POLYOMAVIRUS NEPHROPATHY:
A BRIEF REVIEW WITH SPECIAL EMPHASIS
ON CLINICO-PATHOLGICAL ASPECTS

Mihatsch MJ

Institute for Pathology, University Hospital Basel, Basel, Switzerland

Abstract: From 1995 Polyomavirus (PyV) nephropathy (PVN) has played an important role in solid organ transplant recipients. The disease is caused by a DNA virus, usually the BK variant, more rarely JC virus.

In immune incompetent patients either latent endogenous virus is reactivated, or donated virus can multiply. The frequency of PVN nephropathy (previously 10% or higher) is declining. The disease follows a stepwise course: viruria, viraemia, nephropathy. Nephropathy usually manifests itself during the first year after transplantation. The disease remains clinically silent for long periods, later progressive loss of renal function and renal failure occur. A major risk factor is therapy with potent immune suppressive agents. Morphologically, viral replication produces nuclear inclusions and necrosis, predominantly in the urothelium and tubular epithelium. Inflammation (T and B lymphocytes, monocytes/macrophages and granulocytes) accompanies necrosis. Progression is marked by tubular atrophy, interstitial fibrosis and transplant loss. The virus can be detected by the electron microscope and, better, by immunohistology (preferentially mAb against SV40 Large T antigen). It is often hard to differentiate PVN from an interstitial cellular rejection reaction (Banff 1 A/B). As no effective drug treatment exists, the disease must be diagnosed as early as possible and immune suppression reduced. Screening for polyomavirus reactivation is best done stepwise: search for urinary "Decoy cells" (PyV infected cells), PCR for PyV in the blood and in the case of reduced renal function, renal biopsy. Compliance with a stringent screening algorithm allows early detection and adequate treatment and prevents organ loss.

Key words: Polyomavirus nephropathy, Virology, Clinical presentation, Morphology, "Decoy cells", Differential diagnosis, Screening algorithm.
Introduction

In the summer of 1996 Prof. Gil Thiel (then Head of Nephrology and Transplantation, University Hospital Basel) informed me about unusual cells that he had not previously seen, visible by phase contrast microscopy in native urine samples from certain patients. Urine cytology identified numerous "decoy cells" in the urine and thus active polyomavirus (PyV) infection could be diagnosed. However, this observation did not explain the progressive functional loss in the transplanted kidney.

The renal biopsy from one of these patients revealed nuclear inclusions in the tubular epithelium, that were negative by immunohistochemistry for all viral antigens identifiable at that time. Electron microscopic studies revealed non-enveloped viral particles possessing a paracrystalline structure, which could be classified as belonging to the group of PyV. Subsequently, I learned that commencing April 1996 the patients had been treated with Tacrolimus and Mycophenolate Mofetil (MMF). As in Basel, many colleagues throughout the world were confronted with this new disease pattern between 1995 and 1999 [1–4].

The appearance of polyomavirus nephropathy in transplantation resulted in the rediscovery of a virus that had been looking for a disease since 1971 [5]. Polyomavirus associated nephropathy was first described after renal transplantation, later in a child with congenital immune incompetence [6]. This new nephropathy stimulated virological, clinical and morphological research. Today, we are in a much better position to deal with this insidious challenge and patients need no longer fear transplant loss due to polyomavirus nephropathy.

Human Polyomaviruses

Polyomavirus (PyV) infections are widespread among vertebrate hosts. In humans, 8 distinct human PyVs have been detected [7] which include BK virus (BKV) and JC virus (JCV) named after the initials of the first patients from whom they were isolated [5]. In a healthy adult population, the seroprevalence for all human PyVs exceeds 50% and is highest for BKV [8].

Clinical manifestations of human PyV infections are rare and typically affect immunodeficient patients. Thus, the prototypic manifestation of BKV are PyV-associated nephropathy (PVN) after kidney transplantation and haemorrhagic cystitis after allogenic haematopoietic stem cell transplantation; PyV-associated multifocal leukoencephalopathy is caused by JCV in the brain of patients with HIV-AIDS, with haematological malignancies or receiving modern therapies for autoimmune diseases. Despite considerable research, the route of transmission has not been identified for any of the human PyVs, but
may be oral or respiratory for BKV and JCV. The PyV have a circular double-stranded DNA genome of ~ 5,100 base pairs which can be divided into three parts (Fig. 1): The non-coding control region (NCCR) regulates the expression of the viral early genes encoding the non-structural proteins small T- and large T-antigen in one direction, and in the opposite direction on the other strand, then the viral late genes encoding the capsid proteins VP1, VP2, VP3 [9, 10]. Expression of the multifunctional large and small T-antigen is pivotal for shifting the host cell into the S-phase, thus providing all the building blocks for an efficient viral DNA genome replication. Subsequently, late gene expression is initiated which is characterized by a marked gene dosage amplification effect for the structural capsid proteins and the release of approximately 10,000 – 100,000 virions per cell. Besides the role of the NCCR, key roles of clinical relevance have been attributed to the large T-antigen: for activation of viral replication, oncogenicity, cellular immune recognition, genotyping and diagnostic immunohistochemistry [11] and to the capsid VP1 protein: for defining BKV serotypes, cellular immune recognition, neutralizing and diagnostic antibody responses [12].

Figure 1 – Genome structure of human polyomaviruses BK and JC

**Epidemiology of BKV infection, replication and disease**

Primary infection with BKV occurs mostly without specific symptoms or, rarely, mild respiratory illness during early childhood (5–7 yrs), as indicated by an increasing seroprevalence of up to 90% [13]. Following primary infection, a viremic phase has been postulated during which BKV reaches the reno-urinary tract as the principal site of latency and reactivation [14]. In healthy BKV seropositive, immunocompetent individuals, asymptomatic urinary shedding of BKV is detectable in up to 10%, with low urine BKV loads of < 5 log_{10} genome equivalents (geq)/mL [8]. In kidney transplant recipients, BKV reactivation results in high urinary BKV loads of > 7 log10 geq/mL and the shedding of "decoy cells" is present in BKV loads of > 6 log 10 geq/ml [4–15].
In kidney transplant recipients, BKV reactivation takes place in the donor kidney i.e. in the urothelial cell layer and the tubular epithelial cells. [4, 15]. This was most convincingly shown by FISH analysis of "Decoy cells", which always carried the sex chromosome of the donor, not the recipient (unpublished observation).

*Prevalence of polyomavirus nephropathy and clinical presentation*

Practically all cases of polyomavirus nephropathy (PVN) are caused by BKV, except for some anecdotal reports of JCV-associated PVN [16]. The frequency of PVN is quite variable, ranging from 0% to 10% [17] and also depends on the non-invasive screening procedure and performance of surveillance biopsies [18]. Children and adults are equally affected. In centres with systematic screening programmes, the frequency of histologically proven PVN, but not of BKV reactivation, declines continuously, while centres without screening programmes are still being confronted with an increasing numbers of cases [18].

PVN is extremely rare in native kidneys. It is exceptionally seen in patients with inherited immunodeficiency syndromes, or in heavily immunocompromized patients with solid organ transplants (heart, liver, lung, pancreas) [19]. Today, PVN is the most important viral infection in the renal allograft. CMV and adenovirus infections have very rarely been reported to cause significant allograft pathology.

PVN may occur days to years after transplantation. The earliest case we observed was after 40 days and the latest after 5 years. In 300 published cases, the median time for diagnosis of PVN was 42 weeks [20], in Basel, however, 28 weeks, which we attribute to our screening programme (see below) (Fig. 2). This means that during the first month following transplantation, PVN occurs only exceptionally.

![Figure 2 – Time interval to diagnosis of PVN in cases from literature and 39 cases from Basel. We attribute earlier diagnosis in Basel to our systematic screening programme for polyomavirus in urine and blood (see below)](image)
Clinically, PVN can remain silent for long periods. Stage A (see below) is symptomless. Active BKV infection during this stage can only be diagnosed by detection of "Decoy cells" in urine and/or by PCR testing of urine (screening programme, see below). Later, an increase in serum creatinine is seen in patients with PVN, without any signs of rejection or other systemic symptoms (fever, fatigue). For all practical purposes, only systematic urinary screening after renal transplantation allows early detection of BK-virus reactivation. [21]

The prognosis of PVN seems to be largely governed by the histological stage at diagnosis. The prognosis is very favourable when the disease is recognised in the early, asymptomatic stage. In the past, later stages were associated with graft losses of up to 80% [21]. In the asymptomatic stage of the disease a renal biopsy is not recommended as a screening test for BKN in patients with viraemia. However, whenever renal dysfunction ensues a renal biopsy alone can exclude other accompanying causes of allograft dysfunction.

**Risk Factors in Polyomavirus-nephropathy**

What had happened in 1995/1996 as PVN broke out? Had PVN simply been overlooked previously? The answer is: No! [20]! Tacrolimus and/or Mycophenolate Mofetil were first used as immune suppressive agents for transplantation in Basel in 1996, (earlier use reported in some other centres). This raised the possibility that these highly effective immune suppressants fostered the development of PVN [20].

To date, the question as to the nature of other risk factors has occupied a large number of publications, offering widely differing opinions [20]. On the basis of our own and a majority of other studies, the use of highly potent immune suppressive agents of the Tacrolimus and/or MMF type is particularly relevant. Whether other risk factors are of fundamental significance is questionable. However, these factors probably prompted particularly intensive immune suppression. In the case of Tacrolimus and MMF, there are also clues that the risk of PVN is dose dependent (Tacrolimus > 8 ng/ml, MMF > 2 g/d) [17, 21]. From this evidence we conclude that, for routine practice, screening of urine in patients receiving highly effective immune suppression involving the Tacrolimus and/or MMF type is always advisable. One should never forget that, even years after renal transplantation, the risk of PVN may increase when immune suppression is intensified by Tacrolimus and/or MMF.

**The Histology of Polyomavirus Nephropathy**

The characteristics of PVN [2, 3, 4, 21, 22] are nuclear inclusion bodies in the epithelium and epithelial necrosis (cytopathic effect). The tubular epi-
The epithelium is primarily affected, more rarely the parietal epithelium in the Bowman's space.

The nuclear inclusion bodies are typically sand-like. CMV-like inclusion bodies present less frequently in this manner. Also quite rare are tumour-like enlarged and polymorphic nuclei, without well defined inclusion bodies but with coarse, web-like chromatin (Fig. 3). Similar nuclear changes are seen in "decoy cells" in the urine; the nuclei of the epithelial cells are enlarged. The affected epithelial cells increase in size, break free of the epithelial lining, become necrotic and are sloughed into the tubular lumen. The tubular lumens contain cell debris harbouring viral particles and the cell surfaces of adjacent, unaffected tubular cells are densely coated with virus particles [23]. There remain tubules with rarified epithelial layers and finally a completely denuded tubular basement membrane (Fig. 4). Since the basement membrane remains intact, in con-
A brief review with special emphasis on clinico-pathological aspects 11

Contrast to pyelonephritis, regenerating cells can use the basement membrane as a scaffold permitting even a complete *restitutio ad integrum*. Renal involvement is primarily very focal and not diffuse. This applies to both individual tubular cross-sections and entire kidney allograft. Initially, only a few tubular cells in a particular cross-section are involved whereas all epithelial cells may be affected in advanced cases. At first only a limited number of tubules are involved. Even in late stages affected and unaffected tubules may be found side by side. At the beginning, usually only the collecting duct is affected, later viral inclusion bodies may be found throughout the tubules. Even in advanced stages, collecting ducts are more often involved than distal or proximal tubules [24].

BKV replication typically starts in the medulla and subsequently spreads along the collecting ducts into the cortex. The morphological findings suggest an ascending route of infection in the kidney [24], complicated by a haematogenous spread of viruses as soon as widespread necrosis of the tubular epithelium is present.

The findings described here lead us to postulate the following (possibly oversimplified) patho-morphogenetic sequence (Fig. 5):

1. Infection and amplification of viral replication in the urothelium;
2. Massive backwash of virus into the collecting ducts with accelerated spreading from cell to cell in the tubules;
3. Tubular epithelial necrosis and backwash of virus into the interstitial space and capillaries;
4. Haematogenic re-seeding of virus into the kidneys.

*Figure 5 – Patho-morphogenetic sequence of development of PVN*

If the above correctly describes the sequence of the significant events, then viraemia would always be evidence of early, but significant, intrarenal involvement with tubular epithelial cell necrosis and denudation of the basement membrane. In fact, in cases of viraemia without bioptically proven PVN, a sampling error cannot be ruled out. An early stage of PVN can be easily missed if the biopsy does not contain any medullary tissue.
Methods for Viral Diagnosis

Nuclear inclusion bodies seen by light microscopy, are clues pointing to a viral infection. Additional investigations are required to confirm a polyomavirus infection (Fig. 6).

For routine use we recommend detection of SV40 large T antigen on tissue sections by immunohistochemistry (http://nephropathology.unibas.ch/technical-notes). Staining for large T antigen on paraffin sections is robust and more or less independent of the various light microscopic tissue preparation techniques. Staining for large T antigen can be applied to cytological smears without any problems. We therefore recommend routine immunohistochemical staining for large T antigen in all patients treated with Tacrolimus and/or MMF, regardless of differing opinions published in the literature [21]. A single positive cell for large T antigen allows the definite diagnosis of PVN.

Polyomavirus Nephropathy and Inflammation

During the initial stage of viral replication, with tubular inclusion bodies, but no signs of necrosis, there is no inflammation. As necrosis develops,
inflammatory infiltrates are seen mainly (but not exclusively) around the virus infected tubules. This is always more severe in the cortex than in the medulla [21] (Fig. 7).

Figure 7 – PVN with focal (a) or diffuse inflammation (b) Without inflammation fig. 4
The inflammatory infiltrates consists of T-cells, B-cells and monocytes/macrophages, together with a variable number of polymorphonuclear leukocytes. The latter are particularly evident in regions where tubules reveal extensive epithelial necrosis. Eosinophils are never prominent in PVN.

The composition of the mononuclear infiltrate is similar to that seen in rejection reactions, both qualitatively and quantitatively [25]. Plasma cells are more frequent in PVN (70%) than in rejection reactions (20%) [25]. Plasma cell rich inflammatory infiltrates (> 15% of all mononuclear cells) are seen in half the PVN cases. However, these usually represent late stages of inflammation, rather than early stages, as seen in repeat-biopsies [25]. In plasma cell rich infiltrates, IgM plasma cells predominate in 50% of cases, IgG plasma cells in 30% and roughly equal numbers are seen in the remaining 20%. This situation is in contrast to rejection reactions, where IgG plasma cells clearly predominate. The mononuclear but not the polymorphonuclear cells migrate into the tubules ("tubulitis"). It is noteworthy that plasma cells are also found in the tubules ("Plasma cell tubulitis"), which is hardly ever seen in rejection reactions [25].

In isolated cases with IgG rich plasma cell infiltrates, granular deposits of IgG may be detectable within the tubular basement membranes of infected tubules. There is indirect evidence that these plasma cells produce antibody directed against viral antigens [26]. Viral particles, however, were not seen within the immune deposits in the tubular basement membranes.

Recurrent tubular necrosis, tubulitis, immune deposits in the tubular basement membranes and permanent epithelial regeneration finally result in tubular atrophy and interstitial fibrosis leading clinically to irreversible transplant dysfunction and even transplant loss.

**Morphological Stages of Polyomavirus Nephropathy**

BK viral infection and inflammation can be tied together by describing the morphological stages: PVN can be divided into three stages [27]. Stage A is seen early on (about 9 months after transplantation), stages B and C later (about 16 months after transplantation). Progression from A to B was seen in about 40% of cases, from B to C in about 60% [23].

The different stages (Fig. 7, 8) are relevant for understanding the evolution of PVN with time, evaluating the clinical course, determining the prognosis and eventually for therapeutic decisions.

Stage A is often a chance finding in protocol biopsies, as it is not associated with clinical symptoms.

On this account it is prognostically particularly favorable. PVN heals in more than 75% of cases at stage A [28]. Cases that have reached stages B and
C, rarely if ever heal without residual injury, particularly when renal function is already compromised.

*Figype 8 – Stage C of PVN with prominent tubular atrophy and interstitial fibrosis. For stage A see Fig. 4, for stage B see Fig 7 a,b*

**Polyomavirus Nephropathy and Rejection**

The diagnosis of a rejection reaction with concomitant PVN presents a difficult task [25]. This question is very important for the clinician, as rejection needs increased immune suppression as opposed to a reduction in case of PVN. For diagnostic purposes, the cellular composition of infiltrates (T-, B- lymphocytes, monocytes/macrophages and plasma cells) is not helpful. Tubulitis is equally frequent in both types of lesion. A predominance of IgM-plasma cells is at best a hint of PVN, but does not exclude a rejection reaction. When a stringently and immunohistochemically documented PVN is restricted to the medulla, inflammatory cortical infiltrates with tubulitis may be classified as interstitial cellular rejection (Banff IA/B).

Regardless of the difficulties associated with diagnosing interstitial-cellular rejection (Banff grade IA/B) in combination with PVN, there are morphological characteristics that speak unequivocally of rejection: fibrinoid arterial necrosis, endarteritis, transplantation-glomerulitis, transplantation-glomerulopathy and sclerosing transplantation-vasculopathy, as well as C4d deposition along the peritubular capillaries. Systematic analysis of the different renal compartments, including immunohistochemical staining, finally will allow a clinically relevant diagnosis.

**Decoy Cells**

Polyomavirus infected cells that are excreted into the urine are referred to as "Decoy cells" (DC), "as they can mimic the features of bladder carcinoma cells" [29] (Fig. 9). DC are not just found in patients with renal transplants, they are also a feature of patients without transplants but with restricted immune
competence (pregnancy, tumours, diabetes mellitus [30]. All patients with PVN excrete DC into the urine and these can be readily detected in Papanicolaou stained cell preparations. When numerous DC are excreted they can be readily identified in freshly suspended urine by an experienced nephrologist using a phase contrast microscope. DC are found in urine when more than $10^6$ viral gene copies per ml. are excreted [4].

Figure 9 – Cytospin preparation with many typical "decoy cells"

We recommend that 100 ml of the second morning urine sample be centrifuged within 30 minutes followed by Papanicolaou staining of a cytospin preparation. When the urine cannot be processed immediately, it can be diluted 50% with ethanol for later investigation. The numbers of DC are given as n/10 HPF (Training set for the diagnosis of "Decoy cells": http://vmic.unibas.ch/patho/seminar/index.htm.) We regard < 3DC/10 HPF in urine as insignificant viruria, with 3–10 DC/10 HPF a control investigation is recommended and with more than 10 DC/10 HPF PCR testing of plasma for viraemia is indicated. General rules and borderline values cannot be set, as preparation methods vary between laboratories (smears, ThinPrep, cytospin). PVN can be neither verified nor excluded on the basis of DC excretion levels. A single examination of the urine that reveals 1 DC/10 HPF does not exclude PVN as little as detection of 1,000 DC/10 HPF proves PVN. In our experience with about 1,000 renal transplant recipients, around 30% excrete DC at some timepoint after transplantation, but in a self-limited PyV reactivation in up to 90% of these patients.

In other words, detection of DC reveals reactivation of PyV, but does not prove PVN. If repeated testing fails to reveal urinary DC, PyV reactivation is virtually excluded. Patients who later manifest PVN reveal a progressive increase in DC/10 HPF in urine with time.
Detection of DC in urine is the ideal method of identifying PyV reactivation, but not for diagnosing PVN. Therefore, we recommend PCR testing of plasma when more than 10 DC/10 HPF are detected in the urine. This approach should ensure early diagnosis of PVN in all patients at risk. Other groups advocate the use of PCR in urine instead of urine cytology for DC detection [31]. Although urine cytology for DC has a lower sensitivity for viruria than PCR, it avoids the overestimation of insignificant viruria. Urine cytology for DC has as a good predictive value for viraemia as quantitative PCR and, moreover, is cheap.

**Screening for Polyomavirus Nephropathy**

Biopsy-proven PVN is preceded by a significant increase of BK-viruria and the development of BK-viraemia [32]. Therefore, BK-viruria and BK-viraemia are very useful non-invasive screening parameters allowing early diagnosis of PVN. The key questions in this context are: (i) who should be screened? (ii) how often should one screen?, and (iii) which method should be used for screening?

As clinical risk factors are not sufficiently predictive, we recommend non-invasive screening in all patients receiving current Tacrolimus and/MMF [33]. The screening intensity should ideally be higher during the first six months post-transplant, when the immunosuppression is still at high levels and also at later stages, when immunosuppression is markedly increased following rejection episodes. Screening can be performed using urine (i.e. "Decoy cells" or BKV-PCR) or plasma (i.e. BKV-PCR), and depends on the local experience and available health care resources. At our renal transplant centre, we prefer urinary "Decoy cells" as the primary screening method, because it has a very high negative predictive value [30], is easy to perform and cheap (about 50$US vs. qPCH 500$US in Switzerland) per sample (Fig 10). If significant numbers of "Decoy cells"
are detected, the patient is further evaluated by plasma BKV-PCR. Using this stepwise screening approach, about a third of our patients had urinary "Decoy cells" and 13–19% had BKV-viraemia > 1,000 copies/ml [32–33].

**Therapy of Polyomavirus Nephropathy**

Early diagnosis of PVN and a timely therapeutic intervention is very likely the key element to preserve allograft function and prevent allograft loss. Indeed, if diagnosis of PVN was made late after transplantation, presumably with advanced irreversible damage, many allografts were lost despite therapeutic interventions [34]. By contrast, no allograft losses due to PVN and preserved allograft function were observed in prospective studies using universal screening and early therapeutic interventions [33, 36]. This highlights the importance of an effective non-invasive screening procedure.

Therapeutic interventions for PVN include (i) reduction of immunosuppression, and (ii) agents with antiviral activity (i.e. cidofovir, leflunomide, fluoroquinolones, intravenous immunoglobulins). Several prospective studies have demonstrated that reduction of immunosuppression alone leads to clearance of BK-viraemia in more than 90% of patients [33, 35]. Therefore, reduction of immunosuppression must be regarded as the best and first line therapeutic intervention. The value of anti-viral agents for treatment of PVN is not unequivocally documented. At our centre, we start to gradually reduce immunosuppression if sustained BK-viraemia > 1,000 copies/ml is detected (Fig. 10) [33]. BK-viraemia is used to guide further adaptations of immunosuppression. Several immunosuppression reduction strategies have been evaluated (e.g. first reduction of the calcineurin-inhibitor, first reduction of the anti-proliferative drug) with similar results [32, 35]. This suggests that reducing the overall immunosuppressive burden is likely to be more important than lowering of or discontinuation of a specific drug.

**Conclusion**

Since 1995 polyomavirus nephropathy has emerged as a new threat for renal transplant recipients. Concerted efforts of transplant physicians, virologists, pathologists and many others allowed the problem to be overcome within a few years. Polyomavirus nephropathy is another example of complications brought about by highly potent immunosuppressive agents. Today, intelligent screening programmes allow prevention of polyomavirus nephropathy and avoid permanent damage to the transplanted kidney.

**Acknowledgement**

I thank my former co-workers and colleagues in the field of polyomavirus nephropathy: Fred Gudat, Peter Dalquen, Volker Nickeleit, Eva Kemeny,
Christian Seemayer, Olivier Prince, Stephen Batsford, Stephan Schaub and Hans H Hirsch. For excellent technical assistance I am thankful to Ursula Dürmüller, Rita Epper and Claudia Lautenschlager.

This review is partly based on a recent [37] review and previous reviews, both from our group and other excellent reviews published up to 2006. The reader is referred to these review articles for original literature published until 2005 [9–10, 15, 18, 21–22, 30].

REFERENCES


Прилож. Одр. биол. мед. науки, XXXIII/2 (2012), 5–22


Резиме

ПОЛИОМАВИРУС НЕФРОПАТИЈА: КРАТКА РЕВИЈА СО ПОСЕБЕН АКЦЕНТ НА КЛИНИЧКО-ПАТОЛОШКИТЕ АСПЕКТИ

Михач М.Ј.

Институт за ишемија, Универзитетска болница Базел, Базел, Швајцарија

Од 1995 година полимавирус (PyV) нефропатијата (PVN) одигра важна улога кај примателите на солидни органи за трансплантација. Оваа болест е предизвикана од ДНК вирус, обично варијантата ВК, поредок вирус ЈС.

Кај имуно некомпетентните пациенти или латентниот ендоген вирус се активира, или донираниот вирус може да се мултиплицира. Фреквенцијата на...
нефропатијата PVN (претходно 10% или повисока) е во опаѓање. Болеста се одвива чекор по чекор: вирурија, вирејија, нефропатија. Нефропатијата обично се манифестира во текот на првата година по трансплантацијата. Болеста остава карактеристична, тивка подолги периоди, а подоцна се јавува прогресивно губење на бубрежната функција и бубрежна инсуфициенција. Главен фактор на ризик е терапијата со потентни имуносупресивни агенси. Морфолошки, вирусната репликација преразработува нуклеарни инклузии и некроза, претежно во уротелиумот и во тубуларниот епител. Воспаленето (Т и Б лимфоцити, моноцити/макрофаги и гранулоцити) ја придружува некрозата. Прогресијата е изразена со тубуларна атрофија, интерстицијална фиброза и загуба на трансплантот. Вирусот може да се открива со електронски микроскоп и подобро, со имунохистологија (преразработување mAb кон SV40 Голем Т антиген). Често е тешко да се разликува PVN од реакција на интерстицијално клеточно отфрлање (Banff I A/B). Бидејќи не постои ефикасен лек за третман, болеста мора да се дијагностицира што е можно порано и да се намали имуносупресијата. Скринингот за реактивирање на полимавирусот најдобро е да се прави постепено: пребарување за уринариран "decoy cells" (PyV инфицирани ќелии), PCR за PyV во крвата и бубрежна биопсија во случај на намалена бубрежна функција. Усогласеноста со строг алгоритам за скрининг овозможува рано откривање, соодветно лекување и попречување на загуба на органот.

Ключни зборови: нефропатија на полимавирус, вирусолошки, клиничка презентација, морфолошки, "decoy cells", диференцијална дијагноза, алгоритам за скрининг.

Corresponding Author:

Michael J. Mihatsch
Institute for Pathology
University Hospital Basel
Schönenbeinstrasse 40
CH-4031 Basel
Tel. ++41 61 3287872
Fax: ++41 61 2652230
E-mail: Michael-J.Mihatsch@unibas.ch