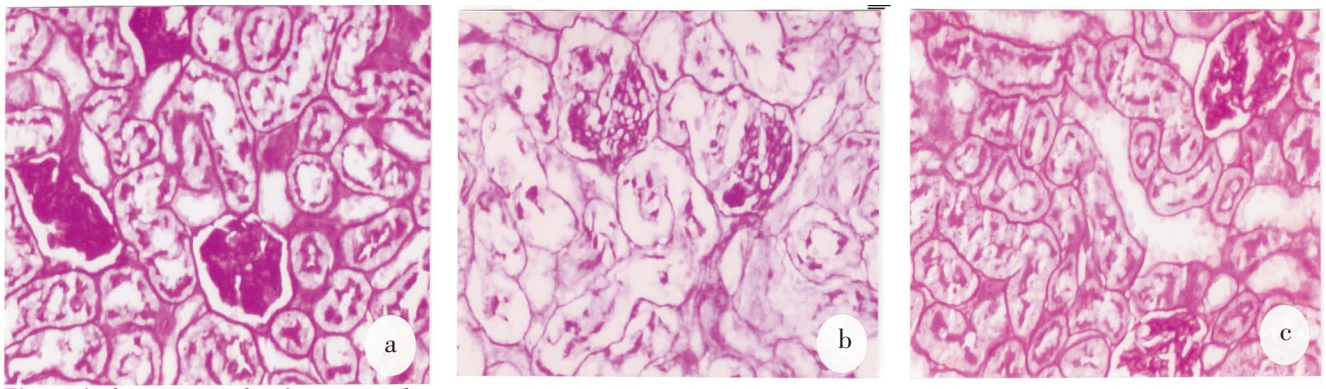

Figure 4. Photomicrographs of PAS-stained sections (300×).
(a) Kidney cortex of a control rat; (b) Kidney cortex of anti-Thy1-treated rat showing decrease of carbohydrates; (c) Kidney of a rat treated with anti-Thy1 and MSCs showing an increase in carbohydrate contents in the glomerulus and renal tubules.

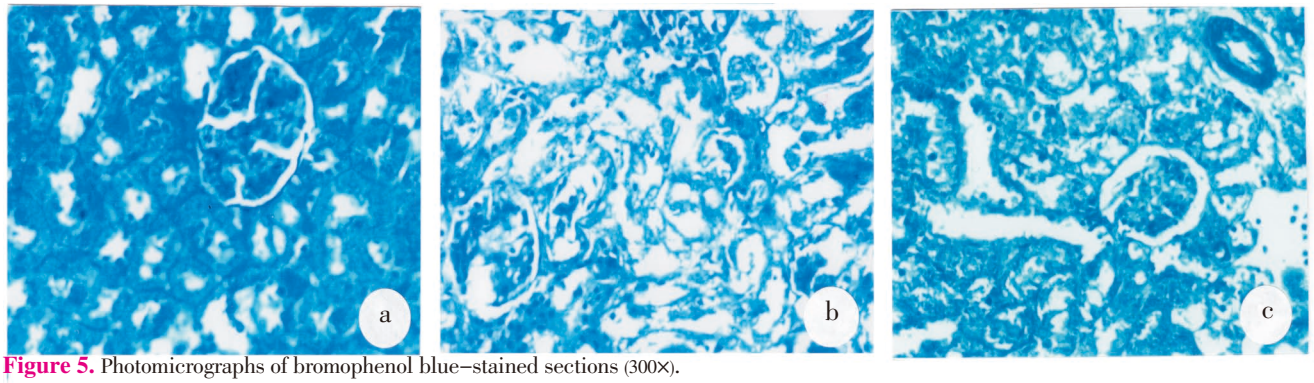

Figure 5. Photomicrographs of bromophenol blue-stained sections (300×).
(a) Kidney cortex of a control rat; (b) Kidney cortex of anti-Thy1-treated rat showing a decrease of total proteins; (c) Kidney of a rat treated with anti-Thy1 and MSCs showing an increase in protein contents in the glomerulus and renal tubules.

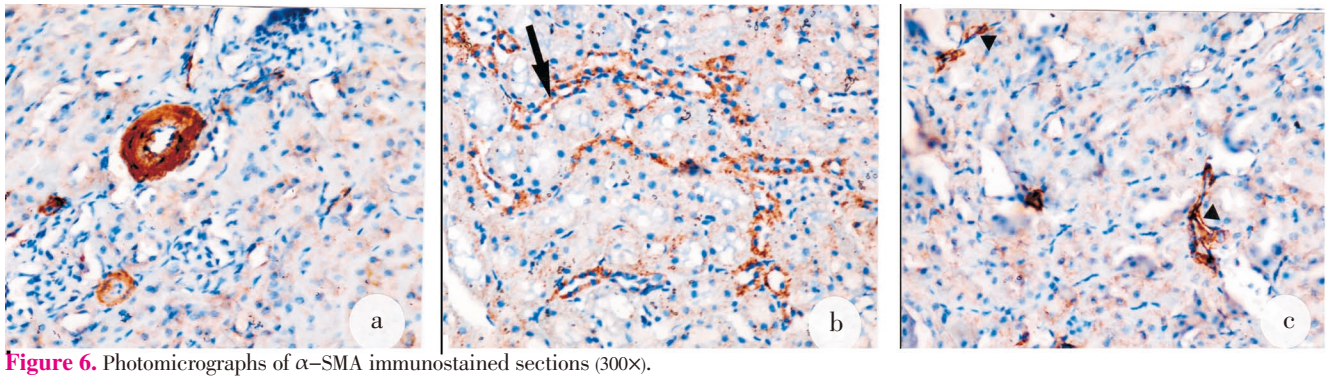

Figure 6. Photomicrographs of α-SMA immunostained sections (300×).
(a) Kidney of a control rat showing expression of α-SMA in renal arteriols; (b) After treatment with anti-Thy1 showing an increase in expression of α-SMA positive fibroblastic cells (arrow); (c) After treatment with anti-Thy1 and MSCs showing a decrease of α-SMA expression (arrow heads).

4. Discussion

The results of the present work revealed that rats injected with anti-Thy1 induced renal injury. Kidney tissue impairments began to appear in rats injected with anti-Thy1 in the form of an inflammatory leucocytic infiltration, hypertrophy of glomeruli, tubular necrosis and congestion of renal blood vessels. The levels of urea and creatinine were elevated in rats treated with anti-Thy1. The kidney tissue also showed reduction of carbohydrates and total proteins. These results are in agreement with those of many investigators. Ulrich *et al*. studied a model of anti-Thy1 glomerulonephritis after a signal intravenous injection[20]. Glomerular damage with matrix deposition, hypercellularity, glomerular scarring and tubulointerstitial damage were recorded in rats after 2 weeks of anti-Thy1 injection. In addition, a high degree of interstitial inflammation and reduction of total carbohydrates deposition in rats was observed. Glomerulonephritis involving glomerular cell apoptosis, inflammatory cell migration, and glomerular cell proliferation was observed in Lewis rats injected with anti-Thy1[21]. Boor *et al*. provided that proliferation of renal fibroblasts, tubulointerstitial damage, interstitial fibrosis, high level of creatinine and reduction of total carbohydrates content were resulted from acute phase of progressive anti-Thy1, 1 glomerulonephritis[22]. Peters *et al*. reported that after

injecting rats with anti-Thy1, the kidney showed chronic progressive glomerulosclerosis accompanied with reduction of total carbohydrates content and protein production[23]. The creatinine level and blood urea nitrogen increased. The pathological process of glomerulonephritis includes inhibition of glomerular capillary and an increase of mesenchymal hypercellularity was observed in rats injected with anti-Thy1 during 5 d after injection. At week 6, total carbohydrates were reduced[2].

In this work, an increase in expression of α-SMA was recorded in kidney of rats injected with anti-Thy1. α-SMA expression is a typical molecular marker of myofibroblasts in many nephropathies[1]. In agreement with the present result, Abbate *et al.* reported that the development of fibrosis in anti-Thy1 treated rat is paralleled by increased expression of α-SMA in the tubulo-interstitial area due to peritubular accumulation of myofibroblasts[24]. Rachmawati *et al.* reported that renal fibrosis induced by anti-Thy1 in rats was observed by an increase of α-SMA expression in tubular interstitial area[25]. Sadakane *et al.* found leucocyte infiltration and an increase in the expression of α-SMA in kidney of anti-Thy1-treated rats due to increase in mesengial matrix accumulation and overexpression of transforming growth factor (TGF-β)[26].

In the present work, anti-Thy1 was found to induce DNA fragmentation in the kidney. These results comes in agreement with many investigators who indicated that anti-Thy1 induced apoptosis in different animals. Sakai *et al.* reported that anti-Thy1 induced necrosis and DNA fragmentation in Wistar rats[27]. Moreover, the glomerular expression of TGF-β, heparan sulfate proteoglycan and chondroitin sulfate proteoglycan were significantly increased. Ott *et al.* examined different markers for cell damage in renal tissue after injection with anti-Thy1 and found that apoptosis plays an important pathophysiological role in glomerulonephritis by restoring tissue structure after proliferation of intrinsic renal cells and infiltration of leucocytes[28]. Wang *et al.* reported that apoptosis was significantly increased in Thy1 nephritis after 5 d of injection[29]. They observed that in DNA damage, the complement C5b-C9 complexes resulted in cell apoptosis by mechanism of sublytic C5b-C9-mediated glomerular mesangial cell apoptosis.

The mechanism of anti-Thy1 glomerulonephritis as an experimental model for mesangial proliferative glomerulonephritis was reported by some investigators[30,31]. Administration of anti-Thy1 to rats leads to proliferative glomerulonephritis, which is characterized by complement dependent injury of mesangial cells, followed by mesangial proliferation. Then transient extracellular matrix (ECM) deposition was observed. Excessive deposition of ECM is the characteristic feature of organ fibrosis. Lots of mediators are involved in the development of scarring and fibrotic conditions. TGF-β is known to play an important role in this process. Generally, TGF-β induces the deposition of ECM through stimulation of ECM production, down-regulation of ECM-degrading proteases and up-regulation of protease inhibitors. By these mechanisms, TGF-β is thought to be involved in the progression of renal fibrosis[32].

In the present work, bone marrow-derived MSCs were isolated from male rats, grown and detected. PCR of *SRY* gene expression was observed in female rats treated with male MSCs. After 28 d, it was observed that MSCs ameliorated the histological and histochemical changes in rats injected with anti-Thy1 antibody. The levels of creatinine and urea decreased. Moreover, the expression of α-SMA and apoptosis decreased after MSCs treatment.

Bone marrow-derived stem cells contribute to cell turnover and repair in various tissue types, including the kidneys[33]. MSCs are attractive candidates for renal repair, because nephrons are mesenchymal origin and because stromal cells are of crucial importance for signaling, leading to differentiation of both nephrons and collecting ducts[34].

MSCs showed *in vitro* properties that resemble those of fibroblasts. In this concern, Lin *et al.* mentioned that MSC can be used in therapy of fibrotic diseases[35]. Other researchers indicated that whole bone marrow-derived cells have been shown to be effective in treating fibrosis development[36,37]. Furthermore, MSC therapies were tested for heart, lung, and chronic diseases and were found to be effective at reducing the fibrotic area and correlated with good outcomes[38]. The present results showed that α-SMA expression decreased in MSCs-treated animals and this proved the antifibrotic effect of MSCs.

MSC was found to secrete high concentrations of growth factors such as VEGF, TGF-β, and hepatocyte growth factor[39]. In particular, proangiogenic effects of VEGF might help to restitute glomerular capillaries better. In contrast, Kunter *et al.* failed to detect any evidence of transdifferentiation of MSC into glomerular, tubular, or renal interstitial cells[40].

It was reported that the mechanism mediating the effects of MSCs can be primarily paracrine. MSCs can express several growth factors such as hepatocyte growth factor, VEGF and insulin like growth factor-1, all known to improve renal function, mediated by their antiapoptotic, mitogenic and other cytokine actions. These paracrine actions of MSCs result in the renal down regulation of proinflammatory cytokines IL-1-β, TNF-α, and IFN-γ, as well as inducible nitric oxide synthase and up regulation of anti-inflammatory and organ-protective interleukin-10, as well as basic fibroblast growth factor, TGF-α and antiapoptotic Bc1-2[41].

There was also accumulated evidence that MSCs have strong immunosuppressive activity. MSCs modulated the immune response by altering the cytokine response of dendritic cells and T cells, by interfering with the development of immune competent dendritic cells, and by favoring the development of regulatory T cells. MSCs

inhibited the activation of T cells that caused by anti-Thy1 nephritis after disease induction. Also, the mode of action seems to involve the generation of soluble mediators with paracrine actions, including IL-6 and macrophage colony stimulating factor[42]. In conclusion, MSCs ameliorates anti-Thy1-induced kidney injury in rats and this may be attributed to paracrine growth factor release.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Comments

Background

Kidney injury is a common clinical entity with high morbidity and mortality rates and ever increasing medical costs. Recently, mesenchymal stem cells (MSCs) have been reported to be an attractive therapeutic cell source for the treatment of renal diseases.

Research frontiers

This study evaluated the effects of bone marrow-derived mesenchymal stem cells on the repair and prevention of kidney injury model induced by intravenous injection of anti-Thy1 antibody into rats.

Related Reports

The data presented in this manuscript showed that bone marrow-derived MSCs contribute to renal repair in experimental glomerulonephritis induced by injection of anti-Thy1 antibody into rats. These findings are in agreement with the previous studies by Tsuda *et al.* (*Am J Physiol Renal Physiol* 2010, 299: F1004-13), who reported that allogenic fetal membrane-derived MSCs contribute to the renal repair in experimental glomerulonephritis by producing paracrine factors.

Innovations and breakthroughs

Kidney disease is a growing public health problem and represents large human and economic problems. A growing body of data suggest that MSCs may improve pathologic conditions involving different organs. This study assesses the the possible beneficial effect of MSCs after kidney injury induced by injection of anti-Thy1 antibody into rats.

Applications

MSCs achieve a great reduction in kidney injury induced by intravenous injection of anti-Thy1 antibody into rats. Additionally, MSCs elicited improvement of renal function. These results support development of MSCs-based approaches for management of renal disease and might offer a greater chance of therapeutic success.

Peer review

This is a good study in which the authors examined the effectiveness of MSCs treatment in animal model of kidney disease induced by anti-Thy1 antibody. The result is interesting and suggests that glomerulonephritis may be successfully treated with MSCs.

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