

## PARTICULARITIES OF INFECTION IN CACHECTIC CHILDREN

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### Abstract

Infections are frequent in childhood, especially in the presence of malnutrition. The etiology of poor state of nutrition can be: incorrect feeding, congenital defects, frequent infections, improper care or a mix of the previous situations. We can diagnose cachexy in children whose BMI is <5 percentiles and under 3<sup>rd</sup> negative deviation.

Authors present four cachectic patients: two children suffering of trisomy 21, who had associated each one heart malformation: first, a boy, N.S., aged 7 had Fallot tetralogy and bacterial endocarditis; second, a girl, P.S, 4 years aged had ventricular septal defect and acute interstitial pneumonia. The third cachectic patient was a girl aged 8, D.C. with Seckel syndrome, admitted for staphylococcal pneumonia; the fourth is a 8 years girl P.ER with spastic tetraparesis, microcefaly, diagnosed with severe sepsis. Only the boy suffering of endocarditis, evolved to MODS and death; the three girls were discharged healed. Trisomy 21 caused immunodeficiency and cachexy also permitted severe infections. Their poor state of nutrition had a combined etiology: congenital defects, improper diet, recurrent infections, inadequate care (two patients lived in orphanage, two girls had only mother). Congenital heart defects could be complicated to endocarditis. In thin children, with birth malformations, pneumonia is frequent. Cachexy in malformed children is an important cause of immunodeficiency which leads to severe, sometimes lethal infections. Infections produce denutrition and cachexy promotes severe sepsis, especially in parentless children.

**Key words:** cachexy, severe sepsis, infection, child.

### Background

The World Health Organization estimates that malnutrition is incriminated for 54 percent of child mortality worldwide, for death of about 1 million children. Even mild degrees of malnutrition double the risk of mortality from respiratory and digestive diseases. This risk is greatly increased in the most severe cases of malnutrition such as cachectic children. According to a 2008 review (15), the authors estimated that 178 million children under age 5 were stunted, most of them living in Africa. A 2008 review (15.) of malnutrition found that about 55 million children suffered of severe acute malnutrition, including 19 million who were cachectic. Pediatric cachexy or wasting syndrome is loss of

weight, muscle atrophy, fatigue, weakness, and significant decrease of appetite in children, despite of their normal birth weight (12). A definition of cachexia is the loss of body mass that cannot be reversed nutritionally: when it occurs in preschool and school children, frequently they had a relative normal weight in their first childhood (according their medical history)(15). Even if the affected pediatric patient eats more calories, lean body mass will be lost, indicating a primary pathology is in place(12). The etiology of poor state of nutrition in children can be: incorrect or insufficient feeding, frequent infections, congenital defects, improper care or a combination of the previous situations. There remain three commonly used measures for detecting malnutrition in children: stunting, (extremely low height for age, under 80 percent of normal), underweight (extremely low weight for age, under 60 percent of normal) and wasting (extremely low weight for height, under 70 percent, NI<0.7)(12). We can diagnose cachexy in children whose BMI is <5 percentiles and under 3<sup>rd</sup> negative deviation (according to WHO 2007 children growth)(13). These measures of malnutrition are interrelated, but studies for the World Bank found that only 9 percent of children of the world exhibit stunting, underweight and wasting. Measurements of children's growth provide the key information for the presence of malnutrition, but weight and height (measurements) alone can lead to failure in recognizing kwashiorkor and to an underestimation of the severity of malnutrition in children.

Infectious diseases, especially respiratory and digestive infections are often found in pediatric population. Sepsis is defined like a systemic inflammatory response syndrome (SIRS) induced by an infection (1,2,3,4). Severe sepsis is sepsis associated to blood hypotension or with hyperglycemia, with hypoperfusion and a single organ damage (5,6). Infectious MODS suppose sepsis with dysfunction of at least two organs (5,7,10). Septic shock means sepsis with hypotension longer than an hour despite a proper fluid rebalancing (9,10,11).

### Material and method

We conducted a study about four cachectic patients, including three girls who were directly supervised by the authors of the paper.

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We used clinical observation worksheets, during their hospitalization in Pediatrics Clinic, Emergency Hospital of Craiova, the length period of study being since march 2013 to april 2014.

Subjects were: two children with trisomy 21, both of them having cardiac malformation and associated medical conditions: the first one, a boy, N.S., aged 7 had Fallot tetralogy and congenital solitary kidney; the second one, a girl, P.S, 48 months aged, had ventricular septal defect, congenital duodenal stenosis and recurrent interstitial pneumonia. Children suffered of L.Down disease lived in orphanage. The third cachectic patient was a girl aged 8, D.C. with Seckel syndrome, admitted for febrile seizures, hypotonia and coma; the fourth was a 9 years girl P.E.R. with spastic tetraparesis, microcephaly, diagnosed with severe sepsis. The last two girls were grown of their alone mothers. We analysed their diagnoses, laboratory findings and the evolution of infection in the same case.

## Results

### Case 1

The boy patient **N.S.**, 7 years and 9 months age, W= 12 Kg, was admitted in First Pediatrics Clinic of Craiova in 27-03-2014 for high fever, hyporesponsiveness, hypotonia, generalized cyanosis, in a child suffering from tetralogy Fallot associated with 21 trisomy. Based on medical history, on clinical examination at admission (which revealed: orthopnea, hypotonia, generalized cyanosis, breathlessness,

tachycardia, 4/6 systolic ejection murmur, late capillary refill time, low blood pression, hyporesponsiveness to verbal stimuli, motor deficit on the right side of the body, and clinical appearance of L. Down disease) and confirmed by laboratory findings (WBC= 13700/mmc, PMN=81%, Ly=15%, Mo=4%; Hb=19,8g%, PLT=87000/ml; INR=1,22; pH=7,25; pO<sub>2</sub>=51,4mmHg; pCO<sub>2</sub>=50,4mmHg; ESR=1mm at 1h/3mm at 2h; CRP=48 mg/l; chest-X-ray revealed heart „en sabot”; cardiac ultrasound: „Ventricular septal defect, aorta „riding” the interventricular septum; suggestive formation like vegetation on tricuspid valve”; abdomino-pelvic ultrasound: „single kidney”; cranial tomography: „Recently cerebral hemorrhagic stroke on cerebral trunk”) the following diagnoses were noted: „Severe sepsis. Unknown etiology endocarditis. Cerebral hemorrhagic stroke on cerebral trunk. 21 Trisomy. Cachexy.” Despite of treatment (hydroelectrolyte and metabolic rebalance, strong antibiotherapy) the patient died at the 8<sup>th</sup> day after admission, but histopathological examination confirmed the clinical diagnosis.

### Case 2

Girl patient **P.S.** (figure 1) 4 years age, weighting 10 kg (at first admission), then has weakened 1 kg, with ventricular septal defect in the context of trisomy 21, had in her past medical history a surgical intervention for duodenal stenosis, several lung infections.



Figure 1: PS-from orphanage.

Based on clinical examination at second admission in 2014 (which revealed: W=9000g, H=83 cm, pale skin, lean tissue absence; peripheral temperature =37,8°C, cough, dyspnoea, tachypnea, bilateral bronchial and crackling rales, 3/6 systolic ejection murmur audible anterior and posterior, and clinical appearance of L. Down disease), according to laboratory findings (Hb=8,8g/dl, WBC=14100/mmc, PMNs=81%, Ly=15%, Mo=4%, PLT=140000/mmc; ESR = 5/10 mm, Prot. =3,3g/dl; Ca= 6,2 mg/dl; serum colesterole = 53 mg/dl, TG=70mg/dl; serum glucose = 49 mg/dl; Na=116 mEq/l, serum iron=53µg/dl; Adler test positive, stool testing positive, abdominal ultrasound found liquid in peritoneal cavity; Conventional chest radiograph revealed bilateral diffuse interstitial infiltrates perihilar and peribronchial; enlarged cardiac silhouette) the following diagnoses were noted: „Interstitial pneumonia. Malabsorbtion syndrome. Iron deficiency anemia. Cachexy. L. Down disease. Mental delay.” The treatment she needed: fluid rebalanced and intravenous aminoacids administration, followed by a high calorie diet; antibiotics: Cefoperazone-Sulbactam. She was discharged respiratory healed, but with the same poor nutritional status, because, in orphanage, she refused food.

### Case 3

D.C., 8-years and 8 months (Figure 2), female, with Seckel syndrome, presented as a transport to the Emergency Room Craiova, First Pediatric Clinic, from another county, secondary to altered metal status and cyanosis of the extremities that lasted for about 30 minutes. On physical examination, patient in critical condition, subfebrile,

agitated, who had short stature with weight being 13 kg, microcephaly, prominent eyes, the characteristic features of „bird-headed dwarf” (pointed nose, micrognathia), dental dystrophy, sequelae of rickets, spastic cough, dyspnea, tachypnea, bilateral bronchial and crackling rales, the aspiration of oropharyngeal secretions revealed purulent secretions, alimentary vomiting, spastic tetraparesis, mental retardation, her mental age being of an one-year-old child. Peripheral blood examination showed Hb=12.6 g/dl, total WBC= 5300/mm<sup>3</sup>, PMN=79%, Ly=11%, Mo=10%, PLT=460000/mm<sup>3</sup>. Respiratory tract culture was performed on tracheobronchial lavage and it was positive: Staphylococcus aureus was isolated. Antibiotic susceptibility test result showed the isolated strain was susceptible to Oxacillin, Linezolid, Teicoplanin, Vancomycin, Rifampicin, Ciprofloxacin, Cefoperazone-Sulbactam and resistant to Penicillin. Conventional chest radiograph revealed bilateral diffuse interstitial infiltrates perihilar and peribronchial, with multiple bilateral confluent reticular opacities. The heart size was within normal. According to the result of culture, the patient was treated with Cefoperazone-Sulbactam, symptomatic medications, fluidifiants of bronchial secretions, oxygen therapy, anticonvulsivant therapy. In pediatric intensive care unit as well as in pediatric ward where she was transferred subsequently in stable condition, her evolution was favorable. After three days from admission, she has got no fever anymore. Prior to discharge, the patient had resumed normal activity.

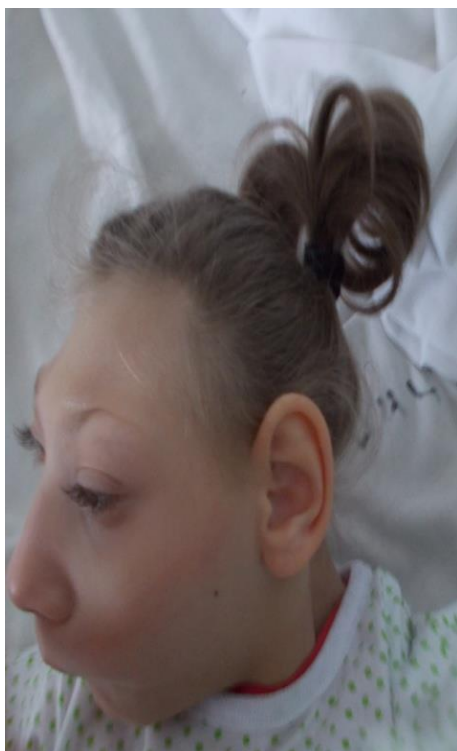


Figure 2: DC-her mother accepted.

Case 4

**P.E.R.**, 8-years female and 7 months (Figure 3), with a past medical history of spastic tetraparesis and intellectual disability, presented as a transfer to the pediatric intensive care unit from an outlying hospital, secondary to altered mental status, due to seizures associated with fever. The patient was born at term by C-section due to umbilical cord around her neck and needed neonatal intensive care. When she was 2-years-old the treatment Pyritinolum was initiated by a pediatric neurologist. On examination, short stature with weight being of 10 kg, Glasgow coma score 10, lethargy, sleepiness, T= 37.9°C, HR= 170, dry skin and mucous membranes, shrivelled and dry skin that lacks elasticity, upper airway sounds transmitted throughout, good bilateral breath sounds, decreased urine output, nuchal rigidity. Peripheral blood examination: Hb=10,4 g/dl,

WBC=12000/mm<sup>3</sup>, PMN=47%, Ly=22%, Mo=4%, 300000/mm<sup>3</sup>, ESR: 25 mm/hr, Astrup parameters: pH=7.29, pCO<sub>2</sub>=33.4, pO<sub>2</sub>=38.8, hypernatremia (160.6 mmol/L), hypokalemia (2.93mmol/L), hyperglycemia (256 mg/dL), ALT: 14U/L, AST: 60U/L. Ocular examination showed normal aspect of the optic disk and retinal blood vessels. General treatment was started: fluid rebalanced and intravenous aminoacids administration. Then, the patient was transferred to the pediatric ward in stable condition on hospital second day. It has been initiated treatment with antibiotics: Ceftriaxonum, then Cefoperazone-Sulbactam, Gentamicin, that lasted to discharge. The total blood cell count decreased to 8000/mm<sup>3</sup>. On the second day of hospitalization, the patient rested with normal temperature. She presented no more seizures. Prior to discharge, girl patient became alert.



Figure 3: PER-we had mother's accept.

**Discussions**

In terms of patient **N.S.** (cachectic, whose BMI= 12, less than 3<sup>rd</sup> percentile, under 3<sup>rd</sup> negative deviation) we note that he fulfilled the diagnostic criteria for sepsis having: fever, leukocytosis, tachycardia. Also, CRP levels greater than 8 times the upper normal and thrombocytopenia can diagnose severe sepsis. In subjects with heart defects, any infection even of the teeth, should be treated with antibiotics, because the risk of bacterial endocarditis is very high. Unfortunately, what we feared for, has happened. Endocarditis with sepsis was vigorously treated with cephalosporins associated with aminoglicosyde, but thrombocytopenia led to fatal intracerebral hemorrhagic stroke. The child, in the context of hypoxia of tetralogy of Fallot, had polycythemia (Hb = 20 g / dl), but even if the initial motor deficit suggested an ischemic stroke caused by a trombus (blood clot), then death was caused by bleeding of cerebral trunk. Obviously, the mother's absence and the heart defect that went uncorrected led to early death. Surgical treatment of congenital heart defects in children with trisomy 21 who live in orphanage, can rarely be

performed in Romania. Repeated infections, lack of family love, Fallot disease marked by hypoxia and mental retard (because of institutionalization and genetic disease), shortage of foster care, led to cachexia that favored sepsis and speeded the tragic end. In children with tetralogy of Fallot, cared and loved in family, survivals were recorded even up to 16 years without surgery, but with a good nutritional status.

**P.S** girl patient with W = 9 Kg and H = 83 cm, compared with normal age, meaned the common measures in four years, W = 17 kg (corresponding to the 50th percentile and SD 0-1) and H = 100 cm (height mean age) found: She wasn't very stunted (83% of the average of her age height) but underweight (extremely low weight for age, 50 percent of normal) and wasting (extremely low weight for height, under 70 percent). She had BMI (PI)= 13, less than 5<sup>th</sup> percentiles and under 3<sup>rd</sup> negative deviation (according to WHO 2007 children growth). Based on laboratory data, we found: hypoglycemia, hypoproteinemia (with edema and peritoneal fluid), hypocholesterolemia, hypocalcemia, iron deficiency anemia, hypotension. The

patient had no bradycardia neither bradypnea, but she lacked Bichat's bubble (like the other three). In conclusion, the patient had a typical third degree malnutrition. VSD (ventricular septal defect) partially explains cachexia, being incriminated other factors, such as: genetic disease, institutionalization, lack of family, lack of appetite due to repeated infections, malabsorption correlated with duodenal stenosis corrected perinatal. It should be remembered that severe malnutrition cause intestinal villous flattening and lactase deficiency, leading to malabsorption, that maintains cachexia. We also know that heart malformations without cyanosis associate often severe dystrophy.(14)

Girl-patient **D.C.** 8 years, 4 months, BMI=13, had the particularities of Seckel syndrome (characteristic features of „bird-headed dwarf”, microcephaly, pointed nose, micrognathia) and was diagnosed with Staphylococcal pneumonia. Staphylococcal pneumonia can develop a staphylococcal pleurisy and is considered a severe clinical form of pneumonia. In the case described, despite of a genetically-Seckel-syndrome, pneumonia was not complicated, being treated with an antibiotic to which Staphylococcus aureus was susceptible: Cefoperazone-Sulbactam. As all genetic diseases, in the Seckel syndrome there is a greater susceptibility to infection. In this case, it was a community-acquired seed of Staphylococcus Aureus, (receptive to Oxacillin) and the patient was discharged cured. The difference, in her case, was the mother's presence. Patient's vital prognosis can be improved by love and good care.

Patient girl, **P.E.R.**, aged 8 years 9 months, with G = 12 kg (BMI= 12), was admitted to the Pediatric Clinic in March 2014 for high fever (40-41°C), febrile seizures (first

episode) refusing food, malaise. Laboratory investigations revealed hyperglycemia (initially 290 mg/dl, then was 170-211mg/dl in ENP with Ringer, 295mg/dl), neutrophilic leukocytosis, thrombocytopenia, elevated ESR. Based on fever, neutrophilic leukocytosis, thrombocytopenia, hyperglycemia, we found severe sepsis as diagnosis. Cachexia associated with hypoglycemia met frequently, especially in the conditions of starvation. In this case, it was necessary differential diagnosis of diabetes onset. Because blood sugar returned to normal without insulin, as the infection heals, the conclusion that was imposed hyperglycemia in context of severe sepsis with unknown origin.

### Conclusion

From all admitted patients in last two years in First Pediatric Clinic, Craiova, the incidence of cachectic children was 1,5%. But cachexy was involved in 25% percent of children who died. Only the boy who suffered from endocarditis led him to MODS and death; the three girls were discharged healed. Trisomy 21 caused immunodeficiency and cachexy also permitted severe infections. The etiology of poor nutritional status was combined: congenital defects, improper diet, frequent infections, inadequate care (two patients lived in orphanage, two girls had single mothers). Pneumonia is frequent in thin children, with birth malformations. Congenital heart defects could have been complicated to endocarditis. Cachexy in malformed children is an important cause of immunodeficiency that leads to severe, sometimes letal infections. Infections produce denutrition and cachexy promotes severe sepsis, especially in parentless children.

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