Recurrent respiratory tract infection due to isolated absence of IgA:

Report of a case

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RECURRENT RESPIRATORY tract infection is often found in bronchiectasis, generalised malignancy, fibrocystic disease or when the patient is receiving prolonged immunosuppressive therapy. An unusual but important cause which has always to be considered is the absence of the globulin, as in agammaglobulinaemia which can either be congenital or acquired. Very rarely, however, the total amount of globulin in the blood may be normal, but there is a selective absence of only the IgA group of the immunoglobulins.

We report here a patient who has a complete absence of the IgA in the serum, saliva and nasal washings presenting as recurrent respiratory tract infection in different parts of his lungs during a follow-up period of almost four years. The aetiology of the recurrent infection posed initially as a diagnostic problem as all the commonly known causes were excluded, and the solution was obtained only after sending his serum for quantitative immunoglobulin estimation. As far as we are aware, no such case has been reported in the literature from either Singapore or Malaysia.

CASE REPORT

L.C.H., a 14-year-old Chinese male, was first admitted to Tan Tock Seng Hospital, Singapore, on 24th November, 1965, with a four-day history of fever, cough and breathlessness. He also had a chronic left ear discharge which was purulent on and off ever since he was a child. There was no history of chronic diarrhoea or arthritis. Clinical examination revealed that he was rather small for his age (4 ft. 9½ ins.), but no other obvious abnormalities were found. Examination of the chest revealed a left pleural effusion. This was confirmed by a chest X-ray which in addition showed streaky opacities in the right first intercostal space, presumably of tuberculous origin.

Investigations.

Total White 13,300. Differential count: Polys. 77%, Lymphocytes 18%, Monocytes 3%, Eosinophils 2%, Haemoglobin Estimation 11.2 gms.%. Sputum for pyogenic culture grew no organisms. A tuberculin test of 1 T.U. was strongly positive (18 mm.). Repeated sputum examination for acid fast bacilli was negative both on direct microscopy and culture.

Progress.

In view of the presence of pleural effusion, a radiological shadow suggestive of Tuberculosis and a strongly positive tuberculin test, he was started on injection Streptomycin ½ gm. daily together with tabs. Para-aminosalicylic Acid 7 gms. and tabs. Isoniazid 210 mgms. daily. On his discharge from the hospital on 19th March, 1966, injection Streptomycin was stopped, but both Para-aminosalicylic Acid and Isoniazid were continued for a total period of two years. He was followed-up regularly as an out-patient in the hospital. At the time of his discharge, his chest X-ray was completely normal except for minimal residual opacities in the right first intercostal space.

He was re-admitted on 20th March, 1967, for fever, and a chest X-ray showed consolidation of the apicoposterior segment of the upper lobe of the left lung. Again there was a leucocytosis and he responded completely to penicillin. Sputum for culture grew no pyogenic organisms. In view of his chronic discharging left ear, he was seen at the Ear Nose & Throat Department at the Outram Road General Hospital where a diagnosis of chronic otitis media was made and Chloromycetin ear drops were prescribed.

His third admission to the hospital was on 10th April, 1967, for similar complaints of fever and cough. This time the chest X-ray showed a complete right upper lobe consolidation. On this admission, a protein electrophoresis was done and this showed: albumin 2.3 gms.%, α_1 globulin 0.4 gms.%, α_2 globulin 0.8 gms.%, β globulin 0.4 gms.%, γ globulin 2.7 gms.%. As fibrocystic disease was considered, the patient's sweat was estimated for total sodium and chloride, both of which were within the normal limit. Again he was treated with injection penicillin and he responded very well.

On 3rd April, 1968, he was admitted to the hospital for the fourth time for a pneumonic consolidation of the posterior segment of the upper lobe of the right lung. Once again he improved with chemotherapy. Since no cause of his recurrent respiratory infection could be found so far, a quantitative estimation of his serum immunoglobulin was carried out, employing a modification of the technique described by Sharpless and LoGrippo, using the micro-double diffusion agar plate (Sharpless and LoGrippo 1965). The results were as follows: IgG 1,460 mgms.%, IgA not detectable quantitatively, IgM 78.0 mgm.%.

Vitamin A absorption test and liver function tests done were all normal. Blood for LE cells was negative, but the R.A. factor was positive.

Bilateral bronchogram done on 6th June, 1968, showed a normal bronchial tree. On 19th June, 1969, immunoglobulin estimation in the serum was repeated: IgG 1272 mgms.%, IgA absent, Igm 92.5 mgm.%. The saliva of the patient, together with his nasal washings, were both sent for quantitative estimation of IgA, and this could not be detected in any of the specimens sent.

Since the last admission, the patient has been followed up regularly and has remained well.

Discussion.

The huge numbers of the anti-bodies found in the serum can be conveniently divided, basing on chemical, physical and immunological characteristics into 5 major immunoglobulin groups – IgG, IgA, IgM, IgD, IgE. Each of these five groups of immunoglobulins have different biological properties and disease states occur where there is either an excess or deficiency in one or more of these immunoglobulin groups. The IgA molecule, like the other immunoglobulins, is composed of two heavy and two light chains and has a molecular weight of 180,000 with a sedimentation coefficient of 7S. Unlike in the serum where nearly all the immunoglobulin groups are represented, IgA is the predominant immunoglobulin in the external secretions of the body such as the saliva, tears, colostrum, nasal and bronchial fluids, gastrointestinal fluids and urine. The IgA found in secretions differs from that found in the serum in that it is 11S instead of 7S due to the presence of a low molecular weight protein, "the transfer piece", attached to the usual IgA molecule. It has been suggested that this "transfer piece" enables the IgA molecule to be secreted by some of the organs in the body (Terry, 1967).

Secretory IgA has been shown to possess antibacterial and anti-viral properties, and is thought to provide an immune protection for the mucous membranes of the body.

Deficiency of IgA can be divided into two groups:–

(a) Deficiency of IgA combined with other

immunoglobulin deficits as in agammaglobulinaemia and Type I and Type II dysgammaglobulinaemias.

(b) Isolated deficiency of IgA (Tomasi, 1968).

Recurrent respiratory tract infection is common to both, but a variety of conditions have been described, associated with the isolated IgA deficiency group. These are hereditary telangiectasia (4 out of 5 patients have deficiency of IgA), cirrhosis of liver, Still's disease, systemic lupus erythematosus and recurrent malabsorption. The last is particularly interesting because the majority of patients with idiopathic steatorrhoea have normal immunoglobulins, although a few have shown isolated absence of IgA.

The exact relationship between IgA deficiency and most of the syndromes it is associated with, such as systemic lupus erythematosus and hereditary telangiectasia, is unknown, although the presence of recurrent respiratory tract infection can be readily explained by a lack of protective IgA anti-bodies bathing the mucous membrane of the bronchial tree. Furthermore, isolated absence of serum IgA in apparently healthy and asymptomatic individuals have been described in 1 out of 700 of the normal population.

The patient we have described is particularly interesting because he presented with the diagnostic problem of recurrent respiratory tract infection of unknown aetiology following treatment for a pleural effusion which was thought to be tuberculous in origin. Bronchiectasis, fibrocystic disease and a few other conditions were all excluded in our investigations. Because it was felt that some lowering of his immune mechanism was responsible, quantitative estimation of his immunoglobulins in the serum and later the IgA in his saliva and nasal washings were done. Chew and his colleagues found that in a survey of the levels of IgG, IgA, IgM in the serum of the normal population in Singapore, employing a modification of the technique described by Sharpless and LoGrippo using the micro double diffusion agar plate, the average levels for Chinese males were as follows:— IgG 774 mgms.%, IgA 206 mgms.%, IgM 73 mgm.% (Chew et al 1969). Using the same method, no IgA could be detected in the patient's serum, saliva and nasal washing.

It must be realised, however, that deficiency of IgA in the serum need not necessarily be accompanied by deficiency of IgA in the secretions, but the converse has not yet been described. The patient described above has a deficiency of IgA in both his serum and his secretions. Rockey and his co-workers described two cases of isolated IgA deficiency in the serum, whose serum IgG were found to be high for some unknown reason, although the IgM was normal (Rockey et al, 1964). It is interesting to note that in our patient, the serum IgG estimated on the two occasions were 1,460 mgms.% and 1,272 mgms.% respectively both of which were much higher than the average IgG level of 774 mgms.% in the normal Singapore Chinese male population as found by Chew et al.

In addition to the recurrent respiratory tract infection, our patient also has chronic otitis media which has been described with IgA deficiency. However, he has no clinical evidence of the other associated syndromes as listed above, and this was confirmed by all the negative investigations, such as the LE cell test and tests for liver function and malabsorption, except for a positive R.A. factor.

Summary.

A 14-year-old Chinese male, presenting with recurrent respiratory tract infection and chronic otitis media due to an isolated absence of IgA in the serum, nasal washings and saliva, is described. The literature regarding the role of IgA and the various syndromes associated with its absence is reviewed.

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