Anesthesia in a Patient with Job's Syndrome (Hyper IgE). Case Report

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Summary: Resende MAC, Pantoja AV, Charruff IA, Magalhães Jr N, Luz P – Anesthesia in a Patient with Job's Syndrome (Hyper IgE). Case Report.

Background and objectives: Job's syndrome (JS), one of the presentations of the Hyper IgE Syndrome, is a rare immunodeficiency. It includes cutaneous abscesses, recurring pneumonias, pneumatoceles, eosinophilia, hyperimmunoglobulinemia E (> 2,000 IU.mL^{-1}), and craniofacial and bone growth changes. This report describes the disease and its anesthetic management.

Case report: The patient is a 13 year old black male, 40 kg, ASA II, with Job's Syndrome diagnosed 6 months prior to this admission. The patient was admitted for elongation of the right femur. He denied use of drugs and prior surgeries; he presented good cervical mobility, interincisive distance greater than 3 cm, Mallampati II, without signs of infection. Preoperative exams were within normal limits. He was monitored with electrocardioscope, SpO_2, non-invasive blood pressure, and $P_{ET}CO_2$. After pre-oxygenation, general anesthesia was induced and he was maintained with sevoflurane. At the end of the procedure, the patient was extubated after reversal of the neuromuscular blockade, and the patient was transferred to the PACU with Aldrete 9, He was discharged from the hospital 72 hours later, without complications.

Conclusions: The choice of anesthetic technique is guided by rigorous observation among risks and benefits for each patient, according to respiratory sequelae, risk of infection, and surgical site. In the patient described here, we considered that neuroaxis anesthesia could be associated with an increased risk of severe infections due to the patient immunologic background. The procedure was safely performed with general anesthesia.

Keywords: Job's Syndrome; Anesthesia, General; Bone Lengthening.

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INTRODUCTION

Hyperimmunoglobulinemia E syndromes are rare primary immunodeficiencies characterized by elevated plasma levels of IgE, eczemas, and recurring respiratory tract and cutaneous infections. Job's syndrome (JS) is one of the presentations of the hyper IgE syndrome, and it is caused by a mutation in the STAT3 (signal transducer and activating factor of transcription 3) gene on chromosome 17q21 with a dominant autosomal inheritance [1]. From the description of two girls with recurring cold skin abscesses, Davis et al. [2] postulated a degree of deficiency in resistance to staphylococcal infection and alluded to the biblical character Job, whose body was "covered with pustules". Typically, it presents as persistent cutaneous abscesses (caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*), and a history of recurring pneumonias, pneumatoceles, hypereosinophilia, elevated serum levels of IgE (> 2,000 IU.mL^{-1}), and craniofacial and bone growth changes. The objective of this report was to present a case of a rare disease and its anesthetic management in a patient undergoing surgery for bone transport through an external fixator.

CASE REPORT

This is a 13 year old black male, weighing 40 kg, 1.50 m tall, with history of normal term delivery and that at 20 days of life developed cold skin abscesses and deep abscesses in the right hip with right femoral epiphyseal sliding, and rib fractures. After culture of the abscesses showed growth a *S. aureus* and *S. epidermidis*, the patient was treated with vancomycin and ceftriaxone for 27 days. He evolved with bacterial endocarditis of the mitral valve, being treated with imipenem for 45 days. Job's syndrome was diagnosed after investigation of immunodeficiency. He was discharged from the hospital after 3 months and followed-up by a multidisciplinary team (pediatrics, cardiology, and orthopedics). Besides right hip and knee deformity secondary to the infectious process, with partial destruction of proximal and distal femoral epiphyseal plates, with shortening of the limb, he developed eczema of the face and three episodes of pneumonia, which were treated without sequelae. The patient was admitted for elongation of the right femur (Figure 1) with a uniplanar Orthofix™ external fixator. His physical status was classified as ASA II.

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He was not taking any drugs and this was his first surgery. On physical exam, he showed good cervical mobility, interincisive distance greater than 3 cm, Mallampati II, and without systemic signs of infection. He had normal cognitive development, was cooperative, and did not receive premedication. Preoperative exams included normal chest X-rays and electrocardiogram; Hb: 12.6 $g.dL^{-1}$; Ht: 38.4%; BUN: 22 $mg.dL^{-1}$; creatinine: 0.49 $mg.dL^{-1}$; glucose: 135 $mg.dL^{-1}$; normal coagulogram; and IgE: 2,100 $IU.mL^{-1}$. Upon arrival to the operating room, he was monitored with electrocardioscope (ECG) on DII and V5 derivations, SpO_2, non-invasive blood pressure on the left upper limb with 5-minute interval measurements, and $P_{ET}CO_2$. After antisepsis with 70% alcohol and infiltration of the skin with 2% lidocaine (20 mg), venous cannulation was performed in the right upper limb with an 18G catheter. After pre-oxygenation for 5 minutes, general anesthesia was induced with fentanyl 150 µg, propofol 80 mg, and vecuronium 4 mg. He was intubated with a 7.0 mm ET tube7 with balloon, and titrated sevoflurane in a calibrated vaporizer was used for anesthesia maintenance. He was ventilated with a circular CO_2 absorber system with VT = 320 mL; RR = 12 bpm; PEEP = 5 cmH_2O; FGF = 2 $L.min^{-1}$ and FiO_2 = 0.4%. Cefazolin 1.2 g was used for prophylaxis. Hemodynamic changes and relevant bleeding were not observed during anesthesia, partly due to the use of a pneumatic tourniquet during 2h10min, whose removal did not cause significant changes. Total anesthesia duration was 3h05min with perioperative hydration with 1,500 mL of Ringer's lactate. At the end of the procedure, the patient was extubated 10 minutes after reversion of the neuromuscular blockade with 0.5 mg of atropine and 1.5 mg of prostigmine. He was transferred to the post-anesthetic care unit with an Aldrete scale of 9. During the procedure, he received 2 g of dypirone, which produced satisfactory analgesia in the immediate postoperative period. He was discharged from the hospital after 72 hours without complications.

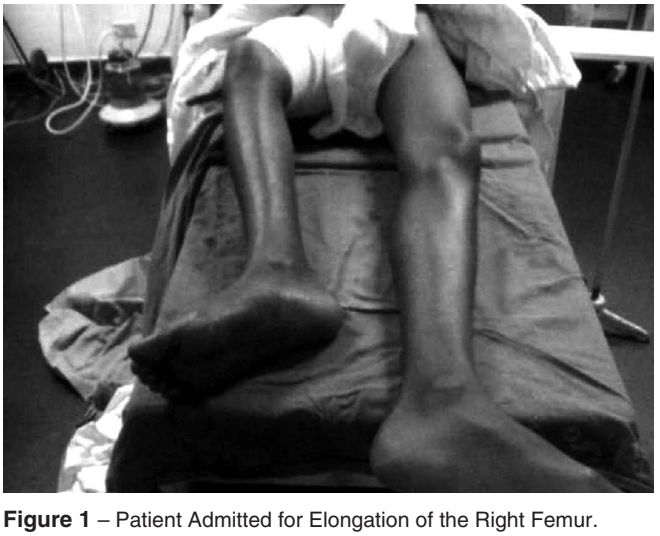

Figure 1 – Patient Admitted for Elongation of the Right Femur.

DISCUSSION

After the original description of Davis et al., [2] in 1966, Buckley et al. [3], who found similar patients with eczema, recurrent skin and lung infections, elevated IgE levels, and skeletal and connective tissue changes, are responsible for the best definition of Job's Syndrome (JS) [3]. Since 1972, a little over 250 cases of JS have been described in the literature, without predominance of gender or race [4,5]. Hyperimmunoglobulinemia E syndrome (hyper-IgE) has two forms: one, dominant, caused by mutations in the *STAT3* gene in chromosome 17q21; and a recessive form, with lower number of pulmonary infections and pneumatoceles, less osteoarticular and odontological involvement, but with more viral infections and vasculitis [6]. When *STAT3* mutations, responsible for most cases of autosomal dominant hyper-IgE syndrome and its multisystem character, were discovered, they explained aspects that intrigued investigators, revealing specific roles regarding wound healing, inflammation, and hematopoiesis [7]. STAT3 is the main signal transduction protein and it is a regulator of several immunologic pathways, and animals with myeloid-specific deletions show hyperexpression of tumor necrosis factor alpha (TNFα) and gamma interferon, but underexpression of IL-6 and IL-10, which promotes excessive production of some proinflammatory cytokines, contrary to those mediated by reduced responses after IL-6 stimulation [8]. In an experimental study, deletion was also associated with generation of osteoclasts and osteopenia, phenotypes seen in patients with hyper-IgE syndrome [9]. Some specific effects related to aberrant regulation of inflammation, at times very intense, such as in lung lesions, other times poor in symptoms, such as in cold abscesses, remain to be elucidated [1]. A group of T lymphocytes shows abnormal function, such as failed chemotaxis with abnormal synthesis of antibodies and cytokines, but with normal phagocytic function. Besides, changes in the proportion of immunoglobulins, with increased production of IgE, while IgG, IgA, and IgM levels, although normal, show qualitative dysfunction. Anti-staphylococcal IgA shows decreased activity, while it might be normal against Gram-negative organisms and streptococci.

Cutaneous manifestations of JS are characteristic; it can manifest as an eczematoid rash in newborns, and pustules and "cold" abscesses with pus that show growth of *S. aureus*. Recurring pneumonias, as well as cutaneous abscesses, can show very little symptoms and, although they show good response to antimicrobial therapy, occasionally, during healing, they evolve to pneumatoceles and bronchiectasis, besides opportunistic infections. Some patients show discrepancy in the growth of their legs. Scoliosis, osteopenia, minimal-trauma fractures, articular hyperextensibility, and degenerative joint disease are among other musculoskeletal changes commonly seen. The facies is considered coarse, with prominent forehead, prominent supraorbital ridge, and widening of the base of the nose [10] (Figure 2). Primary dentition can be retained due to an exfoliative process and that, occasionally, coexists with the second dentition; changes in oral mucosa, elevated palatal arch, and central depressions in the tongue can also be seen [11,12].

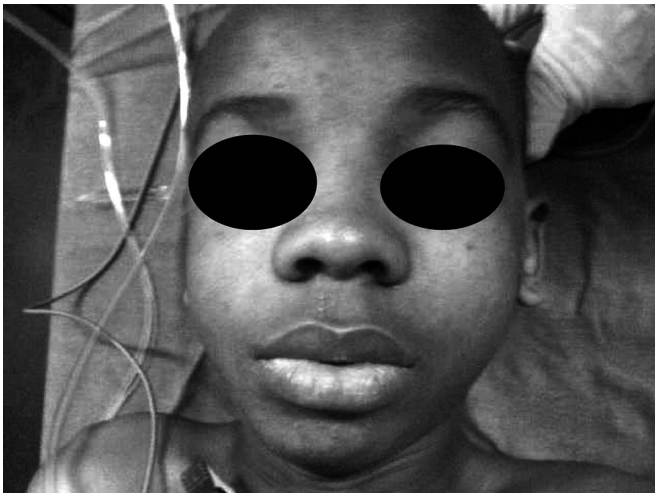

Figure 2 – Patient's Face.

Craneosinostosis and Chiari I malformation, which, most of the times do not require surgical treatment, are among cranial abnormalities in STAT3 deficiency [1]. The presence of aneurisms has also been reported, including in a series of patients undergoing autopsy [13]; those patients also have an increase risk of lymphomas, especially non-Hodgkin [14].

Diagnosis of JS is based on the presence of signs and symptoms associated with elevated serum levels of IgE, usually above 2,000 IU.mL^{-1}, even at birth, but those levels might be decreased in adult life. Serum IgE levels do not show a correlation with eosinophilia, which is very common. In case of acute infection, the leucogram might not show an increase, but neutropenia, although reported, is rare [1,15].

Treatment of patients with this multisystem disease requires a multidisciplinary approach [1]. Recurring infections should be prevented, and local care of cutaneous abscesses with early surgical drainage should be undertaken. Through diagnostic and therapeutic bronchoscopy, pneumologists can improve prognosis of chronic infections and evaluate, along with surgeons, the need of drainage of pleural empyemas or lung resections. Orthopedists should follow-up osteoarticular disease and correct scoliosis and severe bone shortening. Treatment with intravenous immunoglobulin an reduce the number and severity of recurring infections in some patients [16]. The use of *in vitro* gamma interferon showed improved neutrophil chemotaxis; however, *in vivo* it showed inconsistent effects on IgE levels [17].

The choice of anesthetic technique depends on judicious observation of the risks and benefits of each patient. In the patient presented here, it was considered that neuroaxis anesthesia could represent an increased risk of severe infections due to the immunological basis of the patient. Epidural or spinal block anesthesia in patients with chronic skin infections could increase the chances of infections, even with antimicrobial prophylaxis, due to variability of the immune response secondary to previously known deficiency, as justified in one of the first reports of JS, in which general anesthesia was used in a pregnant patient [18]. Abscess formation in JS evolves insidiously, usually without inflammation. When it becomes apparent, the abscess most likely has already caused some neurologic damage, without time for early intervention. We chose general anesthesia due to the possibility that neuroaxis anesthesia could cause severe meningeal infection, even with all antiseptic and aseptic care. On the other hand, Tapper and Giesecke [19] reported a case of spinal block anesthesia in a child with severe pulmonary involvement, with pneumatoceles and empyema. The anesthesiologist should be attentive to the clinical manifestations of patients with JS, such as teeth changes that might hinder airways management; severe scoliosis or joint hyperextensibility when positioning the patient in the operating table; presence of abscesses and undetected skin lesions; and chronic lung infections with cavitations complicated by fungal infections or hemoptysis. A case of prolonged succinylcholine effect, considered an atypical response, in a patient with normal levels of pseudocholinesterase [20], has been reported in the literature.

In the present case, a surgical procedure was safely performed with general anesthesia, without affecting the evolution of the case. The choice of technique should always take into consideration the clinical condition of the patient, protecting the patient, and using good judgment.

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Resumen: Resende MAC, Pantoja AV, Charruff IA, Magalhães Jr N, Luz P – Anestesia en Paciente con el Síndrome de Job (Hiper IgE). Relato de Caso.

Justificativa y objetivos: El síndrome de Job (SJ) es una inmunodeficiencia rara, una de las formas de presentación del Síndrome hiper IgE. El cuadro clínico comprende abscesos cutáneos, neumonías de repetición, neumatoceles, eosinofilia, hiperinmunoglobulinemia E (> 2.000 UI.mL-1), alteraciones craneofaciales y de crecimiento óseo. El relato describe la enfermedad y su manejo anestésico.

Relato del Caso: Paciente masculino, negro, de 13 años, 40 kg, ASA II, con el Síndrome de Job diagnosticado a los 6 meses. Se le admitió para la realización de estiramiento del fémur derecho. Negaba el uso de medicamentos y no tenía antecedentes quirúrgicos, una buena movilidad cervical, una distancia interincisivos superior a los 3 cm, Mallampati II y tampoco tenía señales de infección. Los exámenes preoperatorios fueron normales. Fue monitorizado con electrocardioscopio, SpO2, PANI y PETCO2. Después de la preoxigenación se procedió a la inducción de anestesia general venosa y al mantenimiento con sevoflurano. Al finalizar el procedimiento, el paciente fue extubado después de la reversión del bloqueo neuromuscular y fue derivado a la sala de RPA con Aldrete 9. Tuvo su alta a las 72 horas, sin complicaciones.

Conclusiones: La opción de la técnica anestésica está orientada por la observación de un riguroso criterio entre los riesgos y beneficios específicos para cada paciente, de acuerdo con las secuelas respiratorias y con el riesgo de infección y el sitio quirúrgico. En el paciente en cuestión, se consideraba que la anestesia en el neuro eje podría representar, por la predisposición de base inmunológica, un riesgo aumentado de infecciones graves. El presente caso fue realizado de forma segura con anestesia general.

Descriptores: ENFERMIDAD, Genética: síndrome de Job; TÉCNICAS ANESTÉSICAS, General: venosa.