TEACHING FILE (GRAND ROUNDS)

GRANULOMAS IN CHRONIC GRANULOMATOUS DISEASE

Ira Shah, Anmol Goyal

Clinical Problem :

A 3 years old boy suffering from chronic granulomatous disease (CGD) presented with fever and cough. He was detected to have CGD at the age of 1 year 4 months in view of persistent pneumonia and a positive nitroblue tetrazolium tests (1% cells positive for DHR). At that time he had received a 9 month course of ATT. Subsequently he was on voriconazole prophylaxis till the current episode of fever. On examination, his weight was 10.3 kg and height was 90 cms. On respiratory system, he had decreased air entry on the left side. Other systems were normal. Currently, chest X-Ray showed mediastinal widening with left mid zone haziness. His bronchoalveolar lavage (BAL) grew acinetobacter and klebsiella which were carbapenem and beta lactam resistant for which he was treated with colistin but fever did not subside. Urine culture grew candida for which he was treated with Amphotericin B however fever persisted. CT chest showed multiple large conglomerate necrotic lymph nodes with consolidation in apicoposterior segment of left upper lobe. A CT guided lymph node biopsy was done and sent for tuberculosis (TB), bacterial and fungal culture along with the bronchoalveolar (BAL) fluid. In the meantime he was started on antituberculous therapy (ATT) to which fever subsided. However both BAL & lymph node biopsy did not grow any organism. He was continued on ATT along with itraconazole prophylaxis. Even after 3 months of ATT, his chest x-ray showed no changes.

How should this child be treated?

Expert Opinion :

Chronic granulomatous disease (CGD) is a rare, primary immune deficiency rendering the affected individuals hypersusceptible to bacterial and fungal infections. (1) The actual incidence of CGD is unknown but it has been reported to occur in one child per 200,000 – 250,000 children below 5 years of age with a male predilection of 4:1. (2) Eighty percent of the cases are through an X-linked form of inheritance while the rest are inherited through an autosomal recessive pattern. (3) Cases of CGD usually present with manifestation of respiratory tract, soft tissues, skin, lymph nodes, liver, spleen or bones which is treated with appropriate antibiotics and other surgical interventions. The most common bacterial infections is by catalase positive organism like *S. aureus, Salmonella species* while aspergillus and candida contribute to majority of the fungal infection. (4) Granulomas are formed, which are nodular masses of inflammatory tissue, in the presence of antigenic stimulus or lack of negative feedback from oxygen radicals. (5) In our patient, CT chest showed multiple large conglomerate necrotic lymph nodes with consolidation but cultures were negative, though fever responded to ATT, there was no change on chest X-ray suggestive of noninfectious granuloma. Corticosteroids in CGD are usually contraindicated as it may favor dissemination of infection. (6) However, steroids help to prevent inflammatory complications like granuloma formation, wall thickening around abscesses and organ fibrosis which occurs due to dysregulation in the balance between production of pro and anti- inflammatory cytokines. Corticosteroids help by reducing the excessive pro-inflammatory mediators thereby reducing these exuberant inflammatory responses. (7) Steroids, though have a desirable and rapid effect but patient may develop dependency for long term low dose administration which is a drawback so should be gradually tapered and monitored. (8)

Our patient was started on prednisolone (0.5 mg/kg/day) following which in one month, his X-Ray showed regression of mediastinal nodes as well as the left sided consolidation. Prednisolone was then tapered and stopped in next 15 days. He is on regular follow up. In our patient, steroids helped in regression of pneumonia and nodes by reducing the inflammatory mediators which seems to be the responsible for the lesions which were refractory to antimicrobial therapy.

In conclusion, corticosteroids play an adjuvant role in CGD refractory cases along with appropriate antibiotics.

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From: Medical Sciences Department, Pediatric Oncall, Mumbai, India.

Address for Correspondence: Dr Ira Shah, 1/B Saguna, 271/B St Francis Road, Vile Parle (W), Mumbai 400056, India.

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