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With the introduction of cyclosporine during the 1980s, transplantation has emerged as an effective therapy for a large number of patients with severe kidney, heart, lung, liver, and hematopoietic diseases. As the transplant population grows, surgical pathologists will encounter an increasing number of specimens from transplant recipients. These surgical pathologists play a pivotal role in the multidisciplinary management of transplant recipients. Although much of the approach to handling specimens from transplant recipients is covered in each chapter on specific organ systems, there are some unique aspects specific to the handling of specimens from transplant recipients that deserve special note.

Handling a specimen from a transplant recipient is in many ways guided by an understanding of the complications associated with transplantation. It is therefore useful to keep in mind the pathology unique to transplantation when handling a biopsy or resection specimen from a transplant recipient. These unique situations include (1) Complications related to the primary disease for which the transplant was performed. Specifically, samples must be handled in a way that allows one to diagnose recurrence of the patient's underlying pathology. For example, although electron microscopy and immunofluorescence are generally not helpful for establishing a diagnosis of acute renal allograft rejection, they can be essential for establishing the diagnosis of a recurrent glomerular disease. (2) Complications of the surgical procedure itself. For example, arterial stenosis in the donor segment of an artery is often due to accelerated graft arteriosclerosis (chronic rejection), whereas stricture at the anastomotic site may be related to the surgery. (3) Complications of acute rejection. Acute rejection can develop rapidly and have a devastating impact on the graft and patient survival. Biopsies from transplant recipients are therefore often rushed. Failure to recognize the urgent nature of most transplant biopsies can result in delayed therapy, which can have a devastating impact on patient management. (4) Infectious complications. Infections in transplant recipients are remarkable for the diversity and multiplicity of the organisms involved. Multiple cultures and the up-front ordering of special stains to detect a variety of infectious agents (fungi, bacteria, viruses) are often indicated. (5) Complications related to the patient's clinical treatment. In addition to a host of immunosuppressive agents, transplant recipients are often treated with a variable pharmacopoeia of drugs. They can cause a host of pathologies that may mimic or be superimposed on rejection. The appropriate management of a specimen from a transplant recipient therefore includes a thorough understanding of the patient's clinical history, including a detailed record of the medications the patient is receiving.

In addition to these five general considerations, there are a number of organ-specific guidelines for handling surgical pathology specimens from transplant recipients. These guidelines are frequently updated; as of January 2003, they included the following.

Heart. The International Society for Heart and Lung Transplantation (ISHLT) established a "working formulation" for grading heart allograft rejection in 1990.[4] This working formulation includes a number of technical considerations. Because acute allograft rejection can be focal, the ISHLT standard grading system requires four to

six undivided pieces of myocardium. The individual handling these biopsy specimens should document the number of pieces received. The tissue should be fixed in 10% buffered formalin and paraffin-embedded. Once processed, a minimum of three step levels should be prepared through the block with at least three sections per level. The slides should be stained routinely with hematoxylin and eosin and one slide stained with a connective tissue stain such as a Masson's trichrome. In addition, during the first 6 weeks after transplantation at least one piece should be placed in OCT and fresh-frozen for possible immunofluorescence examination to rule out antibody-mediated rejection.

Kidney. The "Banff" criteria for grading renal allograft rejection were established in 1991.[6] These criteria have been periodically modified, and the current Banff '97 guidelines provide specific recommendations for the handling of biopsy specimens from renal transplant recipients.[7] The recommendation is that seven slides be prepared containing multiple sequential sections. Three of the seven should be stained with hematoxylin and eosin, three with periodic acid–Schiff or silver stains, and one with a trichrome stain. It is also recommended that these sections be prepared at 3 to 4 μm.

Lung. In 1996 the ISHLT presented a revision of the 1990 working formulation for the grading of lung allograft rejection.[8] This revision included the following recommendations for handling transplant lung biopsies from lung transplant recipients. At a minimum, sections of three levels should be stained with hematoxylin and eosin. In addition, one level should be stained with a connective tissue stain to evaluate the biopsy for the presence of submucosal fibrosis associated with the development of bronchiolitis obliterans, and one level should be silver stained for fungi/*Pneumocystis*. In addition, the ISHLT group emphasized that all biopsy specimens should be studied by pathologists with full knowledge of the native recipient disease and the results of the last biopsy and current bronchioloalveolar lavage.

Liver. The Banff system for grading liver allograft rejection was presented in 1997.[9] Their recommendations included that at least two hematoxylin and eosin-stained sections from at least two levels should be prepared from each needle core biopsy.

The criteria for evaluating transplant biopsy specimens for rejection are beyond the scope of this book, but there are some centralized resources. For example, the University of Pittsburgh's website contains both the current diagnostic criteria and standardized templates for evaluating biopsies from transplant recipients (http://tpis.upmc.edu/).

Important Issues to Address in Your Surgical Pathology Report on Transplant Biopsies

- Evidence of recurrence of a patient's primary or underlying disease
- Any complications related to the transplant procedure itself
- Degree of rejection (both acute and chronic)
- Presence of any infections
- Presence of any neoplasms, particularly post-transplant lymphoproliferative disease
- Presence of any complications related to therapy (drug toxicity)
- When appropriate sampling has not occurred, it is essential to note in the pathology report that the biopsy findings may not be fully representative of the changes in the graft.