B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Can a Pompe disease patient be an organ donor?

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To the Editor,

Glycogen storage disease type II, or Pompe disease, also called acid maltase deficiency, is a rare disease affecting lysosomal storage which is characterised by the accumulation of glycogen, mainly in muscle tissue. It is a hereditary autosomal recessive disorder with a deficiency of lysosomal acid α-glucosidase enzyme activity. The two most frequent subtypes of Pompe disease are the infantile and the late onset forms. The infantile form is the most serious and is characterised by cardiomegaly, general muscle weakness, hypotonia, hepatomegaly and death due to respiratory failure before the age of one. The late onset form, also known as juvenile or adult form, appears after the age of one and is characterised by damage to skeletal muscles, which causes progressive muscle weakness and respiratory insufficiency[1]. A prevalence of 1:57,000 in the population is estimated in the late onset form. Before 2006, it was an incurable disease with merely palliative treatment, but the development of recombinant human α-glucosidase enzyme substitution therapy constitutes the first specific treatment[2]. This therapy has allowed the disease's progress to be reduced and/or stopped.

We present the case of a 37 year-old, type 2 non-heart-beating donor with late onset Pompe disease being monitored by our hospital and receiving enzyme therapy treatment. The patient suddenly died at home and was transferred to our hospital as a possible organ donor. Death was certified on arrival at the intensive care unit, with the following biochemical data: normal renal function with serum creatinine level at 0.78 mg/dl and glomerular filtration rate, using MDRD-4, of 85.7 ml/min and altered hepatic profile (GPT [ALT] 150 U/l, GOT [AST] 130 U/l and GGT 160 U/l) already known. Given the rarity of this condition, it was doubted whether a patient with this type of systemic disease could be an organ donor. After reviewing the medical literature, we could verify that there was no information on the subject.

In order to obtain the necessary and useful information that would help us make the correct decision, we consulted the clinical guides on late onset Pompe disease and its systemic damage, deciding to accept the patient as a donor on the absence of data specifically contradicting donation. Although all organs were evaluated, only the kidneys could be used (the liver was rejected due to altered hepatic profile during preservation). The kidneys were transplanted to two recipients aged 27 and 45 without prior transplants. The first recipient was a 27 year-old male with chronic kidney disease (CKD) secondary to Alport syndrome on haemodialysis for three years; the second recipient was also a male with CKD secondary to a polycystic disease on haemodialysis for four years. Sequential immunosuppression with thymoglobulin, micophenolic acid and steroids and late introduction of tacrolimus were used in accordance with usual treatment of a non-heart-beating donor. In both cases there was delayed graft function, as is frequent in kidneys coming from a non-heart-beating donor, subsequently progressively recovering renal function. Neither recipient presented acute rejection immediately following transplant and 18 months after, both showed normal renal function, negative proteinuria and absence of hydroelectrolytic disorders.

Late onset Pompe disease is a multisystemic disorder that can have a wide range of clinical manifestations, including progressive muscle weakness, especially the muscles in the pelvic girdle, and respiratory symptoms, which are the principal cause of morbidity and mortality due mainly to diaphragmatic involvement and involvement of intercostals muscles[3]. Other serious complications are those arising from the presence of intracranial aneurysms, usually underdiagnosed and potentially fatal, and cardiac disturbances, such as Wolf-Parkinson-White syndrome which has been described in some affected patients. Regarding renal disease associated with this condition, isolated cases of electrolytic disorders which mimic Gitelman syndrome with histological findings, in which the presence of glycogen deposits in distal tubules stand out, have been described[4]. A case of nephrotic syndrome has also been reported in a pediatric patient as a complication of high doses of enzyme replacement therapy triggered by immune complex deposits[5].

In conclusion, it is necessary to highlight that there are an increasing number of patients with rare diseases who, thanks to new therapies, have a longer life expectancy. The case described shows that the knowledge of these conditions can allow us to reflect on the suitability of these patients as a source of organ donors.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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Anorexia and megestrol acetate: treatment versus placebo controlled study

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To the Editor,

Loss of appetite is a frequent symptom in a dialysis patient, which causes anxiety and affects perceived quality of life. Deficient food intake as a result of anorexia is the main cause of type 1 uraemic malnutrition, which is not related to intercurrent inflammatory processes[1]. Megestrol acetate increases the appetite and improves the nutritional parameters in patients treated with periodic haemodialysis who suffer from anorexia[2]. Given the subjective nature of anorexia, there is doubt surrounding the extent to which the effect of megestrol acetate can be attributed to a placebo effect.[3] In order to clarify this, we studied anorexia's response to megestrol acetate in a randomised controlled study.

In 2011 and 2012, 122 patients were treated in our haemodialysis unit. 19 of the patients suffered from anorexia, without a known trigger factor. In order to diagnose anorexia, we used the appetite questionnaire from the HEMO and DOPPS studies[4,5] in which the patient has to indicate how he/she regards his/her current appetite on a Likert scale with five possibilities: very good, good, normal, bad or very bad. The patient is then asked whether his/her appetite had improved, stayed the same or diminished in the last four weeks. Anorexia is diagnosed when a patient reports that his/her current appetite is normal, bad or very bad and that it has not changed or has diminished in the last four weeks. The 19 patients were treated randomly with megestrol acetate, 160mg/day (10 patients; 4 males and 6 females), or placebo (9 patients; 4 males and 5 females). We analysed anorexia evolution and evolution of nutrition-related clinical parameters over three months.

Initially, there were no differences between the treated group and the control group with respect to age (73±9 vs. 69±18 years, *P*=.544), time on dialysis (40±46 vs. 47±41 months, P=.731), dry weight (58.1±10.7 vs. 61.9±7.2kg, P=.377), weight loss in the last two months (0.6±1 vs. 0.6±0.5kg, *P*=.903), albumin concentration (3.25±0.62 vs. 3.33±0.57 g/dl, *P*=.781) or dialysis dose (Daurgidas spKt/V 1.70±0.28 vs. 1.79±0.22, *P*=.456). All the patients received dialysis three times a week, with high-flux biocompatible membrane and ultrapure dialysate.

After three months of treatment, 9 out of the 10 patients treated with megestrol acetate and 4 out of the 9 patients treated with placebo reported an improvement in appetite (*P*=.046, Fisher test). Evolution of weight and other nutritional parameters are shown in Table 1. An increase in weight and in concentrations of albumin, creatinine and urea, without modification to dialysis dose, were only observed in the group of patients treated with megestrol acetate. None of these parameters varied significantly in the group of patients treated with placebo.

The feeling of loss of appetite is partly subjective, which can be seen to be influenced by placebo administration. However the stimulating effect on appetite induced by megestrol acetate cannot be exclusively attributed to a placebo effect. The proportion of patients who reported an improvement in appetite following megestrol acetate treatment is higher than that reported by the placebo-treated control group.

Table 1. Evolution of nutritional parameters.

	Megestrol Acetate Group			Placebo Group		
	Baseline	3 months		Baseline	3 months	
Weight	58.1 ± 10.7	59.8 ± 9.9	P = 0.003	61.9 ± 7.2	61.1 ± 7	P = 0.100
Albumin (g/dl)	3.25 ± 0.62	3.49 ± 0.68	P = 0.009	3.33 ± 0.57	3.31 ± 0.46	P = 0.608
Cr (mg/dl)	8.5 ± 2.7	9.7 ± 2.5	P < 0.001	9.2 ± 2	8.7 ± 2.3	P = 0.189
Urea (mg/dl)	136 ± 40	161 ± 52	P = 0.067	141 ± 40	139 ± 50	P = 0.853
Kt/V	1.70 ± 0.28	1.67 ± 0.32	P = 0.587	1.79 ± 0.22	1.83 ± 0.22	P = 0.431