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Letter to Editor

Orthopaedics Section

Correspondence: Knee Effusion with Peripheral Eosinophilia: A Need to Rule out Idiopathic Eosinophilic Synovitis

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Dear Editor,

At the outset, I would like to congratulate the authors of the article entitled-'Knee Effusion with Peripheral Eosinophilia: A Need to Rule out Idiopathic Eosinophilic Synovitis' published in JCDR [1]. However, I regret to mention that the workup mentioned in this article is highly inadequate, before one can come to a definitive diagnosis of eosinophilic synovitis.

I would like to highlight that it is very crucial to rule out history of 'milk allergy', which has been ascertained by finding increased IgG anti milk levels, IgG milk-circulating immune complexes and in vitro T-cell sensitivity to milk as mentioned in the literature [2].

It is must to undertake skin testing for commonly available allergens related to eosinophilia (house dust, Acaridae, feathers, kapok upholstery, ragweed, trees, grasses, pollens, weeds, dog and cat hair, Alternaria, Horrnodendrum). Laboratory testing has to include, in addition to what was undertaken by the author, blood chemistry profile; circulating IgG, IgA, IgM, and IgE; VDRL; antistreptolysin 0 (ASO); with subspecificity assays for antibodies to native DNA (anti-nDNA), Sm, RNP, SS-Pi, SS-B, Scl-70, PM-1, centromere, nucleole and organ-specific autoantibodies [3].

Also, nephelometric assays of C3 and C4; microbiology studies of blood and stool samples for parasites especially Taenia solium as Indian subcontinent is endemic for this infection; serology for HBV and HCV should be included [4].

Minor eosinophilia, in the range of 1-10%, can occasionally be found in haemorrhagic fluids and in the presence of systemic diseases, such as rheumatoid arthritis, rheumatic fever, hypereosinophilic syndrome, parasitic disease and probably many others.

Eosinophilic synovitis has been found in patients with systemic and local parasitic infections, in cancer patients with articular and extra-articular cancerous involvement who received previous radiotherapy and/or chemotherapy and in patients submitted to air or contrast knee arthrography.

In the existing clinical scenario, it is must to rule out low grade septic (pyogenic) arthritis, tubercular arthritis and Juvenile Monoarticular Synovitis (JRA) before finally labelling this condition; so, this essentially warrants the synovial histopathological confirmation [5].

Moreover, it is very important to rule out 'gout', the incidence of which is increasing even though we may agree that the patient was a teenager as various hereditary enzyme linked hyperuricaemic conditions can cause early age hyperuricemia [6].

Finally, it is must to document "eosinophilic infiltration of synovium", which has to be confirmed with Fine Needle Aspiration Cytology (FNAC) or arthroscopic and open biopsy, before coming to a conclusion. Besides, the elevated levels and assessment of IgE in synovial fluid has not been undertaken in this particular case [7].

As far as management of this condition is concerned, it is better to avoid the use of 'Aspirin' as it causes 'Widal Syndrome' [8] and also Ibuprofen [9]. They have the potential to cause eosinophilia; the author has managed the condition with 'Ibuprofen'.

Last is the issue regarding the follow-up of such patients. It is well mentioned in the literature and an established dictum that "Eosinophilic disorders are chronic conditions that require long term treatment for the prevention of clinical manifestations. Morbidity and mortality for many eosinophilic disorders remain high, so they need constant regular monitoring even after initial remission" [10].

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Authors' reply

I would like to extend warm regards to author/s for showing a keen interest in our article.

With reference to article regarding milk allergy, Golding DN reported a case of milk allergy in a 42-year-old patient with recurrent multiple joints pain precipitated after drinking milk. She had history of recurrent urticaria with strong family history of allergic diathesis. Arthrocentesis of right knee joint was performed and 30 mL of synovial fluid was aspirated. Cell count of synovial fluid revealed 82% lymphocytes and 3% eosinophils, while blood count revealed 1.4% eosinophils which were within normal range, so predominant cells in joint in case of milk allergy effusion were lymphocytes [1].

Panush RS et al., also performed prospective reproducible double blinded milk challenges in a 52-year-old patient with active rheumatoid disease since last 11 years. She had history of urticaria after ingestion of shellfish and history of cold related vasospasm. Patient had felt that some food items including milk cause exacerbations of her symptoms. They reported symptomatic exacerbations of symptoms in inflammatory arthritis with intake of milk and dairy products due to immunological hypersensitivity [2].

So, it would be prudent to say that milk allergy and joint effusion should not be looked in isolation. Patient should have personal or family history of allergy or have rheumatic symptoms [1,2]. Nevertheless to say that in milk allergy, predominant cells in synovial fluid analysis were lymphocytes and not eosinophils [1]. There is no evidence that it causes peripheral blood eosinophilia [1]. In our case, patient had a short history of 5 days before presentation (no episodic or recurrent presentation). Patient had no allergic history or family history of allergy and Immunoglobulin E (IgE) level in the blood investigation was normal [3].

With reference of study by Brown JP et al., and conducting skin testing for allergens and other battery of investigations, I would like to highlight the fact that Brown JP et al., had performed all these investigations in their subset of 6 patients because apart from arthritis and joint effusion, all these patients had personal history of allergy (eye/nasal/skin/asthma), positive family history of allergy, increased level of IgE and pronounced dermatographism [4]. Our patient had no personal or family history of allergy and IgE was also normal; so no further investigations in this regard were performed.

In reference to article for performing investigation for Taenia solium, I would like to highlight the fact that we have mentioned in the article that stool examination for ova and cysts was performed and was found to be negative [3,5].

Patients with gout may have eosinophilia but synovial analysis in gout patients predominantly shows neutrophils and not eosinophils [6,7]. So, Gout is not a differential diagnosis in a patient of synovial fluid eosinophilia.

We have performed arthrocentesis at presentation and sent it for routine, biochemical, microbiological, cytological examination and culture sensitivity. There was no evidence for crystals (gout, pseudo-gout), low grade pyogenic or tubercular arthritis on this examination. Further, our patient got improved with treatment and there was no recurrence. Therefore, no further invasive procedures such as biopsy was performed.

In terms of your reference of article regarding estimation of IgE in synovial fluid, Padeh S et al., reported a case of seven-year-old boy who presented with left ankle pain and swelling. Arthrocentesis was performed and patient was started on cloxacillin suspecting as pyogenic arthritis. Subsequently, cultures for bacteria came negative. The patient, however, responded clinically on treatment and was discharged on oral cloxacillin. Patient again presented after one week with swollen left ankle again and generalised pruritus. On physical examination left ankle was swollen, nontender, without temperature changes and range of motion was normal. A second arthrocentesis was performed and then IgE in synovial fluid was performed with other investigations. Authors of this article could only suspect to perform IgE in synovial fluid during follow-up after 1 week as patient had generalised pruritus (allergic manifestation) and clinically there were no signs of inflammatory arthritis with normal range of motion [8]. I would like to say that synovial fluid IgE is generally not the first line of investigation in patient with joint effusion. It is an important investigation to perform if clinician is highly suspicious of synovitis due to allergic cause at first presentation which is quite unusual or get a chance to perform this investigation during follow-up. We did not get a chance to perform a second arthrocentesis and perform this investigation as patient got better during follow-up.

With reference of article of Ibuprofen and eosinophilia, Vogts N et al., reported a case of Pulmonary Infiltrates with Eosinophilia (PIE) [9]. Patients with PIE present with fever, cough, dyspnea, malaise, and rash after 1-2 weeks of drug exposure. This patient was an opiate addict and had taken 72 tablets of ibuprofen and codeine (combination tablets, dose not mentioned). Nonsteroidal anti-inflammatory drugs (NSAIDs) have been incriminated as a cause of PIE and Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) and code in as a causative agent for DRESS [9,10]. Eosinophiliais not an isolated finding with the use of various NSAID's and when present it is associated with adverse systemic manifestations such as fever, rash, lymphadenopathy and internal organ involvement such as liver, pancreas, muscle, heart leading to potentially life threatening condition.

It is unclear to us that why author/s have ignored or may have missed other potentially life threatening condition that occurs in conjuction with eosinophilia after exposure of these drugs and only mentioned eosinophilia as a side effect. In our case, patient didn't take a single dose of Ibuprofen or any other drug before presentation [3]. So, it's safe to comment that Ibuprofen has not caused eosinophilia and she has not developed any systemic manifestation (such as PIE or DRESS) as mentioned above while on treatment.

Lastly, regarding the follow-up, I would say that patient was followed-up for one and half year and patient was well without any recurrence.

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