November 2018

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CASE REPORT

Large mediastinal mass in a 15-year-old boy

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SUMMARY

Hyperimmunoglobulin E syndrome is a rare multisystem inherited disorder characterised by high serum IgE levels, skin disorder causing eczema, dermatitis, recurrent staphylococcal infections and pulmonary infections and various skeletal and connective tissue abnormalities. Common presentation is with recurrent skin and sinopulmonary infections. Several features unrelated to immune system such as characteristic facial features, hyperextensibility of joints, multiple bone fractures and craniosynostosis have been described in the literature. We describe a rare presentation of this disease with invasive aspergillosis presenting as mediastinal mass with extension to mediastinal structures and pulmonary vasculature.

BACKGROUND

Hyperimmunoglobulin E syndrome (HIES) is a rare immunodeficiency syndrome which was initially described as Job’s syndrome by Davis et al in 1966. Pneumonia in these patients is typically caused by infections with Staphylococcus aureus, Haemophilus influenzae or Streptococcus pneumoniae and leads to pneumatoceles, abscesses and behaves as a nadir for fatal infections with bacteria and fungi. Lymphoma is a very important association of this disease and commonly present as mediastinal mass or lymphadenopathy and should always be excluded with biopsy. Fungal infections presenting as a non-resolving pneumonia or mediastinal mass is an important differential in such cases.

CASE PRESENTATION

A 15-year-old boy presented with shortness of breath, cough, haemoptysis and fever. He was in good health until the age of 9 years, he then developed asthma-like symptoms (wheeze, dyspnoea and chest tightness) and recurrent upper respiratory tract infections. His medical history was significant for rashes at birth, recurrent eczema and staphylococcal skin infections. His medical history was significant for rashes at birth, recurrent eczema and staphylococcal skin infections. He was treated initially as a presumed case of asthma/allergic bronchopulmonary aspergillosis with steroids by a family physician which he took for 3 weeks. He did not show much improvement and continued to have symptoms on and off so steroids were stopped.

On physical examination, he was a thin lean boy, of an average built. He had facial dysmorphic features of pinched nose, broad nasal bridge, large ears, new erupting teeth (figure 1) and delayed shedding of primary teeth. Chest examination revealed bilateral wheezes and decreased breath sounds in left lower chest.

Further evaluation with CT scan chest showed large anterior mediastinal mass (figure 3A,B). Bronchoscopy showed normal bronchial mucosa and mucoid secretions were aspirated and sent for microbiology which grew S. aureus (Methicillin sensitive staphylococcus aureus (MSSA)). CT guided biopsy was done which showed chronic granulomatous inflammation with multiple septic fungal hyphae

Figure 1 New erupting teeth (arrow).

INVESTIGATIONS

Laboratory workup showed, IgE levels >7000 IU/mL, beta D glucan >523 pg/mL (cut-off < 60), serum galactomannan was 0.36 (cut-off < 0.5), CBC was normal and his serum electrolytes and liver function tests were normal. Chest X-ray showed left lung collapse and mediastinal widening (figure 2). Further evaluation with CT scan chest showed large anterior mediastinal mass (figure 3A,B). Bronchoscopy showed normal bronchial mucosa and mucoid secretions were aspirated and sent for microbiology which grew S. aureus (Methicillin sensitive staphylococcus aureus (MSSA)). CT guided biopsy was done which showed chronic granulomatous inflammation with multiple septic fungal hyphae.

Figure 2 Chest X-ray showing mediastinal widening (arrow pointing left) and left lower lobe collapse (arrow pointing down).
Rare disease

Aspergillus stained with Periodic acid-Schiff-Diastase stain (PASD) (Figure 4) and fungal culture performed on the tissue sample grew Aspergillus flavus. Cardiothoracic surgery and infectious disease consultation was taken and he was started on voriconazole.

Further workup revealed raised IgG level (sub class study not available) and normal IgA and IgM. Flow cytometry was done (CD3 + total T-lymphocytes, CD4 + T helper cells, absolute count CD8 + T regulatory cells, absolute count CD19 + total B-lymphocytes and absolute count CD56 + Natural killer cells) which showed reverse CD4+/CD8+ ratio and rest normal. STAT3 mutation is not available. Patient was diagnosed with HIES on the basis of his clinical features and NIH scoring system (59 score).

DIFFERENTIAL DIAGNOSIS
- Malignancy, as the patient presented with mediastinal mass.
- HIES as the patient had characteristic facial abnormalities along with high IgE levels.
- Chronic infections like TB and fungal infection (aspergillosis).
- Paediatric chronic granulomatous disease.

TREATMENT
Patient was started on voriconazole 200 mg two times per day.

OUTCOME AND FOLLOW-UP
The patient showed dramatic improvement of symptoms and significant decrease in the size of mediastinal mass after 4 months of therapy (figure 5A-D). He was treated with antifungal therapy for 1 year due to the slower resolution of the disease process (mediastinal mass) as assessed by the serial CT chest images.

DISCUSSION
Autosomal-dominant hyper-IgE (Job) syndrome, is a result of negative mutations in signal transducer and activator of transcription 3 (STAT3) and a link between STAT3 mutation and recurrent infection and connective tissue abnormality has been widely described in literature. Recurrent bacterial pneumonias, attributed to dysfunctional STAT3, frequently lead to bronchiectasis and formation of pneumatoceles. Fungal pneumonias, typically aspergillosis have been described in literature as a cause of significant morbidity and mortality.

Lung complications following respiratory infections are common in HIES. These pulmonary lesions facilitate secondary infections with opportunistic pathogens (e.g., Aspergillus fumigatus, Pseudomonas aeruginosa), which are not among the initial...
Recurrent pulmonary infections lead to premature death in patients with HIES; early diagnosis and treatment can be lifesaving and can lead to a significant reduction in morbidity and mortality. To best diagnose and treat, we should be familiarised with the clinical and laboratorial aspects of the disease. Besides the infections, we should not forget the risk of malignancy that is associated with HIES.

**Contributors** MGA performed the literature search and wrote the manuscript. ABSZ and FNQ reviewed the manuscript and the case.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent** Parental/guardian consent obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**