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Review

Anti-vimentin antibodies in transplant and disease

Tigran Divanyan[a], Ernesto Acosta[a], Dhruv Patel[a], Don Constantino[b], Reynold I. Lopez-Soler[c,*]

[a] Albany Medical College, Albany, NY, United States
[b] Transplant Immunology Laboratory, Albany Medical College, Albany, NY, United States
[c] Division of Surgery, Section of Transplantation, Albany Medical Center, Albany, NY, United States

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ABSTRACT

Non-HLA antibodies are recognized as a potential source of antibody mediated rejection following transplantation. The epitopes which lead to production of these antibodies are a result of tissue disruption, specifically endothelium, secondary to inflammation and injury. Vimentin is a cytoskeletal protein involved in many aspects of cellular organization, signaling, and proliferation. Recently, antivimentin antibodies have been shown to be important not only for rheumatological autoimmune diseases, but also cardiac and renal transplant dysfunction. In cardiac transplant recipients, antivimentin antibodies are associated with coronary artery vasculopathy and chronic graft loss. In renal transplantation, antivimentin antibodies are detected prior to transplantation and are also correlated with chronic graft dysfunction. In renal transplant recipients, antivimentin antibodies seen prior to transplantation are thought to be secondary to chronic endothelial injury during hemodialysis and therefore more prevalent prior to renal transplant than cardiac transplantation. In this review, we will examine the generation and pathogenesis of antivimentin antibodies. Given that these antibodies appear to be associated with both post-cardiac and -renal transplant dysfunction, developing standard detection paradigms may be important for risk stratification prior to transplantation. Finally, understanding the pathogenesis of antivimentin antibodies may lead to the development potential therapies in order to improve long-term survival.

1. Introduction

Antibody mediated rejection (AMR) is an important source of graft dysfunction following transplantation, contributing to both acute and chronic rejection. Even though anti-HLA antibodies have been commonly described as the source of AMR, non-HLA antibodies have also recently become important in the pathogenesis associated with both chronic and acute humoral rejection. In fact, AMR secondary to non-HLA antibodies must be considered, in patients with no detectable donor-specific antibodies and a negative pre-transplant crossmatch that develop clear signs of AMR.

It is thought that the source of the epitopes leading to some, if not most, of these non-HLA antibodies is the endothelium as it is the "first responder" in inflammatory and ischemia/reperfusion injury. Anti-endothelial cell antibodies have been identified in both the setting of renal and cardiac post-transplant AMR [1,2]. One of the antigens that have come to some prominence recently is the intermediate filament protein, vimentin [3]. Vimentin monomers and dimers polymerize to form the basis of the cytoskeleton in fibroblasts, smooth muscle cells and endothelial cells. These protein networks allow for the maintenance of cellular structure in addition to contributing to cell signaling and proliferation [3–10]. Vimentin is the target of numerous kinases involved in signal transduction, cell motility, and differentiation [11,12]. In addition to this, vimentin expression has been shown to direct changes in cell shape, modulate focal adhesions, and alter the expression of membrane-associated proteins [13].

For close to 40 years, there has been a connection between antivimentin antibodies and autoimmune diseases such as Rheumatoid Arthritis [14]. Additionally, antivimentin antibodies have been associated with certain types of cancer [15,16]. However, more recently, antivimentin antibodies have become important in the development of post-renal and -cardiac transplant dysfunction (see Table 1). In this

Abbreviations: AVA, antivimentin antibodies; mAb, monoclonal antibody; RA, rheumatoid arthritis; ACA, anti-citrullinated vimentin; CAV, cardiac vasculopathy; CAN, chronic allograft nephropathy; AMR, antibody mediated rejection; CAD, coronary artery disease; IF/TA, Interstitial Fibrosis and Tubular Atrophy (*CAN (Chronic Allograft Nephropathy) has been replaced by IF/TA)

* Corresponding author at: Albany Medical College, Department of Surgery, Division of Transplantation, 43 New Scotland Ave., Albany, NY 12208-3479, United States.

E-mail addresses: divanyt@amc.edu (T. Divanyan), acostae@amc.edu (E. Acosta), pateld3@amc.edu (D. Patel), constad@amc.edu (D. Constantino), lopezsr@amc.edu (R.I. Lopez-Soler).

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Table 1
Key articles related to AVA in cardiac and renal transplantation.

Title	Organ	Author	Year	Type of Rejection	Summary
Antivimentin antibodies are an independent predictor of transplant-associated coronary artery disease after cardiac transplantation	Heart	Jurcevic S, et al.	2001	Humoral	Mean titers of AVA were significantly higher in patients who developed transplant associated coronary artery disease than those who remained disease free
Autoimmunity to vimentin potentiates graft vasculopathy in murine cardiac allografts	Heart	Mahesh B, et al.	2015	Humoral	Autoimmune response to vimentin accelerates CAV progression in murine cardiac allografts
Autoantibodies to Vimentin Cause Accelerated Rejection of Cardiac Allografts.	Heart	Mahesh B, et al.	2017	Humoral	AVA, in conjunction with the alloimmune response, are necessary for accelerated rejection.
Incidence and early outcomes associated with pre-transplant antivimentin antibodies in the cardiac transplantation population.	Heart	Young RK, et al.	2015	Humoral	AVA are common in the cardiac pre-transplant population with a higher incidence in the young. Detectable AVA levels did not correlate with either early post-transplant rejection or graft survival.
C4d deposition is correlated with the level of antivimentin antibody in rat kidneys undergoing chronic allograft nephropathy	Kidney	Yang L, et al.	2008	Humoral, Chronic	AVA were detected 8- and 12-weeks after surgery. AVA were not detected prior to transplant. IgG against AVA were detected 4–6 weeks post-transplant. Elevated AVA concentration with associated C4d staining were correlated with development of IF/TA
Vimentin Antibodies: A Non-HLA Antibody as a Potential Risk Factor in Renal Transplantation.	Kidney	Carter V, et al.	2005	Humoral, Chronic	Patients with biopsy-proven IF/TA had elevated IgM AVA concentrations within the first 3 months post-transplant. This was seen in association with *de novo* HLA-DQ2 alloantibody production
Immunoglobulin isotype switching of antibodies to vimentin is associated with development of transplant glomerulopathy following human renal transplantation	Kidney	Gunasekaran M, et al.	2017	Humoral, Chronic	Elevated IgG AVA (but not IgM) concentrations post-transplant were correlated with graft dysfunction in patients with biopsy-proven IF/TA
Anti-vimentin Antibodies Present at the Time of Transplantation May Predict Early Development of Interstitial Fibrosis/Tubular Atrophy	Kidney	Lopez-Soler RI, et al.	2017	Humoral, Chronic	Elevated IgG AVA concentration was seen in patients with early (< 5 yrs.) IF/TA. Twofold increased risk for early IF/TA with pre-transplant AVA concentration > 15 μg/mL

review, we will discuss the possible pathways for the development of antivimentin antibodies and their association with autoimmune rheumatologic diseases. We will also discuss the current thinking on their role in both cardiac vasculopathy and interstitial fibrosis and tubular atrophy. These autoantibodies are part of an enlarging group of non-HLA antibodies which may contribute to chronic loss of cardiac and renal grafts following transplantation and therefore could be attractive markers for the diagnosis of graft dysfunction as well as possible targets for intervention to improve outcomes.

2. Generation and pathogenesis of antivimentin antibodies

It is unclear how vimentin expression leads to the development of antivimentin antibodies as it is not traditionally expressed either on cell membranes or secreted in serum. However, multiple studies have shown that vimentin can be aberrantly expressed and released in serum and on the cell surface of a number of immune and non-immune cells [17]. Vimentin is also a target of Caspases during inflammatory states which may lead to the exposure of antigenic vimentin peptides in apoptotic cells (Fig. 1, [18,19]). In fact, it is the aberrant expression of vimentin in serum secondary to inflammation derived from ischemia/reperfusion injury, infection, or rejection following transplantation that may allow for the formation of anti-vimentin antibodies (AVA). Following tissue injury, vimentin is readily accessible to the host immune system, making it a target for immune response. Interestingly, post-translational modifications such as citrullination may also be important for generating an immune response and in fact has been associated with autoimmune rheumatologic diseases (Fig. 1). For the unmodified vimentin, Tomiyama et al studied the epitope of AVA using the V9 mouse monoclonal antibody (mAb), and identified the epitope to be in the C-terminal domain (Fig. 1, [20]). This study also established the presence of a cross-species conserved asparagine at position 417 that was critical for antibody binding [20]. These data also show that the V9 mAb was able to recognize these partial vimentin protein epitopes [20]. Other studies determined that the interaction of vimentin and immunoglobulins is mainly carried out through a 30kD peptide located close to the amino-terminal part of the vimentin molecule indicating significant variability in the antigenicity of vimentin for creating AVA(Fig. 1, [21]). In addition, although these circulating antibodies have been linked to chronic post-transplant dysfunction, vimentin has also been shown to be aberrantly expressed on the cell surface of platelets and has been shown to aggregate platelets independently causing damage to vascular endothelium [22]. This provides yet another mechanistic role for injury.

The source of antigenic vimentin can be linked to inflammation, injury and hypoxia. As an intermediate filament expressed in endothelial cells, vimentin may be presented to the immune system regularly secondary to endothelial cell injury from infection and/or trauma. However, vimentin-specific T-helper memory cells and B-cells appear to remain quiescent until self-tolerance is broken, and IgG and IgM antibodies appear post-transplant. Ischemia/reperfusion injury of the graft either prior to transplantation or following transplant (secondary to infection or inflammation) may also be enough to unveil vimentin antigens and trigger an immune response. Previous studies have shown that during pro-inflammatory states, vimentin can be aberrantly expressed at cell membranes and secreted into serum [23–25]. Specifically, vimentin has been shown to be secreted by macrophages under inflammatory conditions. In the study by Mor-Vankin et al, they show that expression of TNF-α leads to vimentin secretion by activated macrophages, while expression of IL-10, an anti-inflammatory cytokine, is blocked [26]. Thus, the aberrant expression of vimentin during pro-inflammatory states may also contribute to the generation of antivimentin antibodies. Tissue injury may contribute the development of AVA, specifically the “shedding” of endothelial proteins following vascular injury during hemodialysis. This idea is bolstered by studies performed on patients on chronic hemodialysis which showed a

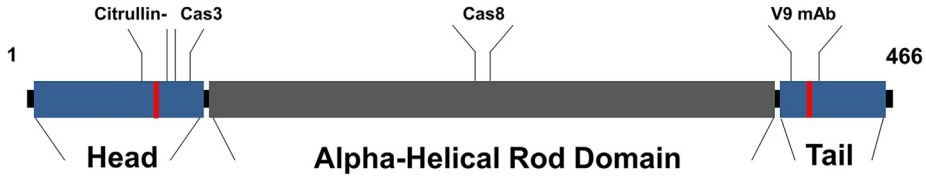

Fig. 1. Antigenic components of vimentin involved in generation of AVA. Vimentin is a 466 amino acid peptide that can be separated into 3 domains (head, intermediate filament and tail). Four notable sites on the vimentin peptide are identified: (a) *citrullin-*, (b) *Cas3*, (c) *Cas8*, and (d) *V9 mAb*. (a) *citrullin-* is the site at which the peptide is citrullinated, which normally occurs at the arginine (R) residue (noted in red) in the sequence SAVRARSSVP between residues 66–75 [36]. (b) *Cas3* is the site at which Caspase 3 cleaves vimentin at the sequence DSVD/F between residues 82–86 [21]. (c) *Cas8* is the site at which Caspase 8 cleaves vimentin at the sequence IDVD/V between residues 255–259. (d) *V9 mAb* is the epitope at which the mouse monoclonal antibody binds vimentin between residues 411–423 with the crucial asparagine (N) residue at 417 noted in red [23]. Current literature in cardiac transplantation has not yet elaborated on specific antigenic epitopes of vimentin leading to the development of AVA.

high incidence of AVA (15.4%) in sera while no AVA we found in 82 healthy control subjects [27]. Finally, ischemia/reperfusion injury following organ donation may also result in the generation of vimentin autoantibodies, as elevated levels of antivimentin antibodies were detected in the sera of non-heart beating donor recipients 1- and 6-months following transplant when compared to standard brain-dead donors [28]. These data indicate that antigenic vimentin leading to AVA can be mediated by various mechanisms resulting in the exposure of vimentin (whole or in part) to immune pathways leading to the development of AVA.

3. Antivimentin antibodies in immunological diseases

Antivimentin antibodies have been associated with human autoimmune diseases such as Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus for close to 40 years [29–32]. In the case of RA, anti-citrullinated vimentin (ACV) antibody is implicated in RA pathogenesis by their induction of osteoclastogenesis. Harre et al show that ACV antibodies bound to osteoclast surfaces and lead to induction of osteoclastogenesis and bone loss [33]. They hypothesized this to be a link between the adaptive immune system and bone metabolism, with osteoclast surface binding of ACV antibodies, leading to subsequent activation of the adaptive immune system and release of cytokines, such as TNF-α. Their work characterized the epitope of the ACV, and found it to be in the N-terminal region within amino acid positions 56 and 77 [33]. The presence of ACV antibodies in sera has been shown to be a powerful diagnostic marker for the diagnosis of RA with a sensitivity of 82% and specificity of 98% [34,35]. More importantly, these data clearly show not only the possible pathogenic role of antivimentin antibodies but also potentially point to novel therapies that may be able to be applied in transplantation. Specifically, antibody minimization therapies commonly used for anti-HLA antibodies may be applied in the setting of AVA to improve graft function/survival, but also understanding the development o AVA may allow us to change pre- and post-transplant management paradigms to minimize antibody exposure.

4. Antivimentin antibodies in cardiac transplantation

Three-year survival following cardiac transplantation approaches 75% while 5-year survival ranges from 60 to 72%. However, one of the major causes of long term loss of heart allografts is coronary artery vasculopathy (CAV) developing in 30–40% of heart transplant recipients within 5 years [36]. The causes of CAV are multifactorial, with chronic or acute AMR as one of the main components [37].

In cardiac transplant recipients, the presence of anti-vimentin antibodies is associated with cardiac vasculopathy and correlated with worse graft outcomes [(Fig. 2, 38,39]). In fact, the presence of vimentin autoantibodies was shown to induce early humoral rejection in cardiac grafts [40,41].

The source of antigenic vimentin may stem from apoptotic endothelial cells which express vimentin on their surface during all stages of acute rejection following transplant [42]. One study analyzed sera from 148 patients and found an association between the presence of donor HLA-specific antibodies in acute rejection and coronary artery vasculopathy (CAV) with the development of antibodies to vimentin and myosin. Induction of high CD4+ TH1 cells specific to cardiac self-antigens that secrete IL-5 and IL-17 played a major role in the development of vimentin antibodies that lead to AMR and CAV. These CD4+ cells also decrease their IL-10 secretion, demonstrating a possible breakdown of tolerance to vimentin leading to inflammation (Fig. 2, [43]). Cardiac transplantation in mice treated with both antivimentin antibodies and vimentin reactive TH1 Cells resulted in accelerated rejection in vimentin-immunized mice compared to controls. Immunized mice had increased CD8+ T-cells and enhanced vascular deposition of C3d, CD41, P-selectin, as well as increased vimentin and C3d levels on apoptotic leukocytes, endothelial cells, and platelet/leukocyte conjugates [40]. Pathological analyses of non-human primates undergoing acute rejection following cardiac transplant with CAV-type lesions revealed strong C4d, C3d, and C5b-9 staining associated with AVA staining. These studies indicate that AVA binding can stimulate CD8+ T cell-mediated inflammation leading to acute humoral rejection [42].

Barber et al detected self-restricted CD8+ T-cells bound to vimentin tetramers in two of six cardiac transplant recipients using A*02:01 vimentin binding tetramers [44]. A study looking at 109 patients found that mean titers of IgM AVA were significantly higher in patients who developed transplant vasculopathy than those that remained disease free 1, 2 and 5 years post-transplant, and IgG AVA was detected at the time of diagnosis of AMR in the absence of donor specific HLA antibodies (Fig. 2, [17,38]). Pre-transplant levels of AVA, however, do not seem to play a role in the development of AMR or CAV. Incidence of antibodies prior to transplantation and their association with early rejection was investigated at Johns Hopkins from 2004 to 2012. This study found that AVA positivity pre-transplant did not predict rejection in the first 24 months post-transplant [45]. Additionally, a study looking at cardiac transplants in Cynomolgus monkeys found that absolute levels of pre-transplant AVA IgG and IgM had no correlation with post-transplant peak titer in any experimental group [42].

Regarding treatment, mycophenolate mofetil was found to be more effective than azathioprine in decreasing post-transplant AVA levels in a 86 patient cohort [46], and a separate study found patients taking tacrolimus developed less AVA than patients taking cyclosporine [47].

In conclusion, while not predictive of CAV, it seems that AVA may be playing an additive, but not necessary, role in the setting of acute and chronic AMR leading to CAV. Presence of CAV in animals without AVA suggests that alloantibody may be all that's needed, however AVA appearance post-transplant can accelerate the development of CAD and ultimately lead to graft failure [42].

5. Antivimentin antibodies in renal transplantation

Interstitial fibrosis and tubular atrophy is seen in up to 20% of transplant recipients following transplantation and is a major cause of long-term renal transplant failure [48]. It is thought that one component of IF/TA is chronic antibody-mediated injury from alloantibodies as well as autoantibodies [49]. Similar to studies in cardiac transplantation, the presence of AVA flowing renal transplantation has also been

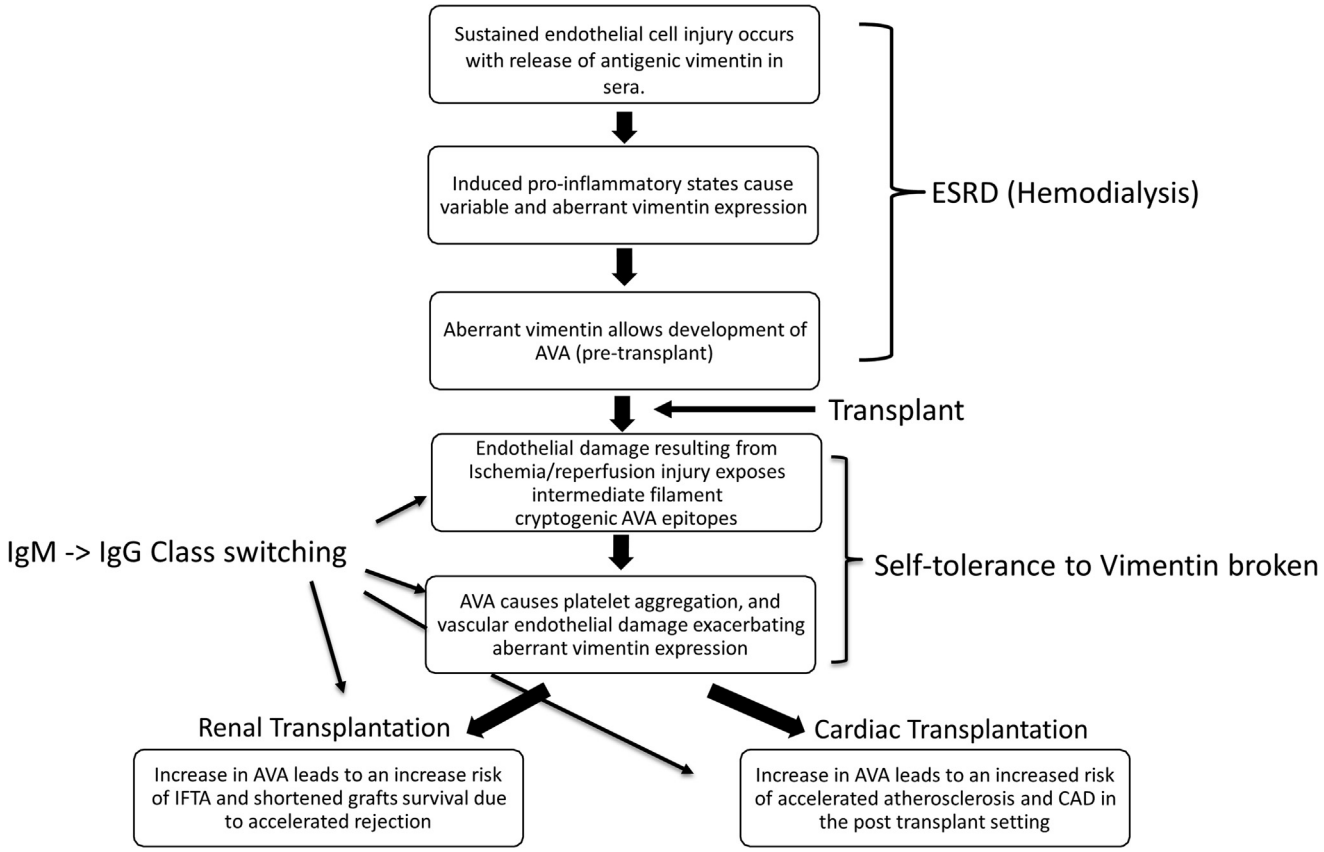

Fig. 2. Possible pathway for AVA-directed damage in cardiac and renal transplant recipients. Formation of AVA in ESRD patients on HD is likely a result from continuous endothelial damage during A-V Fistula cannulation. This allows for the exposure of antigenic vimentin in sera and production of AVA. Though atherosclerosis and chronic injury from diabetic vasculopathy may contribute to endothelial damage and subsequent release of antigenic vimentin, it likely does not result in large boluses of vimentin in serum. Therefore, this initial pattern of AVA formation is not seen in the pre-cardiac transplant patient population. Following transplantation, ischemia/reperfusion injury of both cardiac and renal grafts results in endothelial damage/shedding which provides an additional bolus of vimentin epitopes in sera. In addition, exposure of aberrant vimentin expression on the surface of platelets as well as damaged endothelial cells allows for damage from preformed AVA, potentiating the release of more vimentin in sera. During this time, self-tolerance to vimentin appears to be broken through repeated signalling from continued antigenic exposure and inflammation. Additionally, class-switching from IgM to IgG class occurs allowing for the formation of pathogenic AVA. Following subsequent episodes of immune activation from acute rejection, infection, or injury; formed AVA now result in continued and persistent damage that accumulates over time resulting in permanent graft injury.

associated with chronic graft dysfunction (Fig. 2). Animal studies in non-human primates found AVA in 31/37 recipients with IF/TA. It was shown that though some immunosuppressants specifically those blocking CD40/86 delay AVA formation, they don't prevent IF/TA [50]. Following renal transplant in rats *de novo* AVA was detected 8- and 12-weeks after surgery where pre-transplant sera was free of AVA with a gradual increase in IgG around 4 weeks after transplant. Elevated AVA levels with C4d deposition were correlated with development of IF/TA. Interestingly, cyclosporine use resulted in higher AVA titers compared to rats treated with mycophenolate mofetil [51].

Human studies showed similar results. Sera from 48 patients with IF/TA was compared to non-transplanted renal failure patients. Patients with biopsy proven IF/TA had high levels of IgM AVA (P = .008) that developed within the first 3 months post-transplant remaining elevated in the subsequent studies especially in those patients with patients with antibodies to HLA-DQ2. The study shows that there is not only a role of AVA in the development of IF/TA but also an additive effect when anti-HLA antibodies are present [52]. In a recent retrospective study of 70 renal transplant recipients, there was an increase in the amount of AVA in patients with IF/TA vs controls 4 years after transplant (P = .0003 by year 4) [53]. There was however no difference in the AVA concentration at the time of transplant [53]. Another study also determined that elevated AVA concentrations post-transplant was correlated with the finding of graft dysfunction. However, although there was an increased IgG AVA in patients with IF/TA, there was no difference in IgM concentration [54].

Work from our laboratory analyzing the sera of 97 transplant patients between 3 and 12 years after transplant quantified the concentration of AVA and then correlated the levels with the presence of IF/TA. Our studies showed higher AVA concentrations in patients with early IF/TA (< 5 years) vs. controls (32.2 vs. 14.36 μg/mL). In fact, we found that a pre-transplant AVA concentration > 15 μg/mL conferred a 2-fold higher risk of early IF/TA [55]. These data, similar to cardiac transplantation, show a definitive correlation between the development of AVA and graft dysfunction although there are differences in their biology and presentation (Fig. 2).

6. Antivimentin antibodies and liver transplantation

There have not been many studies linking post-liver transplant dysfunction and antivimentin antibodies. Previous studies have shown correlation between inflammatory states in liver secondary to viral hepatitis and the development of antivimentin antibodies [56]. Immunoblotting showed that sera from patients with acute viral hepatitis reacted with 57 kD vimentin in triton-cytoskeletal extracts of fibroblasts. These results show that autoantibodies to vimentin are present in sera from patients with acute hepatitis A, B and non-A, non-B HCV [57]. Finally, a study by Abdeen et al showed that chronic hepatitis patients

had a higher mean antibody concentrations of ACA in sera compared to controls (P = .001), and the titers were able to distinguish patients with fibrosis or cirrhosis from those without [58]. These data, though not directly analogous to post-transplant studies, show the creation of anti-vimentin antibodies during inflammatory states and therefore argues for analyzing the sera of liver transplant patients (especially those with viral hepatitis as the cause of their liver dysfunction) with rejection for the presence of these antibodies

7. Discussion

Antivimentin antibodies have been associated with autoimmune diseases, cancers, fibrosis, and post-transplant dysfunction. However, the pathogenesis of vimentin antibody production is not clear. Based on human and animal studies, vimentin in and of itself may be immunogenic when released by tissue damage secondary to inflammation and injury. Injury to endothelium secondary to physical injury (hemodialysis) and inflammatory processes as well as ischemia/reperfusion results in a bolus of endothelial vimentin leading to immune processing [25,59,60]. The presence of AVA in hemodialysis patients as well as non-heart beating donors supports the idea of endothelial injury as a source of AVA [28,61]. However, it appears that expression of pathogenic AVA is induced following transplantation and/or injury (ischemia/reperfusion, infection, or rejection) of the new graft where cytokine production in concordance with exposure of new antigenic vimentin either stimulate production of new AVA or is able to overcome the anergy seen prior to transplantation in renal transplant recipients.

Currently there is very little data on the role for these antibodies in the setting of liver, lung, and pancreas transplantation. However, data from oncological studies have shown a possible role for vimentin as a maker of pancreatic cancer progression [15]. Data from pulmonary fibrosis studies have shown that antivimentin antibodies may be associated with worsening pulmonary injury [62]. Finally, there is some additional data showing the importance of antivimentin antibody associated with hepatic inflammatory processes [58]. Clearly, more work needs to be done in order to determine whether these antibodies are important for post-transplant function in lung, liver, and pancreas transplants.

The consequences of AVA production vary with the organ transplanted which is likely secondary to the specific nature of the disease process for each type of recipient (cardiac and renal). Specifically, chronic endothelial cell damage is more common in renal failure patients on hemodialysis. This pre-immunization idea is corroborated by mice data where treatment with vimentin prior to transplant results in accelerated cardiac vasculopathy [40]. However, pre-transplant levels of antivimentin antibodies do not seem to correlate with post-transplant development of CAV, where, even though there is a strong correlation between anti-vimentin antibodies and graft dysfunction, the presence of anti-vimentin antibodies prior to transplantation did not predict the risk of rejection at 1 year and graft survival at 1 and 2 years [45]. Likely, the antigenicity of vimentin is related to the depth of endothelial injury resulting in the exposure of vimentin (whole or in part) in order to allow for the development of auto-antibodies during hemodialysis. Supporting this idea renal transplant recipients appear to develop AVA much earlier than cardiac transplant recipients. It's likely that these AVA are more readily formed secondary to having B and T cells exposed to vimentin prior to transplantation which are more readily activated during the inflammatory state associated with transplantation (Fig. 2). However, differences in AVA damage when comparing cardiac and renal transplantation could also stem from the increased production of IgG AVA in renal transplant recipients. Class switching from IgM to the more pathogenic IgG subtypes could be due to increased exposure of vimentin in kidneys following injury where *de novo* vimentin expression is detected in renal tubular epithelial cells in addition to interstitial fibroblasts, glomerular cells and endothelium [53,63,64].

8. Conclusions

Antivimentin antibodies are clearly pathogenic following transplantation. However, it is unclear how the presence of these antibodies should change treatment paradigms in the post-transplant settings. This becomes more complicated when there is also no associated graft dysfunction by clinical parameters. The presence of AMR on biopsy specimens with concomitant detection of DSA almost always lead us to strategies such as, B-cell depletion, intravenous immunoglobin administration, plasmapheresis, proteasome inhibitors, and complement inhibitors, but it is not clear how much/which therapy to use and what endpoint to target when AMR is detected in cardiac and renal transplant recipients with no associated anti-HLA antibodies. Our understanding of the importance of non-HLA antibodies, including AVA, in post-transplant graft dysfunction continues to evolve. As our knowledge about these antibodies increases it may become important to determine AVA and other non-HLA autoantibody concentrations as part of the pre-transplant evaluation as a way to risk stratify patients prior to transplant. In addition, the detection of these antibodies may change post-transplant care by 1) increasing and expanding post-transplant auto-antibody detection protocols to include non HLA-antibodies and 2) changing transplant immunosuppression therapies aimed at minimizing antibody mediated injury. Finally, more work needs to be done to determine the true risk in cardiac vs. renal transplant recipients. Given the propensity of renal transplant recipients to be exposed to antigenic vimentin while undergoing hemodialysis, it is likely that they are at an increased risk of post-transplant AVA-mediated injury and therefore measuring the pre-transplant levels of AVA may be important in determining post-transplant immunosuppression regimens while cardiac transplant recipients may not be exposed to such increased risk (Fig. 2). Either way, prospective studies looking the association between developing de novo AVA and subsequent graft dysfunction will allow us to determine the need for monitoring AVA. Still, given the cost and manpower associated with detecting, evaluating and possibly treating these patients, much work remains to fully understand the risk conferred by the development of AVA. As part of this initiative, we have begun analyzing antivimentin antibodies in a prospective manner in all of our kidney transplant recipients in order to determine whether there are any effects on post-transplant renal graft function and survival. We hope this will expand our knowledge about the importance of AVA in transplantation and potentially change our practice, possibly improving post-transplant outcomes.

Conflict of interest

There is no conflict of interest.

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