Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: https://www.tandfonline.com/loi/irnf20

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Kemal Agbaht, Funda Pepedil, Alper Kirkpantur, Rahmi Yilmaz, Mustafa Arici & Cetin Turgan

To cite this article: Kemal Agbaht, Funda Pepedil, Alper Kirkpantur, Rahmi Yilmaz, Mustafa Arici & Cetin Turgan (2007) A Case of Kaposi's Sarcoma Following Treatment of Membranoproliferative Glomerulonephritis and a Review of the Literature, Renal Failure, 29:1, 107-110, DOI: 10.1080/08860220601039551

To link to this article: https://doi.org/10.1080/08860220601039551

Published online: 07 Jul 2009.

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Renal Failure, 29:107–110, 2007
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ISSN: 0886-022X print / 1525-6049 online
DOI: 10.1080/08860220601039551

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CASE REPORT

A Case of Kaposi's Sarcoma Following Treatment of Membranoproliferative Glomerulonephritis and a Review of the Literature

Kemal Agbaht and Funda Pepedil
Hacettepe University, Hacettepe Medical School, Departmant of Internal Medicine Ankara, Turkey

Alper Kirkpantur, Rahmi Yilmaz, Mustafa Arici, and Cetin Turgan
Hacettepe University, Hacettepe Medical School, Departmant of Nephrology Ankara, Turkey

Kaposi's sarcoma (KS) is an unusual tumor principally affecting the skin of the lower extremities. Although the association between KS and renal transplant has been well documented, there are a few KS cases in the literature associated with membranoproliferative glomerulonephritis or other glomerular diseases. This report presents a patient with membranoproliferative glomerulonephritis (MPGN) who developed KS following treatment with long-term medium dose glucocorticoid and short-term additional immunosuppressives. The KS cases associated with glomerulonephritis are also reviewed. KS is a rare complication in glomerular diseases that may (or may not) be related to immunosuppression. Hence, immunosuppression treatment should be carefully planned in glomerulonephritis treatment and avoided if they are not essentially necessary.

Keywords membranoproliferative glomerulonephritis, Kaposi's sarcoma

INTRODUCTION

Kaposi's sarcoma (KS) is an unusual tumor principally affecting the skin of the lower extremities.[1] It occurs in four clinical forms: *classic* KS, human acquired immunodeficiency syndrome (AIDS)-related *epidemic* KS, African type *endemic* KS, and *transplantation-associated* (due to immunosuppression) KS.[2] There is a well-known relation between KS and human immunodeficiency virus (HIV).[3] There were also KS cases reported in patients who had immunosuppressive treatment in different settings, such as rheumatoid arthritis, polymyositis/dermatomyositis, vasculitis, systemic lupus erythematosus, polymyalgia rheumatica, Behçet's syndrome, and after renal/liver/cardiac transplantation, Wegener's granulomatosis, bullous pemphigoid.[4–6] In almost all of the cases, human herpesvirus-8 (HHV-8) has a role in KS development,[7] and most of them have a history of high dose and/or long-term immunosuppressive treatment.[4] Although KS has been reported in such different rheumatologic settings, it was rarely associated with glomerulonephritis other than AIDS or post-transplant states. Indeed, only four such cases were found, before that in the present report.

The current report concerns a patient with membranoproliferative glomerulonephritis (MPGN) who developed KS following treatment with long-term medium dose glucocorticoid and short-term additional immunosuppressives. The KS cases associated with glomerulonephritis were also reviewed.

CASE REPORT

A 52-year-old woman referred to our center with a complaint of newly onset purple colored lesions on her left leg. Her medical history revealed a diagnosis of MPGN since 1997. She had been taking prednisolone 20 mg per day for seven years without any interruption. The patient had received additional immunosuppressive drugs during the last six months because of ongoing and/or resistant proteinuria. First, azathioprine 125 mg per day had been added to steroid for about five and half month's duration. Following the discontinuation of azathioprine, cyclosporine and mycophenolate mofetil had been tried for several

Address correspondence to Asst. Prof. Mustafa Arici, MD, Hacettepe Medical School, Department of Nephrology, Sihhiye, Ankara, 06100, Turkey; Tel.: +90 312 305 1710; Fax: +90 312 311 3958; E-mail: marici@hacettepe.edu.tr

weeks in order to control proteinuria. The immunosuppressive treatment had been given up two days before admission to our hospital due to the sudden appearance of lesions on her legs.

Upon physical examination, blood pressure was 140/90 mmHg. She had both periorbital and pretibial edema. There were red-purple papules becoming confluent to form a big plaque of 24 × 9 cm on the anterior side of her left leg surrounding the ankle. She had another lesion on her left popliteal region which was a 2 × 2 cm bluish-purple papule with erythema at the base (see Figure 1).

Laboratory investigations showed hemoglobin: 7.3 g/dL, hematocrit: 21%, white blood cell (WBC) count: 3.8 ($\times 10^3/mm^3$), platelet: 182 ($\times 10^3/mm^3$), blood urea nitrogen: 17 mg/dL, serum creatinine: 0.8 mg/dL, albumin: 2.9 g/dL, total cholesterol: 229 mg/dL, triglycerides: 227 mg/dL, HDL: 80 mg/dL, LDL: 103 mg/dL, VLDL: 45 mg/dL. Protein excretion was 6680 mg/day. Serology of hepatitis B and C was negative. Echocardiography showed no abnormality. Anti-nuclear antibody, anti-dsDNA, and extractable nuclear antibodies were negative. Renal venous thrombosis was ruled out by Doppler ultrasonography.

In order to control blood pressure and proteinuria, ramipril plus hydrochlorothiazide (5/12.5 mg) were added to losartan 100 mg/day. Acetylsalicylic acid 100 mg/day was also prescribed. The dose of simvastatin was adjusted according to lipid profile.

In addition to these supportive measures for MPGN, an evaluation of KS was performed. Pathologic examination of the lesion on the left popliteal region revealed early stage KS. An examination of serum samples for HIV by ELISA method revealed negative results, and antibodies against HHV-8 were positive at high titer. Computed tomography of the thorax and abdomen showed no visceral organ involvement. The glucocorticoid treatment was tapered accordingly and then stopped. External radiotherapy was planned for the lesions on the leg (see Figure 1). New lesions, however, were recognized on her left foot, left anterior trunk, and left arm during radiotherapy. Following radiotherapy, paclitaxel 80 mg/m^2 per week added to treatment. After six weeks of treatment, KS lesions regressed noticeably but not completely.

Figure 1. The lesion at the left leg, lateral aspect.

DISCUSSION

Kaposi's sarcoma is a rare tumor of endothelial cell origin.[8] The relation between KS and immunosuppression is well documented.[4–5] It is seen in about 0.1% renal, liver, and cardiac transplant patients secondary to immunosuppressive treatment.[9–13] The development of a tumor is not directly related to the dose or the duration of steroid used.[14]

Infection with HHV-8 is almost always required but not enough for the tumor development.[15] HHV-8 is an oncogenic virus from the herpes virus gamma group family. It affects the coding of the cytokines and factors that promote cellular multiplication, apoptosis, and immune responses, resulting in endothelial cellular transformation.[7] It has been suggested that immunosuppressives such as glucocorticoids and cyclosporine do not activate the lytic cycle of HHV-8 or modify the cell survival, thus promoting cancer progression by a direct cellular effect.[16]

There are KS cases reported following treatments with corticosteroid therapy of various rheumatologic,[4] dermatologic,[17–19] hematologic (ITP),[20] and gastrointestinal[21,22] disorders. Nephrologists are also familiar with KS because of immunosuppressive treatment following renal transplantation, and they encounter it in HIV-infected patients as well, though less frequently. The relation between glomerulonephritis and KS, however, is not well established, and there are only a few cases reported in the literature (see Table 1).

MPGN is identified in approximately 10% of renal biopsy specimens. It could be classified as idiopathic or secondary according to etiology. MPGN could be presented in three distinct types in context of histopathology: type I, type II, type III. Even though a majority of MPGN patients are children or young adults, adults could be affected by type I MPGN and rarely by type II MPGN. The etiology of secondary MPGN consists of infections (hepatitis C and B, infective endocarditis, shunt nephritis, Schistosoma nephropathy, and mycoplasma infection), rheumatologic diseases (systemic lupus erythematosus, scleroderma, Sjögren syndrome, sarcoidosis, mixed essential cryoglobulinemia) and malignancies (carcinoma, lymphoma, leukemia).[23] In general, one-third of patients with type I MPGN

Table 1
Kaposi's sarcoma cases associated with glomerulonephritis

Renal disease	Immunosuppressive Treatment	Kaposi's sarcoma development	Co-existent disease	Treatment	Outcome	Reference
Membranous glomerulonephritis (MG)	None	One month after diagnosis of MG	None	Local radiotherapy	Cure	24
Membranoproliferative glomerulonephritis (MPGN)	Prednisolone	Months later	Castleman disease, Hemolytic anemia	Bleomycin and radiotherapy	Exitus	25
Focal glomerulosclerosis	• Prednisolone 25mg/ 48 hours, 15 months; then 1 mg/kg/day eight months • Cyclosporine 3mg/kg/day, 10 months • Cyclophosphamide 100mg/day six months	Two years later	None	Vinblastine boli	Cure	26
Diffuse MPGN	Prednisolone 40mg/day, three months	One year later	Multicentric Castleman disease	Undesignated	Undesignated	27
Membranoproliferative glomerulonephritis	• Prednisolone (20 mg/ day, seven years, for short courses 60 mg/ day) Azathioprine (125 mg/ day, six months) • Cyclosporine (two weeks) • Mycophenolate mofetil (two weeks)	Seven years after immunosuppression	None	Local radiotherapy and Paclitaxel (weekly)	Improvement	Current case

will have a spontaneous remission, one-third will have a progressive disease, and one-third will have a disease process that will wax and wane but never completely disappear. The treatment of type I MPGN is based on the underlying cause of the disease process. Low-dose, alternate day prednisone may have a beneficial effect on improving renal function.[23]

Although the association between KS and renal transplant has been well documented, there are a few KS cases in the literature associated with MPGN or other glomerular diseases (see Table 1). In three cases, there was a history of immunosuppressive medications. KS was also developed in a membranous glomerulonephritis case without immunosuppression. It was suggested that there may be a different mechanism other than immunosuppression in association of glomerular diseases and KS development.[24]

Although no relation was documented with the dose and/or duration of glucocorticoids or other immunosuppressives, the patient in this case has been disadvantaged by using long-term glucocorticoid treatment and recent augmentation of immunosuppressives. As the treatment of MPGN is debatable, long-term immunosuppression was unnecessary, even dangerous in this particular case.

In conclusion, Kaposi's sarcoma is a rare complication in glomerular diseases. It may be related to immunosuppression, but there may be other mechanisms apart from immunosuppression. Hence, immunosuppression treatment should be carefully planned in glomerulonephritis treatment and avoided if they are not essentially necessary.

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