ACADÉMIE NATIONALE DE MÉDECINE

New developments in transplantation: the challenge of surgical prowess in the face of alternatives.

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Three recent examples invite us to recall the technical, ethical and patient information conditions which allow a surgical advance, sometimes spectacular, to take place as a modality of progress in therapy, in the current state of knowledge and alternatives.

In November 2020, a lung transplant was performed at Foch Hospital in Suresnes on a patient with terminal respiratory insufficiency due to SARS-CoV2 infection. Transplantation, in this exceptional indication, has been performed in several dozen patients worldwide (21 cases in the USA), either to treat Acute Respiratory Distress Syndrome (ARDS) or, more often, to treat the fibrosing sequelae of patients dependent on extracorporeal circulatory or respiratory assistance. The indications of this treatment, which could give rise to ill-considered hopes in a context of graft limitation, are still evolving. They must take into account the severity of a transplant in a context of persistent viral infection and the possibility of regression of fibrosing lesions.

On January/13, 2021, a bilateral upper limb allograft involving the shoulder, performed at Edouard Herriot Hospital in Lyon, declined in many ways the register of the exceptional: a) the 48 year old patient, who had lost both upper limbs following an electrocution accident 20 years ago, had had a liver transplant for acute liver failure in 2002, and was therefore on a well-tolerated immunosuppressive dual therapy; b) the logistics of the operation (15 hours and nearly 50 caregivers, including 15 surgeons and 5 anesthetists) performed under extra-renal perfusion in order to avoid the ischemia-reperfusion syndrome of the transplanted tissue mass. The technique consisted of a "classic" transfer to the right arm (made possible by the persistence of a proximal humerus segment and an excellent scapular belt) and the stabilization of the left upper limb by suspension of the humerus proximal end from the scapula in the absence of a humerus stump. Despite all these difficulties, the aftermath was straightforward.

Having succeeded to develop formidable compensatory capacities, the patient was informed that there was no guarantee of a functional recovery apart from the possible flexion of the elbows, that there will be probably no sensory-motor recovery of the hands, and that, in the event of the graft removal, the attempt would be made to keep longer stumps for a better

adaptation of the apparatus. However, this unusual operation allowed a radical change in the patient's abilities and, above all, the restoration of the image of his body integrity. In the future, advances in brain-controlled devices could make this type of transplantation unnecessary.

On February 12, 2021, the birth at Foch Hospital in Suresnes of a child after a uterine transplantation performed in March 2019 was the happy outcome of the response to the desire for maternity of women with an absence of uterus but with functional ovaries, either congenital (100 to 200 cases per year in France) or acquired (uterine malformation, adenomyosis, hysterectomy for hemostasis or for cancer). For women who do not wish to give up having a child, uterine transplantation is then in balance with adoption, a commitment of generosity and self-sacrifice facing with numerous obstacles (small number of children to be adopted, delays of nearly 18 months, long investigations and formalities, multiple uncertainties), and with surrogate motherhood (GPA), prohibited in France but not in neighboring countries (approximately 400 French children born each year from GPA carried out abroad. The conditions for uterine transplantation, successfully developed in Sweden since 2015 were the subject of a report by the French National Academy of Medicine (1) and have recently been clarified on the basis of the first 45 published cases (2). In addition to the technical difficulties of collecting the graft and of its implantation in the recipient, there is also an oocyte harvest, a reimplantation of the embryo, a caesarean section and a secondary hysterectomy after one or two pregnancies. The ethical questioning must also take into account the uncertainties about the long-term effects of immunosuppressants on the mother and child and on the child development in a transplanted uterus coming, most often, from a close relative but, in certain cases, from an anonymous donor.

The French National Academy of Medicine, in its role of support and dissemination of medical progress:

- welcomes the remarkable contribution of French medical and surgical teams to the development of therapeutic alternatives in extreme medical situations;

- underlines that the spectacular side of these technical and organizational challenges should not make us forget that their indication remains rare, concerns rigorously selected cases, and cannot dispense neither from an objective evaluation of the results at a distance, nor from a continuous research of alternative solutions;

- recalls that the media coverage of these events, although recently authorized by the Public Health Code, requires caution because of the generally very painful human dimension involved;

- recommends the continuation of ethical reflection and support, including financial support, for medical research allowing the application of exceptional therapies in medical situations with no indisputable traditional and innovative solutions.

1) Report of the French Académie Nationale de Médecine (presented by R. Henrion and J. Milliez). Bull Acad Natl Med 2015; 199, n°6 :921-942.

2) B.P. Jones et al. Human uterine transplantation: a review of outcomes from the first 45 cases. BJOG 2019; 127:1310-1319