Clinics in Surgery

Editorial
Published: 03 Aug, 2017

Transplantation Surgery and Related Basic Sciences

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Editorial

Transplantation is an interesting treatment procedure. A patient, who has an organ failure, in need of life support devices, incompatible with life without them, and suffering from a disease severely lowering the quality of life, is treated by replacing the failing organ. Principles of vascular and general surgery are used during the procedure, but surgery is not the sole part of the procedure, transplantation is much more than that. There is an orchestration of many procedures that must be harmonized with precision. Patients are prepared for transplantation by fine tuned medical means, molecular graft-recipient matching using proper genetic and molecular biology lab techniques. After the operation, keeping the donor organ in the patient by immune modulation and prophylaxis measures for the complications are the essentials for a successful transplantation. In its' nature, transplantation is a life saving procedure. To perform a transplantation, a graft organ or tissue donated by a healthy donor is always necessary.

Transplantation is an old idea in the history of medicine. Men always dreamed of the possiblity to survive longer and be more powerful, even imagined different elements of strong species living on the same body, mythology has several descriptions of this. Two World Wars and major local combats experienced in 20th century gave lessons to men; the importance of manpower and health, to survive longer and better, the ways of quick wound healing, support of wounded patients with engineered aid devices, looking for quick ways to rehabilitate them, forced scientist to explore and invent some unusual new procedures, that provide prolongation of life. In treating burns which are the most common wounds in war, skin grafts were taken from cadaver donors in the war field was a good idea at first. Grafting was useful for a temporary skin wound covering, but soon, it was realized that, it was not treating the patient, the major problem being recipients not tolerating and rejecting grafts from allo cadaver donors. This was the nature's reaction to foreign tissue antigens as a survival strategy acquired by lots of experience during the evolution. This reminded doctors of the importance of the immune system to stay alive. Immune system was the second to physical bariers of the body to protect and to survive. During the WW years, lots of experiments, inventions and applications of the inventions were done, new technologies in basic sciences had improved. Medicine developed fast, alongside with all these; new diagnostic techniques and tools were invented and applied that detect biological problems early and correctly, which made doctors realize the importance of the basic sciences in medicine. Immunologic and genetic discoveries helped transplantation develop, thanks to hardworking dedicated scientists. The main problem was the inflammatory reaction and its' involvement in rejection reaction to foreign tissue mediated by the immune system. As knowledge of the immune system accumulated in time, more information was provided on its behavior coexisting with an allograft. What an allograft is, the rejection reaction and how to create a tolerant state to an alloorgan of the failed organ in the body was understood better.

The most important antigens that differ self from nonself or foreign tissue were;

- Blood group antigens which are located on endothel and
- Major histocompatibility antigens located on every nucleated and immune cell's surface.

The complement system and coagulation system were very important during immune responses. With the aid of tolerance studies, the spesific immune reactions, the acquired immun system activities which are very important in transplantation reaction are understood. The acquired immune system was acting accordingly with the nonspesific signals coming from the innate system during the transplantation procedure.

Many organ transplant trials were done with no acceptable success because of the natural reaction of rejection. During these trials it was understood that the procedure needed multidisciplinary and translational works to develope as a treatment. It was postulated that genetic similarity might be a way to success. First successful transplantation was performed in Boston, USA, in December

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Received Date: *24 May 2017*
Accepted Date: *28 Jul 2017*
Published Date: *03 Aug 2017*

Citation:
Titiz Mİ. Transplantation Surgery and Related Basic Sciences. Clin Surg. 2017; 2: 1576.

1954, an identical twin brother with no genetic disparities donated one of his kidneys to his brother, a chronic renal failure patient. Since the experimental research on transplantation warranted a multidisciplinary approach, different clinics of the hospital helped each other to be successfull. The members of the first transplantation team were; Joseph E. Murray, a Plastic Surgeon, John Merrill (Nephrologist), J. Hartwell Harrison (Urologist), Gustave Dammin (Pathologist) and a Psychiatrist [1].

Later, as research and medical developments went on, related basic sciences improved by sharing information gained from the several experiments done around the world, especially on the topics of organ preserving, ischemia – reperfusion problems, organ sharing, new selective drug inventions to decrease immune reactions, better combinations of them for less toxicity helped transplantation be a routine therapeutic procedure for organ failure. Today almost any organ or tissue can be transplanted with safety and acceptable success. The only major problem in transplantation today that is not solved is shortage of donor organs. We learned that not all transplanted patients react the same to the allograft. Immunsuppressive drug protocols do not provide or ensure the same benefit to all patients. Drugs were preventing the rejection reaction but with a cost of many side effects and toxicities. The treatment should be tailored for each patient differently according to the condition, the immunologic status of the patient and the biologic properties of the graft organ. As the rule; patient reacts to the allograft and the allograft reacts to the body. The balance must be achieved by means of logical use of immune modulating medicines to reach optimal results. Accumulated lessons from clinical trials, reported outcomes and evidence collected taught us that clinical transplantation must be supported by the translational studies from the basic science laboratories. Clinical problems must be studied together with appropriate models designed in the labs to increase scientific knowledge for better outcomes, and results generated in labs should be tested in clinical conditions. Translational studies helped doctors to discover the big problem why we had failed to have long posttransplant graft and patient survival. At the early years, we believed the immunmodulation strategy of T cell control was the most important step against rejection, then tolerance was not understood with all its dimentions. Although transplantation had become successful in short term with this method, long term results were not as expected. Later, it was understood that the major problem in the long run was, for not quite understood reasons, inadequate immunsuppression and subclinical chronic humoral activity against the allograft and graft injuries that it caused. That finding has shifted the attention of the researchers to the pretransplant sensitization problems caused by suboptimal matchings and the humoral theory developed [2]; the importance of immune memory, existing antibodies to HLA, their amount, phenotypes, subgroups, B cells and plasma cells was explored further. Searching the patients sensitivity level and anti-HLA memory status pretransplantation helped us to match organs with the appropriate recipients. In clinical practice, to overcome the suboptimal HLA matchings, patients were immunosuppressed more and that increased the risk of viral infections. Infections are immune system triggers and, as a principle, activated immune system is not desired following transplantation. Keeping these in mind, may provide us with more rational patient selection, for offered rare and precious donor organs, reaching higher graft and patient survivals.

In today's clinical transplantation studies there are almost no surgical technical problems, but problems related to long term graft and patient survival are still subject to research.

Generally it is agreed that:

- Good HLA matching, naturally, is very important, although it is not possible to applicate during the routine practice of donor organ – patient matchings.
- Ischemia and reperfusion injury is a very strong inflammatory event happens during transplantation and a powerful immun system stimulator. What possible is, shortening the ischemic storage period, may help reduce the reperfusion inflammatory reactions. Keeping the intensity of the immune reaction low by reducing the ischemic period and proper immunmodulations after reperfusion is also very important for having a near tolerant state.
- The immune condition the patient is in during transplantation, is a parameter that must be well evaluated and understood fully, and tailoring the posttransplant immunmodulation accordingly is very important.
- All possible prophylactic measures should be taken against infection, especially viral infections not only as an infection prophylaxis but keeping the immun system function low as much as possible.
- Education of the patients, having their contribution on possible unwanted events by regular and close patient monitoring are important for long term success.
- Transplantation has social and ethic and economical aspects. Taking care to ethical measures, better and just matching of donor organs with the recipients, better outcomes increase the trust to the procedure and may help people donate more. A more responsible approach to use the resources logically may make transplantation to be a more economic procedure that lowers the unnecessary expenses.

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