Short reports

The hyperimmuno-globulinaemia E and recurrent infections syndrome in an adult

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Abstract

A 27 year old white woman with a history of chronic eczema and episodes of serious infection of the chest, skin, and bone presented with acute respiratory failure. She was found to have a spontaneous right pneumothorax and a pneumatocele in the left upper lobe. Despite a left upper lobectomy she was left with chronic respiratory failure, bullous lung disease, and bilateral bronchiectasis. The hyperimmunoglobulinemia E and recurrent infections syndrome was diagnosed only in adult life.

In 1966 Davis *et al* reported the association of frequently infected eczematous dermatitis, sinusitis, acute pulmonary infections and recurrent cold abscesses caused by *Staphylococcus aureus* in two white girls with red hair. They named the clinical syndrome "Job's syndrome" after the Biblical character.¹ Two further children with eczema, multifocal infections, a dysmorphic syndrome, and a high serum IgE concentration were reported by Buckley *et al* in 1972.² One hundred and thirty cases of the "hyperimmunoglobulinaemia E and recurrent infections" syndrome have now been published. We report a case in which the diagnosis was made only when the patient reached adulthood.

Case report

The patient, a secretary born in 1956, was admitted to the intensive care unit of the University Hospital of Rennes in July 1984 for acute respiratory failure one month after treatment for an abscess in the left upper lobe. She had a medical history of serious infections: mammary abscess at three weeks, repeated dental, nasosinusal and bronchial infections throughout childhood, numerous episodes of staphylococcal infected eczema, osteomyelitis of the fifth right metatarsal treated in 1969, staphylococcal spondylitis of

T12-L1 in 1971, abscess of the buttock in 1973, and abscess of the right breast in 1984. During adolescence she developed idiopathic right dorsal and left lumbar scoliosis. At 20 she developed asthma. On examination she had a right pneumothorax, which was drained with a chest tube. On the chest radiograph a large bulla was apparent in the left upper lobe (fig 1). A left upper lobectomy was performed. Surgery confirmed that the bulla was compressing the underlying parenchyma. The postoperative course was uneventful. Chest radiography and ventilation and perfusion scintigraphic studies showed that the left lower lobe had inflated satisfactorily, though the images suggested underlying lung disease. She was left with regular suppurative sputum. The patient was admitted to the chest clinic in September 1986. On examination she had cyanosis, finger clubbing, and wheezing. The skin bore scars secondary to the previous episodes of infected eczema, and there was an onychomycosis of the right thumb. Chest radiography showed bullous lesions at the base of the left lung and increased shadowing in the opposite lung (fig 2). Computed tomography confirmed bilateral bullous dysmorphies and bronchiectasis. Forced vital capacity (FVC) was 1.55 litres (47% predicted), FEV₁ 1.01 l (34% predicted), FEV₁/FVC 65%, and steady state carbon monoxide transfer 60% of predicted. Arterial oxygen tension (PaO₂) was 54 mm Hg (7.2 kPa), arterial carbon dioxide tension (PaCO₂) 39 mm Hg (5.2 kPa) and pH 7.39. There was no clinical, electrocardiographic, or echographic evidence of cor pulmonale. Investigations showed a slightly raised eosinophil count ($5.4 \times 10^9/l$). Serum IgE levels were considerably raised on at least four determinations (>4000, 10 500, 12 500, 14 880 IU/ml; normal <150 IU/ml). Radioallergosorbent tests

Figure 1 Chest radiograph showing right pneumothorax and left upper lobe pneumatocele.

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Accepted 27 April 1990

Figure 2 Chest radiograph showing bullous lesions of left lower region and contralateral lung shadowing.

gave strongly positive results for *Staphylococcus aureus* (9.3 PRU/ml, class 3) and *Candida albicans* 20 PRU/ml, class 4). Serum IgG was 15.9 (N 6.4–13.5) g/l, IgM 0.6 (N 0.6–2.8) g/l, IgA 1.3 (N 0.7–3.2) g/l. Cell mediated immunity was depressed in vivo (the Mantoux test and Méricux Multitest gave negative responses) and partially in vitro: lymphoblastic transformation tests were normal with phytohaemagglutinin and concanavalin A, and weak with pokeweed mitogen and recall antigens (varidase, protein purified derivative) and in mixed lymphocytic culture. Neutrophil chemotaxis was decreased; tetrazolium nitroblue reduction after phagocytosis of latex particles and chemoluminescence of neutrophils were normal. Serological testing for human immunodeficiency virus gave a negative result. In view of these signs a diagnosis of hyperimmunoglobulinaemia E syndrome was made. Renal amyloidosis and chronic respiratory insufficiency developed in the following years.

Discussion

The hyperimmunoglobulinaemia E syndrome is a rare disease, which usually appears before the age of 2^{3,4} and only exceptionally in adults.^{3,5} Clinical features include: recurrent infections^{3,4,6} affecting mainly the skin, lungs and sinus, which may be of bacterial (*Staphylococcus aureus*, *Streptococcus pneumoniae*, or Gram negative bacilli) or fungal origin (*Candida albicans*, *Aspergillus* spp); eczematous dermatitis, which is frequently infected;^{3,7,8} and a dysmorphic syndrome, with retarded growth, coarse facies, and prognathism in some patients.² Other disorders that have been described include asthma (about 10% of patients), and osteogenesis imperfecta, craniostenosis, and axial osteoporosis (half of all patients).⁸ Eosinophilia is frequently present; lymphopenia is rare. The serum complement level is normal. Humoral immunity is disturbed and serum IgE levels are substantially raised (more than 4000 IU/ml). IgE studies show a specificity for *Staphylococcus aureus* and *Candida albicans*. Serum IgG and IgD concentrations are frequently increased.

The anamnestic reaction to vaccines is weak and there is no reaction to neoantigens. On the other hand, there is often an immediate skin reaction to inhalant or food allergens without any corresponding clinical problem. Study of cell mediated immunity shows a normal E rosetting count, decreased CD3 and CD8 lymphocytes, and a normal CD4 level.⁹ Lymphoblastic transformation tests often give normal results for mitogens but only weakly positive results for recall antigens or in mixed lymphocytic culture. Half the patients have no delayed skin hypersensitivity. Neutrophil and monocyte functions are normal, apart from an irregular anomaly of neutrophil or monocyte chemotaxis (or both) that fluctuates with time.^{3,4,8} Tissue eosinophilia is frequently seen in chronically infected lesions but there is no granulomatous reaction, which could be an argument in favour of an abnormal cellular response.⁴ Several diseases may be associated with the hyperimmunoglobulinaemia E syndrome: systemic mastocytosis, membranoproliferative glomerulonephritis, systemic lupus erythematosus, Hodgkin's disease and non-Hodgkin's lymphoma.⁴ The complications of the hyperimmunoglobulinaemia E syndrome are mainly respiratory: chronic bronchitis and bronchiectasis,^{3,5} though empyema, pneumothorax, and bronchopleural fistulas have been reported also.¹⁰ The frequency of pneumatoceles is remarkably high and surgical excision is often necessary.^{3,4,8} Infections may affect vital organs and may be fatal.⁸ There may be less severe forms of the disease. The incidence of respiratory infections and their bronchopulmonary complications is such that lung specialists should be aware of the hyperimmunoglobulinaemia E syndrome.

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for a 52 year old plumber with extensive malignant pleural mesothelioma, who had been admitted with impaired consciousness and left sided long tract signs and whose computed tomogram showed at least four cerebral metastases, two in the brainstem and two in the right parietal region. Both of these tumours were subsequently confirmed at necropsy. In addition, there was extensive tumour affecting the pericardium, epicardium, and myocardium and extending extensively through the peritoneum.

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I agree with Dr Lewis that the small number of published cases of antemortem diagnosis of cerebral metastases in pleural mesothelioma may be due to underreporting. Unfortunately, I do not have data to support or refute this contention. I reviewed about 200 cases of pleural mesothelioma in 1986-87 and was surprised to find that many physicians were unaware that the tumour often metastasised.

Over the last few years I have developed a strong interest in research examining how scientific data are used in the courts and in public policy decision making.¹ Through my work in the asbestos area I became aware that injured workers seeking compensation through the courts often faced defence attorneys who vigorously questioned a diagnosis of pleural mesothelioma if metastatic disease was present. This prompted me to review a large number of cases coming to necropsy, and document the occurrence of metastatic spread, which was quite common.² This report also cited earlier studies further supporting this fact.

With the incidence of pleural mesothelioma increasing, cerebral metastases will undoubtedly be found more often. I hope that information such as that detailed by Dr Lewis will find its way into medical publications. In this way confusion concerning the natural history of this disease will be avoided.

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Local anaesthesia for fiberoptic bronchoscopy

We read with interest the report by Dr A R Webb and colleagues (June 1990;45:474-7) in which they compared transcricoid injection of lignocaine with the traditional "spray as you go" technique. They found the transcricoid technique to be more effective.

On reading the "Methods" section of the paper, one finds that both groups of patients received topical anaesthesia with lignocaine, but that the location and timing of administration differed. Patients who received transcricoid anaesthesia had lignocaine delivered to the subglottic space in an anteroom several minutes before the passage of the bronchoscope, whereas the other group of patients received a topical application of lignocaine to the upper surface of the vocal cords about 1 1/2 minutes before the bronchoscope was passed between the cords. There were further applications to the bronchi during the procedure.

In these circumstances it is not surprising that the group given transcricoid anaesthesia should cough less. It is likely that the lignocaine which was introduced into the trachea would spread widely in the bronchial tree during the coughing bout which followed the injection. It is also likely that the lignocaine would anaesthetise the inferior and medial surfaces of the vocal cords as it was removed from the bronchial tree by coughing and ciliary action. The bronchoscope is in contact with these surfaces of the vocal cords during bronchoscopy, but the "spray as you go" method would have anaesthetised only the upper surface of the cords. In the absence of any subglottic anaesthesia, one would expect the patient to cough and experience discomfort as the bronchoscope was passed into the unanaesthetised trachea and bronchial tree.

We have evolved a non-invasive technique for the instillation of local anaesthesia into the subglottic space and trachea. It is our practice to anaesthetise the nose and the upper surface of the vocal cords by the techniques described by Dr Webb and colleagues. We then position the bronchoscope directly above the vocal cords and we introduce 2-4 ml of 4% lignocaine as a bolus during inspiration. This enters the trachea and main bronchi and produces a cough similar to that occurring after transcricoid injection of lignocaine. We then wait two to three minutes before proceeding with the bronchoscopy and we find the operating conditions to be as good as those described after transcricoid lignocaine.

Our technique avoids a transcricoid injection but it has two potential disadvantages. Firstly, it may add one to two minutes to the duration of the bronchoscopy; we find this to be an acceptable delay. Secondly, our technique requires an experienced bronchoscopist to guarantee subglottic placement of the lignocaine. In difficult cases where both hands are required to optimise the position of the bronchoscope, we get an assistant to introduce the subglottic bolus of lignocaine while we observe the vocal cords through a lectroscope or on a video monitor.

We would therefore agree that transcricoid injection of lignocaine may have certain advantages, especially as it will achieve good anaesthesia of the glottis and trachea for trainee bronchoscopists. We suggest that experienced bronchoscopists might prefer to administer anaesthesia by the above non-invasive technique at the cost of a slight increase in operating time.

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We read with interest the article by Dr A R Webb and others (June 1990;45:474-7). Transtracheal injection of topical anaesthetic has been widely used for bronchoscopy, bronchography, and endotracheal intubation since this method was first suggested by Caynut¹ in 1920. Hitherto, a few complications, such as cellulitis, breakage of the needle, and pretracheal abscess, have been reported.²⁻⁴

Previous reports recommended inserting the needle perpendicularly to the skin through the cricothyroid membrane. This may cause laceration of the trachea as a result of coughing while the local anaesthetic is injected, and we witnessed a case of bleeding due to tracheal laceration many years ago. We therefore devised this technique to prevent this potential complication. A 23 gauge

Diagram illustrating the technique of transtracheal injection with a bent needle.

hypodermic needle is bent aseptically about 45° at a point 1 cm from the tip with a cap of the needle. A bent needle, attached to a 5 ml syringe containing 3 ml of anaesthetic, is inserted perpendicularly into the trachea through the cricothyroid membrane. Easy aspiration of air confirms that the needle is within the tracheal lumen. Then the syringe is directed cephalad at an angle of about 90° while air is aspirated and the needle is advanced about 0.5 cm. This procedure makes the bent part of the needle parallel to the anterior wall of the trachea (figure). Thus there is no possibility of traumatising the trachea or dislocating the needle while the anaesthetic is instilled even if the patient coughs persistently.

We have used this technique for more than 20 years before endotracheal intubation and also for instillation of saline or mucolytic agents for treating and preventing post-operative pulmonary complications together with diazepam⁵ and midazolam. No troublesome complications have been noted after more than several thousand injections, confirming the safety of this technique.

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CORRECTION

The hyperimmunoglobulinaemia E and recurrent infections syndrome in an adult

In the paper by J-P L'Huillier *et al* (September 1990;45:707-8), the 4th line from the end of p 707 should read "(0.54 × 10⁹/l). . ."