Management of recurrent lung infections in a case of hyperimmunoglobulinemia E (or Job's) syndrome

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The diagnosis of hyperimmunoglobulinemia E (hyper IgE) or Job's syndrome was made in a five-month-old girl with chronic staphylococcal mastitis, elevated serum IgE and abnormal neutrophil chemotaxis. After multiple hospitalizations for severe skin infections, right upper lobe bullae were found and treated by lobectomy when the patient was three years of age. Thereafter, the patient was repeatedly hospitalized for pneumonia while on cloxacillin prophylaxis and receiving regular chest physiotherapy. When she was 12 years old, pulmonary deterioration (increased frequency of pulmonary infections, hemoptysis, radiological destruction of the right middle lobe) led to a right middle lobectomy. Since this intervention, the patient has had an improved quality of life, takes part in regular sports activities, without recurrence of severe pulmonary infections, and has had near normal pulmonary function studies. A concerted medicosurgical therapeutic regimen can control severe pulmonary complications in patients with this rare syndrome.

Key Words: *Hyperimmunoglobulinemia E syndrome, Job's syndrome, Lung abscess*

Prise en charge des infections pulmonaires récurrentes dans un cas d'hyperimmunoglobulinémie E (syndrome de Job)

RÉSUMÉ : Le diagnostic d'hyperimmunoglobulinémie E (hyper IgE) ou syndrome de Job a été posé chez une fillette de 5 mois présentant une mastite staphylococcique chronique, un taux élevé d'IgE sériques et un chimiotactisme des neutrophiles anormal. Après de nombreuses hospitalisations pour des infections cutanées graves, une bulle a été décelée dans le lobe supérieur droit et traitée par lobectomie à l'âge de trois ans. Par la suite, la patiente a été hospitalisée plusieurs fois pour des pneumonies malgré une prophylaxie à la cloxacilline et une physiothérapie pulmonaire régulière. À l'âge de 12 ans, une détérioration pulmonaire (fréquence accrue des infections pulmonaires, hémoptysies, signes radiologiques d'une destruction du lobe moyen) a nécessité une lobectomie du lobe moyen. Depuis cette intervention, la patiente a vu sa qualité de vie s'améliorer et participe à des activités sportives régulières sans nouveaux épisodes d'infections pulmonaires graves. Ses épreuves de fonction pulmonaire sont proches de la normale. Un régime thérapeutique médicochirurgical concerté peut enrayer les complications pulmonaires graves chez les patients souffrant de ce rare syndrome.

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THE HYPERIMMUNOGLOBULINEMIA E (HYPER IGE) OR Job's syndrome is a rare disease with elevated IgE and a defect in immune function (1,2) resulting in repeated sino-pulmonary tract infections in childhood which eventually lead to serious pulmonary destruction and respiratory compromise (3,4). This report describes a patient with hyper IgE syndrome and severe pulmonary complications who now has acceptable pulmonary function and enjoys a good quality of life because of a complete medicosurgical therapeutic regimen including tailored pulmonary surgery, physiotherapy and bronchodilator therapy.

CASE REPORT

The five-month-old patient was diagnosed with hyper IgE syndrome when she presented to the pediatric clinic with a history of chronic right breast discharge since birth, chronic seborrheic dermatitis, perforated otitis media and left cervical adenitis. Family history was positive for a maternal uncle with repeated cutaneous abscesses, pneumonia and multiple bouts of otitis media as a child, two maternal aunts with childhood cutaneous abscesses, and several other maternal relatives with chronic severe pustular lesions of the face and scalp. Physical examination revealed an active well looking afebrile child with infected facial eczema, normal chest, cardiovascular and abdominal examination, left posterior cervical adenitis and a right breast abscess. Laboratory workup revealed an increased serum IgE level (113 U/mL, which later increased to 15,000 U/mL) and decreased chemotaxis (assessed by the Boyden chamber technique [5]). Leukocyte count was $21,000 \times 10^9/L$ with 8% polymorphonuclear cells, 88% lymphocytes, 1% monocytes and 2% eosinophils. Culture of scalp, breast discharge and the cervical abscess were positive for *Staphylococcus aureus*. Review of her chart showed a positive *S aureus* culture of the umbilicus at two days of age.

By the age of three years, the patient had had three hospitalizations, the first for right leg and perianal abscesses, the second for conjunctivitis and an infraorbital abscess, and the third for severe purulent conjunctivitis. All were culture-positive for *S aureus*. The episodes occurred while the patient was on oral cloxacillin prophylaxis and she responded well to antistaphylococcal intravenous antibiotics. Also, at 14 months old, she was found to have congenital dislocation of the hip and later an associated genu valgum, which required three hospitalizations for surgical correction.

At the age of three years the patient began to develop pulmonary complications. While she was hospitalized for a severe campylobacter gastroenteritis, routine roentgenograms showed large bullae occupying the entire right lung field. The patient was asymptomatic and had normal blood gases. Perfusion lung scan showed almost complete loss of perfusion to the entire right lung but normal left lung perfusion. After four weeks of cloxacillin the patient had slight dyspnea on effort, and repeat chest roentgenograms showed bullae originating in the right upper lobe and compressing the right middle and lower lobes (Figure 1). Two months later the patient underwent a right superior lobectomy, which was

Figure 1 Posteroanterior (top) and lateral (bottom) chest radiographs obtained at the age of three years demonstrate several large pneumatoceles involving the entire right upper lobe and compressing the adjacent middle and lower lobes

Figure 2) Posteroanterior chest radiograph (**top**) and computed tomography section through the carina (**bottom**) obtained at the age of 12 years show, besides right upper lobectomy changes, consolidation and volume loss of the reoriented middle lobe containing multiple air-filled cavities, some of which represent bronchiectasis

well tolerated with an uneventful postoperative course. At the time of surgery the middle and lower lobes were noted to be normal. Pathology examination showed multiple bullae within chronically inflamed pulmonary tissue.

Over the subsequent eight years, the patient was hospitalized three to four times per year for pneumococcal or

Figure 3) Posteroanterior chest radiograph (**top**) and computed tomography section through the carina (**bottom**) obtained at the age of 14 years show a normal postlobectomy chest appearance

Haemophilus influenzae pneumonia, localized to the superior portion of the right lung, while on oral cloxacillin prophylaxis. The patient began to experience symptoms of chronic cough and diminished exercise tolerance, and at 12 years of age she had occasional episodes of mild hemoptysis.

While the patient was hospitalized for another bout of pneumonia, chest roentgenogram and computerized tomographic (CT) scan demonstrated multiple air-filled cavities surrounded by pulmonary opacities occupying the upper third of the right lung field (Figure 2). Bronchoscopy showed

unremarkable scar tissue at the site of surgery, 80% stenosis of the right middle lobe bronchus, and abundant white secretions in the right and left main bronchi. Bronchial lavage culture was positive for *S aureus* and *H influenzae*. Bronchography revealed numerous cavities unpenetrated by contrast medium, distortion of right middle bronchus and no evidence of bronchopleural fistula. Pulmonary function studies suggested a mild obstructive pattern with a forced expiratory volume in 1 s (FEV₁) of 71% and a forced vital capacity (FVC) of 90% of predicted values. The patient responded well to intravenous antibiotic therapy, but over the next year had further frequent hospitalizations for right upper lobe pneumonia; a repeat CT scan showed persistence of the cavities as well as atelectasis of the right middle lobe with occasional areas of bronchiectasis. A second perfusion lung scan showed diminished perfusion of the upper right lung. Based on the laboratory evidence of damaged middle lobe parenchyma and the patient's clinical deterioration over one-and-a-half years, the patient underwent a right middle lobectomy at the age of 13, from which she made a rapid recovery with an uneventful postoperative course.

In the following two years, the patient has had an improved quality of life, with normal daily activities including sports, and near normal pulmonary function studies showing normal lung volumes (greater than 90% of predicted values) and arterial blood gases, a mild obstructive spirometry pattern (FEV₁ 66% and FVC 83% of predicted values with a rise to FEV₁ 76% and FVC 89% after inhalation of a beta₂-agonist). She has also had only one three-day hospitalization for mild pneumonia during this time. She is still on oral cloxacillin prophylaxis, long term regular inhaled beta₂-agonist therapy and has daily chest physiotherapy, which has helped to prevent any further complications.

The chest radiograph and CT scan obtained at the age of 14 showed a normal post lobectomy appearance (Figure 3).

DISCUSSION

Job's syndrome, first reported by Davis et al in 1966 (1), derives its name from the biblical figure Job, who was afflicted with "boils from the sole of his foot unto his crown" (JOB 2:7) by Satan. In 1972 Buckley et al (2) made a major advance in delineating the syndrome. The disease is characterized by: repeated cutaneous, ganglionic, sinus and pulmonary infections usually of staphylococcal, streptococcal or *H influenzae* origin; eczematoid dermatitis that is usually superinfected; facial dysmorphism and coarse facies; retarded growth; and, rarely, limb deformity (6). The syndrome shows characteristic hyper IgE, many hundred times above normal, a mild chemotactic defect and eosinophilia (7,8).

Pulmonary involvement is usually important and can compromise the patient's pulmonary function to the point of severely reducing the quality of life and finally leading to death. Aggressive early antibiotic therapy together with chest physiotherapy must be instituted in order to keep pulmonary damage to a minimum. As seen in our patient, repeated pulmonary infections may lead to lung destruction with bulla formation and bronchiectasis. A full pulmonary workup in-

cluding bronchoscopy with bacterial cultures, CT, ventilation scan and pulmonary function studies is indicated in these patients when involvement is severe, in order to optimize medicosurgical therapy.

There are few treatment modalities that have proved to be beneficial for patients with hyper IgE syndrome (7,8). Until the underlying pathogenesis is more fully understood, a complete pulmonary therapeutic regimen including discussion of early tailored surgery is warranted for these patients. Anecdotal experience drawn from our patient and other previous case reports (3,4) suggests that removal of the damaged lung parenchyma can reduce morbidity and improve pulmonary function significantly when conservative measures fail to control repeated respiratory infections. The two surgical procedures performed in our patient are in accordance with previous reports in hyper IgE syndrome. Pneumatoceles have been reported to be frequent in hyper IgE syndrome patients; usual persistence with secondary infection is common (9). Also, current practice guidelines in thoracic surgery advise a lobectomy for localized bronchiectasis in the presence of symptomatic and recurrent pneumonia refractory to medical treatment, recurrent hemoptysis and adequate predicted postoperative lung function (10). Surgery combined with an aggressive medical regimen with frequent follow-up visits reduce hospitalizations, optimize pulmonary function, improve the quality of life and allow a child with a chronic debilitating illness to live normally.

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