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RESEARCH ARTICLE

HYPER IGM SYNDROME: ABOUT 2 CASES

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Abstract

Hyper-IgM syndrome is a rare combined immune deficiency linked to a mutation most frequently found in CD40.The diagnosis is usually made in the presence of recurrent infections, particularly pulmonary, digestive and others. Through to the dosage of lymphocyte subpopulations and after elimination of other differential diagnoses, the diagnosis of hyper-IgM syndrome can be confirmed.

The objective of this work is to emphasize the presence of the diagnosis of hyper-IgM syndrome, the interest to search for it to avoid the repercussions on the growth especially and the survival.

Results: We reported the case of 2 patients the first one a 4 years old patient diagnosed at the stage of complication by a DDB which presented infections essentially pulmonary with repetition in front of this table a dosage of immunoglobulin's was required which was in favor of syndrome of hyper-IgM. And a second one the 10 years old, this patient who had as history a brother who died of the same symptomatology, repeated ear infections, digestive infections such as gastritis with HP; a zona the immunoglobulin dosage objectified a hyper-IgM syndrome. Both patients were put under immunoglobulins with good evolution.

Conclusion: The hyper IgM syndrome is still rare but should be suspected as any immune deficiency in front of repeated infections. We have illustrated in this work two cases that have evolved well with treatment and how certain complications can be avoided by early diagnosis.

Introduction:-

Hyper IgM syndrome is a rare immune deficiency first described by Rosen and Al in 1961, when he described primly the clinical condition of two brothers who had recurrent infections (2). In the work of Brutin was described for the second time when who found an elevation of IgM with a low level of IgG (3).

It is a combined deficiency linked to a mutation of CD40 expressed by B lymphocytes resulting in a low secretion of IgG with IgA and a high or normal secretion of IgM.

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The physiopathology of this syndrome is very complex and gives as clinical expression ENT, pulmonary and especially digestive infections with a predilection of opportunistic infections, with intracellular tropism.

The interest of this work is to pay attention to the diagnosis of the hyper IgM syndrome and to search for it in front of digestive and pulmonary infections in order to be able to ensure a certain balance after the establishment of the treatment before the installation of complication like the DDB

Observation of the first case:
This is a 4-year-old female child who presented since birth with recurrent respiratory infections > 8 times/year. The patient presented during the first hospitalization with a productive cough predominantly in the morning with bronchorrhea and night sweats in a context of altered general condition, and fever calculated at 39. On clinical examination, the patient had a globular thorax, subcutaneous chest indrawing and diffuses bilateral sibilant rattles on auscultation. On general examination, she was underweight (-2DS) according to the WHO curve, without statural delay, and a right basal atelectasis was seen on the thoracic radiography. The thoracic CT scan showed a dilatation of the right basal bronchi, cylindrical type. In view of the history of infections, an immunological assessment was requested which showed a normal level of IgM and IgA with values of 0.881 and 0.772 respectively, with IgG collapsed below 1.64. Other etiologies were eliminated, namely tuberculosis and cystic fibrosis, and HIV serology was negative.

The patient was put under antibiotic prophylaxis with amoxicillin-clavulanic acid for 10 days every month for 3 months associated with an infusion of immunoglobulins at a dose of 0.5g/kg/month. The evolution was marked by clinical improvement and quality of life of the patient.

Observation of the second case
A 10-year-old female patient was hospitalized for HP gastritis and intercostal shingles. She presented with repeated ENT and respiratory infections at the rate of two infections per month, she was hospitalized for frontoethmoidal sinusitis, having undergone a tonsillectomy at the age of 8 years, and she had a brother who died in the same context at the age of 18 years, An immune deficiency was suspected in view of her history of repeated infections and confirmed by an immunoglobulin assay which showed a low IgG level of 3.4 g/l and IgM of 1.781 g/l, The patient then developed a productive cough with chronic morning bronchorrhea for more than 1 month. A thoracic CT scan was done but it did not show any bronchial dilatation; the patient was then put on immunoglobulins at a dose of 0.5g/kg/month and on antibiotic prophylaxis: trimetoprim-sulfamethoxazole at a dose of 20mg/kg/d

Discussion:-

Hyper IgM syndrome is a combined immune deficiency initially named "dysgammaglobulinemia", in 1979 the world health organization changed its nomenclature to IgM immunodeficiency syndrome (1). In 1993 five heterogeneous groups showed that the mutation in CD40L, which is responsible for this deficiency. However, some groups had a normal CD40L (6,12).

In fact, it is secondary to the high or normal production of IgM type immunoglobulins, which may be related to a decreased production of other immunoglobulin isotopes or an absence of their production (13).

The incidence and prevalence of this syndrome was difficult to estimate, according to the European national registry of immune deficiencies was around 0.3% to 2.9%, the incidence in Spain was 1/20 million; in America the incidence was close to 1/100000 (5). In this work there were two cases in the region that were diagnosed, it could probably be a lack of awareness of the diagnosis.

Another series was reported in Rabat in 2017 about the immunological profile of patients with SHIGM. 12 out of 15 cases were reported to be consanguineous, which could explain the slightly higher number of cases than in other countries. In Asia, consanguinity was incriminated (8), whereas in Taiwan, there was no link with consanguinity (9).

The first clinical signs are of the type of pulmonary or ENT infection with repetitions generally appear at an early age before 4 years (5), especially for the X-linked hyper-IgM subtype without having a correlation between the age of diagnosis and the appearance of clinical signs. A study on the immunological profile has shown an appariation of the symptomatology between the age of 7 days and 16 months (7), which is consistent with the two clinical presentations in our work.

Several factors can trigger this syndrome, in particular opportunistic infections such as mycobacteria, toxoplasmosis, gondiosis and cryptosporum (1).

Rare cases have been reported in the literature, the example of an observation was described in Italy that had repeated respiratory infections, other etiologies such as TBK and alpha-antitrypsin deficiency and GERD were eliminated and then a dosage of immunoglobulins and lymphocyte subpopulations to objectify an increase in IgM with low concentration of other isotopes. The patient was subsequently complicated by bronchial dilation. Treatment consisted of infusion of immunoglobulins every 3 months (16).

Repeated infections were the main evocative symptom, with a predominance of pulmonary infections in 47% of cases, chronic diarrhea in (30%) and recurrent purulent otitis in third place (23%) which is in line with our work (10). In another study, diarrhea was the first complaint and constituted 50% (12). They may have autoimmune manifestations such as inflammatory arthritis, inflammatory bowel disease, biological pancytopenia, and especially neutropenia (14,15).

Progression to BMD was not uncommon (7). It can also include a delay in weight and height, which is secondary to repeated infections, as well as bronchiectasis or a lymphoproliferative syndrome (11).

Our second case did not evolve into DDB, which could be explained by the efficacy of cotrimoxazole-based antibiotic prophylaxis for its primary ID.

Conclusion:-

Hyper IgM syndrome is a syndrome that remains rare. We have illustrated in this work the clinical and biological presentation of 2 cases diagnosed in the Marrakech-Safi region and we have cited the evolution under immunoglobulin.

SHIGM must be sought in front of pulmonary and digestive infections especially with repetitions are confirmed by the rise of IgM with a fall of the other stereotypes, coupled with the genetic study. The treatment is based essentially on the control of the exacerbation as well as the infusion of immunoglobulins and essentially on antibiotic prophylaxis.

The evolution and the different therapeutic approaches should be investigated in the future.

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