A 6-month-old female infant was referred for evaluation of failure to thrive and episodes of cough and shortness of breath for three days. She was born with a weight of 4750 gr, following a full-term normal pregnancy as the second child of consanguineous Turkish parents. In her family history; her brother died due to metabolic acidosis with an unknown etiology when he was eight months old. Her physical examination findings were as follows: weight 5700g (25-50 p), height 55 cm (3-10 p), head circumference 39 cm (3-10 p), blood pressure 80/50 mmHg (<90 p/<90 p), pulse rate 180 beats/min, respiratory rate 60/min, and body temperature 37°C. The patient was found to have skin pallor and altered sensorium. There were wheezing and fine crackles in her respiratory examination and her liver was palpable 2 cm below the right costal margin. Laboratory data were as follows; hemoglobin (Hb) 9.2 gr/dl, hematocrit (Htc) 28.5%, white blood cells (WBC) 24,700/mm³, platelet count 499,000/mm³, erythrocyte sedimentation rate 58 mm/h, serum creatinine 4.4 mg/dl, urea 102 mg/dl, creatinin clearance 8 ml/min/1.73 m², total protein 5.4 gr/dl, albumin 3.3 gr/dl, sodium (Na⁺) 141 mmol/l, potassium (K⁺) 3.5 mmol/l, calcium (Ca++) 9.6 mg/dl, phosphorus (P) 9.8 mg/dl, pH 7.24, pCO₂ 28 mmHg, bicarbonate 11 mEq/l, base excess -14. Urinary sodium 54 mmol/l (N: 40-220 mmol/l) and chloride 126 mmol/l (N: 112-150 mmol/l) levels were normal. Plain abdominal radiography showed big kidneys which were almost at bone density (Figure 1). Renal ultrasound scan and abdominal computed tomography demonstrated hyperechogenic kidneys with intensive medullary calcinos and bilateral nephrocalsinosis, respectively. Fundoscopic and echocardiographic examinations revealed diffuse photoreceptor dystrophy and significantly dilated cardiomyopathy, respectively. Based on these clinical and laboratory findings, the patient was commenced on chronic peritoneal dialysis treatment. Iron replacement therapy (5 mg/kg/day orally) was also started on admission. Five months after the onset of the disease, erythropoietin (EPO) treatment (150 IU/kg/week) was started. 

**Figure 1:** Plain abdominal X-ray showing calcified kidneys, bilateral nephrocalsinosis, big and nearly bone density kidneys (a). Also, note long bone fracture (arrow).
ek, subcutaneously) was initiated due to persistence of anemia. On the 8th month follow up, she received blood transfusion (20 ml/kg, red cell pack) and EPO dose was increased to 300 IU/kg/week due to failure to respond to combination of iron and EPO treatment and persistance of her anemia. On the subsequent follow-up, she was transfused three additional times. On the 10th follow up, she remained anemic despite treatment (Hb: 6.4 gr/dl, Htc: 19.3%, MCV: 96.6 fl). Furthermore, her peripheral blood smear showed macrocytic anemia. Potential cause of macrocytic anemia was searched and normal folic acid (> 24 ng/ml; N: 3-12 ng/ml) and low vitamin B12 (155 pg/ml; N: 196-940 pg/ml) levels were determined. Furthermore, bone marrow aspiration revealed significantly decreased cellularity and increased histiocytes. The patient also experienced multiple pathological long bone fractures during her follow-up.

QUESTIONS

1. What is the most likely causes of end stage renal disease in the infancy period?

2. Which causes should be considered in the differential diagnosis of this EPO resistant anemia? Which process should be done to confirm EPO resistant anemia?

3. How can this condition be treated?