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Arthritis in Hypogammaglobulinemia

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Majority of children with hypogammaglobulinemia present with recurrent and severe lower respiratory tract infections and the diagnosis in such cases is usually clinically obvious. In some children, however chest infection may not be very prominent at presentation and instead joint involvement may be the major clinical finding. Such patients have been misdiagnosed as having juvenile rheumatoid arthritis(l). We report two such cases whom we treated recently. This type of presentation of hypogammaglobulinaemia has not been previously reported in the Indian literature.

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Case Reports

Case 1: A five-year-old boy presented with history of swelling in various joints for last 9 months for which he had been receiving treatment elsewhere To begin with he had swelling of left shoulder joint which was painful and was associated with fever. Arthrocentesis was done as aspirate showed a purulent exudate. He underwent arthrotomy and received antimicrobials for

3 weeks for a presumed staphylococcal infection. As there was no improvement in symptoms even after one month, he was given antituberculous therapy for 3 months, but without significant improvement. One month after this, he developed swelling of left knee joint for which again arthrocentesis was done and antituberculosis therapy was continued. All these aspirates were sterile. Swelling of these joints persisted till the child presented to us. On direct questioning there was history of repeated chest infections but these had never been severe enough to warrant hospitalization or intravenous antimicrobials. There was also history of recurrent draining ears in the past. There was no family history suggestive of immunodeficiency. On examination, he was severely malnourished (weight 10 Kg, expected 18 Kg). He was febrile and had pallor and clubbing. Pulse rate was 140/min and blood pressure 90/60 mm Hg. There was marked irritability. His systemic examination was unremarkable. Ear drums were intact. The left knee and left 5th interphalangeal joint were swollen, tender and there was limitation of movements. Movements at left shoulder joint were also limited. Investigations showed a hemoglobin of 7.5 g/dl, total leulocyte count 29,000/ cu mm with 89% polymorphs. He had sterile blood culture. Mantoux test was non reactive, ASO titers were < 200 IU, C reactive protein was positive, rheumatoid factor was negative and brucella titer in serum was < 30 IU. X-rays of the involved joints showed only soft tissue swelling. Fine needle aspiration cytology of left knee joint showed non specific inflammatory changes and cultures for bacteria and fungi were sterile. Technetium scanning of left knee showed increased perfusion. He had normal nitroblue tetrazolium dye reduction and negative HIV serology. His serum IgG was 9 mg/dl (N at this age = 929±228), IgA was 28 mg/dl (N = 93±27) and IgM was 24 mg/dl (N = 56 ± 18)(2). He was started on intravenous cefotaxime, amikacin and cloxacillin for 3 weeks followed by oral cloxacillin for 3 more weeks and given intravenous immunoglobuins (IVIG) 0.4 g/kg every 3 weeks. He had significant clinical improvement with this treatment; he became afebrile, irritability almost disappeared, but the swelling in the joints persisted, though no new joint swelling appeared. He was given oral erythromycin for 6 weeks for a presumed mycoplasma arthritis. The parents continued IVIG therapy for approximately 2 months after which they decided to discontinue treatment due to financial constraints.

Case 2 : A three-year-old boy presented with history of repeated respiratory infections from 6 months of age, fever for 3 months, a swelling over occipital area of scalp for 1 month and swelling of right elbow and ankle joints for last 10 days. On examination he was febrile and pale. There was alopecia and a discharging sinus on the scalp over the area where he had swelling one month back. His weight was 10.2 kg (expected 14 kg) and height was 83 cm (expected 95 cm). In systemic examination both lungs showed crepitations, more on left than on right side. There was redness and tenderness in right elbow joint and movements were restricted in right ankle joint. His hemoglobin was 8.6 g/dl which fell to 6.2 g/dl over next 20 days. Peripheral blood film showed microcytic hypochromic anemia. X-ray chest was suggestive of brochopneumonia and X-rays of involved joints showed only .soft tissue swelling. His blood culture as well as pus from scalp abscess were sterile for bacteria and fungi. He had negative Mantoux test. At admission, a possibility of disseminated staphylococcal infection was kept and he was started on intravenous cloxacillin and

gentamicin followed by oral cloxacillin for 3 more weeks Nitroblue tetrazolium dye reduction was normal and he had negative HIV serology Ig G level was < 100 mg/dl (N at this age = 929±228), IgA was 20 mg/dl (N = 93±27) and IgM was 40 mg/dl (N = 56 ± 18) (2) Lymphocyte subset analysis using monoclonal antibodies was done on a Flourescence Activated Cell Sorter (FACS) CD 19 +ve cells were 0.02%, thereby confirming the virtual absence of B cells IVIG therapy and oral erythromycrn were given keeping a possibility of arthritis due to mycoplasma infection At discharge, he was afebrile, scalp wound had healed and both joints had become less inflammed He is continuing to receive IVIG therapy every 3-4 weeks Follow up after 12 months has shown that the right elbow joint has become nontender and there is only slight restriction of movements His ankle joint is still somewhat swollen but the movements are not painful His current weight is 14 kg and height 96 cm

Discussion

Recurrent sepsis, sinusitis, otitis media and pneumonia are the usual presenting complaints in patients with hypogammaglobulrnemia(3) Some of the children, however, can present with arthritis as the major clinical finding Though immunodeficiency as a cause of arthritis is well described m standard text books(4), it is often missed by treating physicians as is exemplified by our two patients as well Clinically it resembles oligoarticular JRA, but may progress to polyarticular disease(l) There is usually no radiographic evidence of joint destruction Such patients have a normal erythrocyte sedimentation rate, negative rheumatoid factor and negative antrnuclear antibodies(l) Both of our patients had oligoarticular presentation and no evidence of tissue destruction on X-rays

Significant joint involvement in children with hypogammaglobulinemia can result from bacterial, mycoplasma or viral *(sp* echovirus) infections Lederman *et al* (5) had shown presence of arthritis in 19 out of 53 patients of agammaglobuhnemia (35 8%) Out of these, 8 were caused by bacterial pathogens, 1 by adenovirus and no organisms were isolated from remaining cases The etiology of aseptic arthritis remains uncertain(5) In patient with hypogammagobulrnemia, if routine cultures are negative, the working diagnosis should be kept as mycoplasma arthritis until proved otherwise(6) Routine cultures were sterile in both of our patients.

Like all children with hypogammaglobulinemia, those who present with arthritis also require prolonged IVIG therapy Appropriate antimicrobials should be given in the initial phase depending on the organism isolated Majority of such children show significant improvement with these measures, as evident in *Case 2.*

It is important to recognize hypo-gammagobulrnemia as a cause of arthritis in children as it prevents many unnecessary invasive investigations and toxic medications to the child and avoids unnecessary mental and economic burden to the families

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