Case report 1

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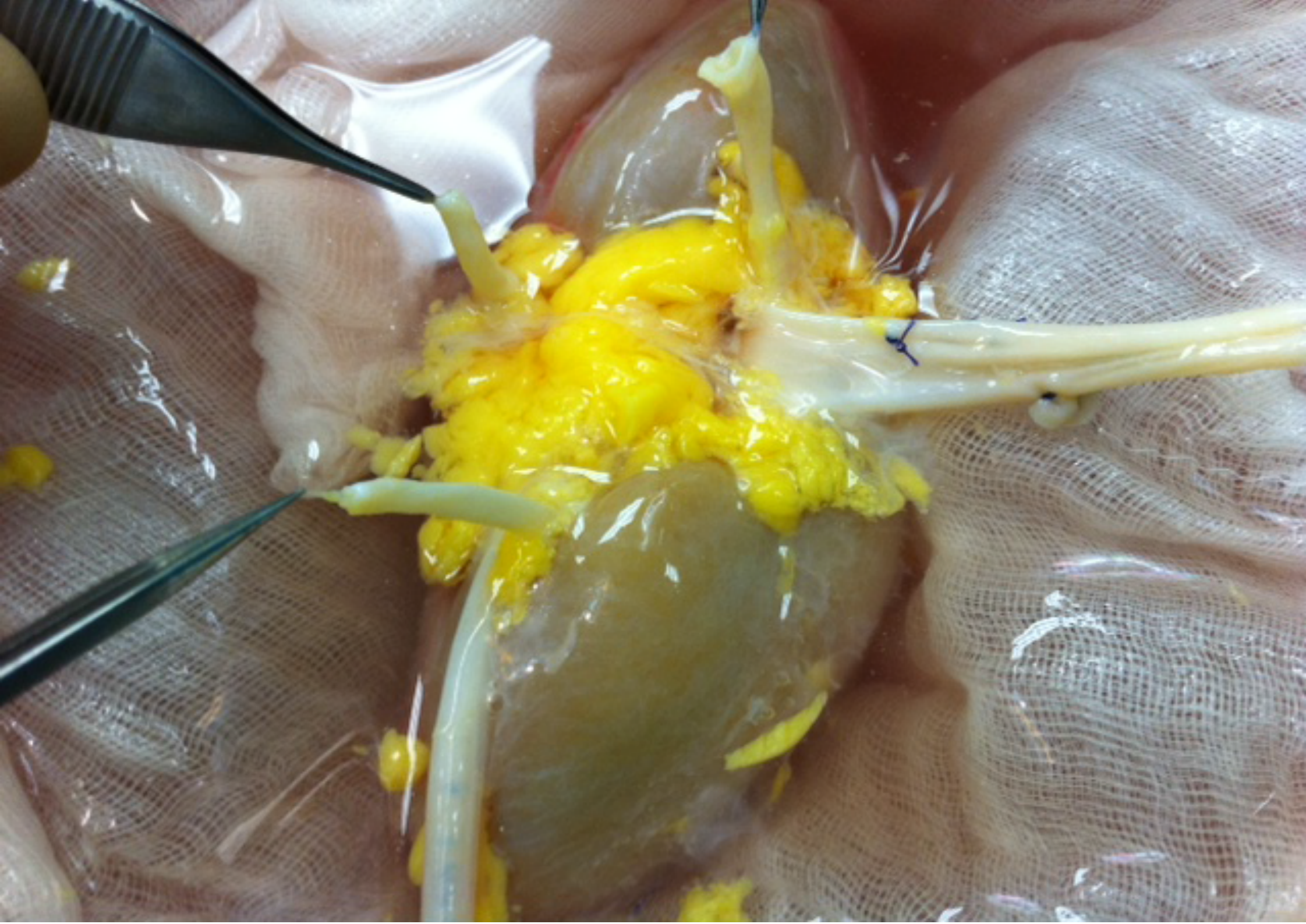
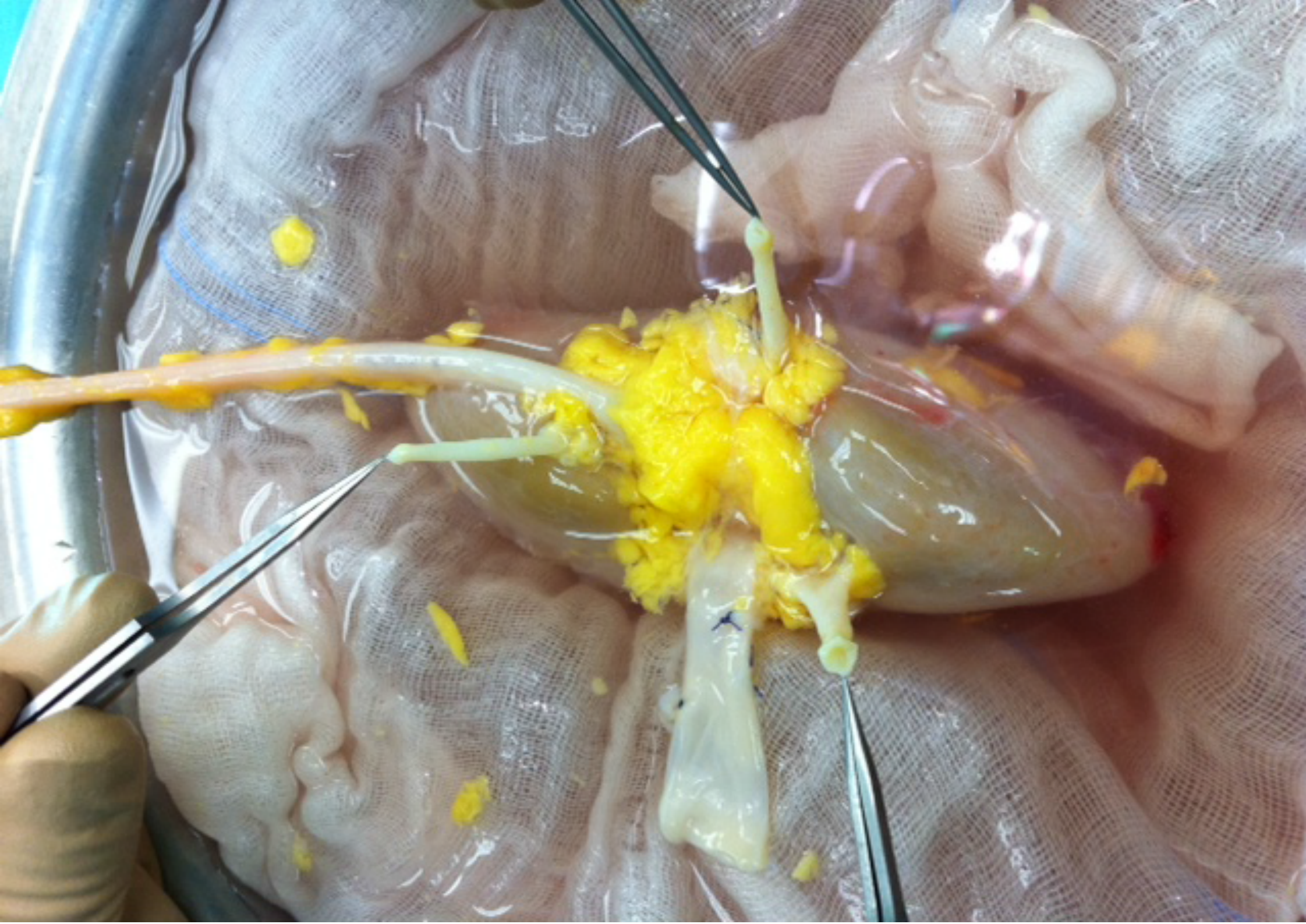
Bambino Gesù
OSPEDALE PEDIATRICO

- Male: d.o.b. december 23rd 1989
- Primary renal disease: reflux nephropathy
- 2003 First graft: LRD (father) lost for renal artery thrombosis (protein C deficiency)

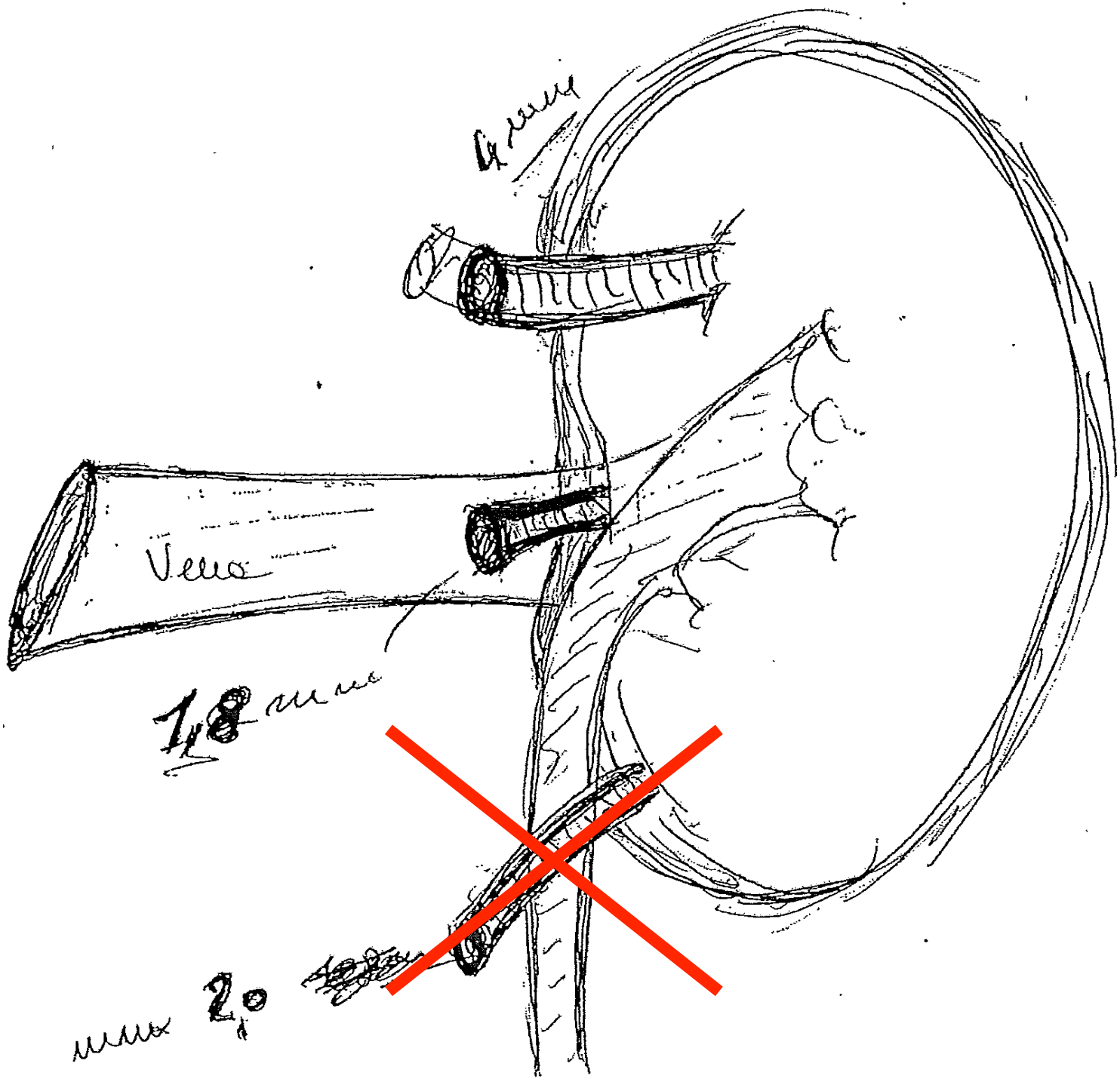
- PRA:98% class I and 48 % II
- Prohibited antigens:
  - Class I: A2, A9, A10, A28, A29, A31, B17, B18 Bw6;
  - Class II: DQ2, DR3 DR17
- Waiting time on the list: 9 years
- Enrolment in the national sensitized patient list

- 2011: Kidney available with **no prohibited antigens**
- Difficult vascular situation

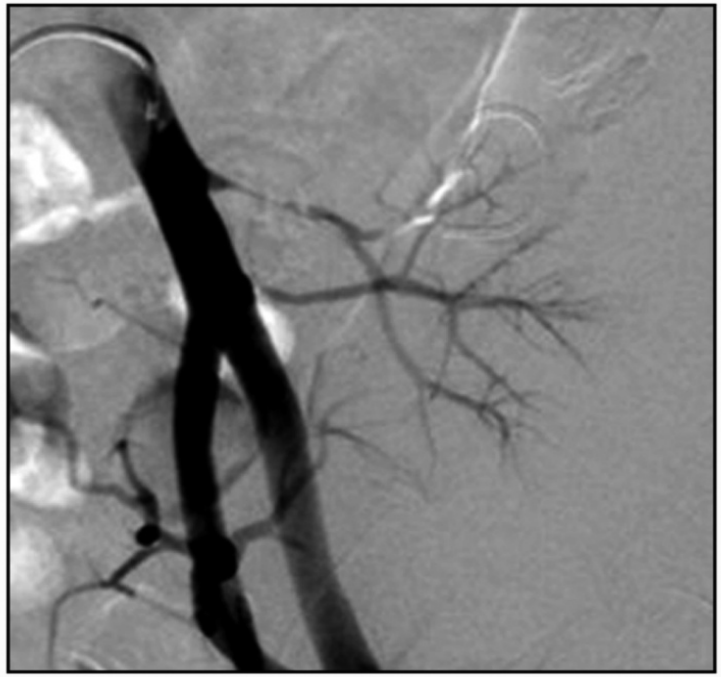




- Extensive discussione with patient and family
- Kidney was accepted


Уши
1,8 мм
мин 2,0

- Severe hypertension, not responding to treatment



hypertension

Pediatric series:

- Prevalence 60 to 80%
- Often resistant to treatment

Treatment (Minneapolis 1660 pts)

- 95% of pts receives at least 1 antihypertensive drug 1 year post transpalant e 75 % after 5 years
- Blood pressure control did not improve in the last 10 years

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Causes

- Immunosoppressant
  - CsA
  - Steroids
- Rejections
- Native kidneys
- Renal artery stenosis (even mild)

Treatment (Minneapolis 1660 pts)

- ACE inhibitors – ARBs 30%
- Beta Blockers: 30-35%
- Calcium antagonists: 70 %
- Other drugs < 10%

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OBG Monitoring: yearly

- 24 hour monitoring 1 /year
  - Ophtalmology visit
  - Heart ultrosound for Left ventricular mass
- whenever needed: Magnetic resonance angiography and / or arteriography

Case report 2

Bambino Gesù
OSPEDALE PEDIATRICO

- Male, 18 yo
- Atypical HUS 6 months
- Peritoneal dialysis started at 12 months
- **First renal transplant at the age of 7**

- II day post op: cardiac arrest due to hyperkalemia
- CPR immediately started.
- Cardiac activity restored in 10 minutes

- 2 hours later: urine output ceased
- 12 hours later: fever (39°C), hypertension (165/95 mmHg)
- Platelets: 120.000/mm^3
- Renal histology on day 5 showed diffuse renal parenchyma hemorrhage with evidences of thrombotic microangiopathy (TMA).

Genetic evaluation

- No mutations in genes known to cause aHUS : *CFH*, *CFI*, *MCP*, *CFB* and *C3*
- Serum anti-CFH autoantibodies, evaluated by ELISA, were not detected.
- No *CFH/CFHR* hybrid gene,
- In 2009, he was found to carry an isolated heterozygous missense Thrombomodulin mutation: P501L

- Thrombomodulin (THBD) is a ubiquitous transmembrane glycoprotein expressed by endothelial cells that accelerates the inactivation of C3b
- *THBD* mutations were expected to represent a low risk for post-transplant relapse because most of the protein is membrane bound.
- For this reason the patient was enlisted for a second renal tranplantation

- Risk of recurrence was considered to be low
- However, thrombomodulin also exists in a soluble form in plasma, which increases during inflammation and vascular injury
- Moreover patient had already lost a graft for a possible HUS relapse
- We decided to protect this patient and asked for a compassionate delivery of Eculizumab

- Unfortunately Eculizumab was not provided as a prophylactic treatment by manufacturing company and could not be obtained.
- For this reason we decided to start plasmapheresis

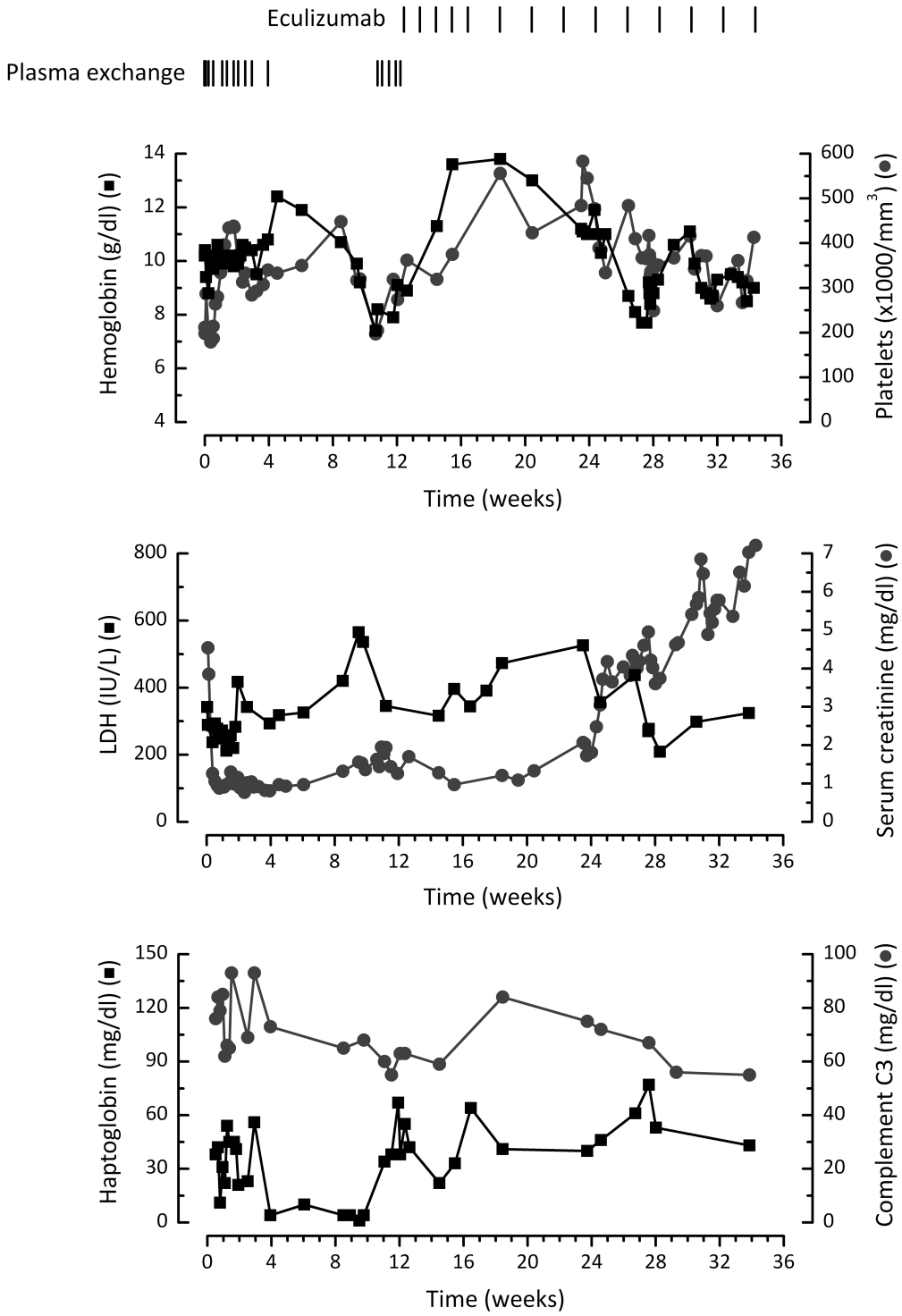
- II transplantation February 2011.
- standard immunosuppression: basiliximab, prednisone, FK506 and mofetil mycofenolate
- Plasmapheresis were performed during the first 3 weeks after transplantation

- 2 months later: mild increase in serum creatinine (1.56 mg/dl)
- Renal biopsy: normal .
- Creatinine spontaneously recovered to 1.26 mg/dl in one week.
- Three weeks later: creatinine 1.94 mg/dl, platelets 197.000/mm^3 , hemoglobin levels 7.4 g/dl
- second biopsy: recurrence of HUS.
- C4d negative.

- Five daily plasma exchange sessions were performed
- Then eculizumab was started (dosage according to body weight (600 mg weekly for 4 weeks, 900 mg on week 5 and 900 mg every 2 weeks thereafter)
- Prompt improvement of renal function

- 5 ½ months later a biopsy proven C4d negative acute rejection occurred (type 1B according to the Banff classification);
- glomerular changes consistent with a recent episode of TMA were still present, although markedly improved
- 3 methylprednisolone pulses; plasma creatinine stabilized but increased again to 4.32 mg/dl a few weeks later after an episode of severe gastroenteritis complicated with dehydration (weight loss: 2.5 Kg in one night!).

- Seven months after transplantation a new biopsy was obtained, showing persistence of cellular rejection.
- The patient failed to respond to a second cycle of steroid pulses;
- Renal failure rapidly progressed to end stage and the patient was started again on hemodialysis and eculizumab treatment was stopped.


Eculizumab
Plasma exchange
Hemoglobin (g/dl) (■)
Platelets (x1000/mm3) (●)
Time (weeks)
LDH (IU/L) (■)
Serum creatinine (mg/dl) (●)
Time (weeks)
Haptoglobin (mg/dl) (■)
Complement C3 (mg/dl) (●)
Time (weeks)