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ASSOCIATION BETWEEN PHLYCTENULAR CONJUNCTIVITIS AND INTESTINAL PARASITES

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Abstract

This study was carried out on fifty children suffering from Phlyctenular keratoconjunctivitis and attending ophthalmology outpatient clinics of Sohag University Teaching Hospital and Sohag Ophthalmology Hospital, of them 30 (60%) male and 20 (40%) females with age range from 6months to 14 years. Fifty stool samples were collected and examined microscopically for detection of any parasitic infection. 12(24%) cases were infected with *Hymenolepis nana*, one (2%) case was infected with *E. hyistolytica*, one case was infected *Enterobius vermicularis*, one case was infected with *Giardia lamblia* and one case was infected *Tenia* spp., regarding to age and sex distribution of the disease, male gender and age ranged from 6-8years were more affected, rural children were more affected than urbans one.

Keywords: Phlyctenular keratoconjunctivitis, Children, Gastro-intestinal parasites

Introduction

Phlyctenular keratoconjunctivitis is a nodular inflammation of the perilimbal tissues that occurs secondary to an allergic hypersensitivity response of the cornea. There are two distinct types of phlyctenular lesions: corneal and conjunctival. Patients typically present with symptoms of tearing, ocular irritation, mild to severe photophobia and a history of similar episodes (Hochedez *et al,* 2003). It is a disease occurring mainly in children. In Egypt it is very common, constituting about 20% of cases of acute conjunctivitis. The disease has been associated with systemic disorders such as Behçet's disease, tuberculosis, HIV and rosacea among others. It is known to be an allergic response of the corneal and conjunctival epithelium to an endogenous toxin. The most accepted theory was that this toxin is a tuberculoprotein (Hashida *et al,* 2003). Al-Hussaini and Saoudi (1968) found that tuberculoprotein did not seem to be a factor in phlyctenular eye disease in Egypt. Bakly (1929) attributed a high incidence of phlyctenular eye disease in Port-Said, Egypt, in association with ascariasis. Jeffery (1955) found that *Ascaris lumbricoides, Ancylostoma duodenale, Enterobius vermicularis,* and *Entamoeba histolytica* are responsible for a number of eye diseases, phlyctenulosis being the commonest. Al-Hussaini *et al*. (1977) in Egypt found that phlyctenular eye disease was often associated with *Hymenolepis nana* (dwarf tape worm).

This preliminary study, pointed to *H. nana* as having an important role in the aetiology of phlyctenular eye disease, suggested the need for more evidence.

Patients, Material and Methods

This study was carried out from September 2013 to August 2014. Fifty children suffered from Phlyctenular keratoconjunctivitis were selected from ophthalmology outpatient clinics of Sohag University Teaching Hospital and Sohag Ophthalmology Hospital, of them 30 (60%) male and 20 (40%) females with age range from 6 months to 14 years. Other 50 patients of the same age, sex and not suffering from Phlyctenular keratoconjunctivitis were also selected to be used as control group from outpatient clinics of Sohag University Hospital, 27 of them (54%) were male and 23 of them (46%) were females. A written consent was taken from the parents of the children after they had been informed about the nature of the test. Detailed history was taken which include age,

sex, and residence, loss of weight, abdominal pain and diarrhea. Fresh stool samples were collected in clean, dry, sterile, plastic containers, labeled and examined as fresh as possible or stored at 2-8ºC until examined. If the material was stored, 10 % formalin was used as preservative. Stool samples were examined macroscopically to the gross appearance (Consistency, Colour, odour, presence of blood or mucus and presence of any macroscopic parasites). Microscopic examination by direct saline wet mount, iodine wet mount, formol-ether concentration technique & simple flotation methods were done (Garcia, 2007) by low and high power for eggs, larvae and protozoa.

Statistical analysis: Data was organized, tabulated and statistically analyzed using SPSS software statistical computer package version 13 (SPSS Inc, USA). For quantitative data, the mean and standard deviation were calculated. The difference between two means was analyzed using students (t) test and for comparison between more than 2 means one way analysis of variance (ANOVA test) was used. For qualitative data number and percent distribution was calculated. Significance was adopted at $P < 0.05$ for interpretation of results of significance.

Results

In the present study, 16 cases (32%) of the Phlyctenular keratoconjunctivitis associated with parasitic infections and 34 Cases (68%) free of parasitic infections. In control group it was found that 7 cases (14%) (6 cases with single infection and one case with mixed infection) associated with parasitic infections and 43 cases (86%) free of parasitic infections (Figs. 2-6). Regarding to types of parasitic infections, it was found that 12 out of 50 cases (24%) was infected with *Hymenolepis nana*, one case (2%) was infected with *Entamoeba histolytica*, one case (2%) was infected with *Enterobius*, one case (2%) was infected with *Giardia lamblia* and one case (2%) was infected with *Taenia* species. In control group, there was only 2 cases (4.0%) infected with *Hymenolepis nana* (Tab. 1). Regarding to age, it was found that one case out of 15(6.7%) less than 6 years old were infected, 13 out of 25(52%) from 6-8 years old were infected, 2 cases out of 10(20%) more than 8 years old were infected (table 3 & 4). Regarding to residence, it was found that 14 positive cases out of 32 cases (43.8%) in rural area and 2 positive cases out of 18 females (11.1%) in urban area (Fig. 1). As regarding to gender, it was found that 11cases out of 30 boys (36.7%) were infected and 5 cases out of 20 girls (25%) were infected (Tab. 2).

Table 1: Distribution of parasites in cases of Phlyctenular keratoconjunctivitis.

Results	Patients (n= 50)		Control (n=50)		P-value
	No.	%	No.	%	
Hymenolepis nana	12	24.0	2	4.0	0.004*
Entamoeba histolytica	1	2.0	3	6.0	0.617
Enterobius vermicularis	1	2.0	2	4.0	0.558
Giardia lamblia	1	2.0	1	2.0	--
Tenia species	1	2.0	0	0.0	--
Total positive	16	32.0	7	14	0.032*
Total negative	34	68.0	43	86.0	

* P-value < 0.05

There was marked increase in number of patients infected with *H. nana* in Phlyctenular keratoconjunctivitis cases. In controls, only 2 cases (4.0%) were infected with *H. nana* with P-value = 0.004* indicating significance difference between cases and controls.

Table 2: Sex distribution of parasites in cases of Phlyctenular keratoconjunctivitis.

Results	Male (n= 30)		Female (n= 20)	
	No.	%	No.	%
Positive	11	36.7	5	25.0
Negative	19	63.3	15	75.0

There was statistically non-significant increase in number of parasites associated with Phlyctenular keratoconjunctivitis in males.

Table 3: Age distribution among cases.

Age	Patients (n= 50)		Control (n= 50)		P-value
	No.	%	No.	%	
< 6 years	15	30.0	17	34.0	0.834
6 - 8 years	25	50.0	22	44.0	
> 8 years	10	20.0	11	22.0	
Mean ± SD	7.40 ± 2.13		7.11 ± 2.44		0.305

Disease was higher at 6-8years of age and mean value was represented ±SD.

Table 4: Distribution of parasites in relation to age

Results	<6 years (n=15)		6-8 years (n=25)		>8 years (n=10)		P value
	No.	%	No.	%	No.	%	
Positive	1	6.7	13	52.0	2	20.0	0.008*
Negative	14	93.3	12	48.0	8	80.0	

Chi-square test * **P-value** < 0.05

Discussion

Phlyctenular keratoconjunctivitis (PKC) is a noninfectious inflammatory process; presumably resulting from type IV hypersensivity reaction to systemic antigens, it usually occurs in children and young adults (Ardoin *et al*, 2007). While the condition has been described as a complication of staphylococcal blepharitis, *Mycobacterium tuberculosis* and intestinal parasites are other possible causes (Doan *et al,* 2005). *Hymenolepis nana* was discovered by Bilharz in 1851 in the small intestine of a native boy at necropsy in Cairo, Egypt. It affects 10% of children in Egypt and Sudan. A total of 62-63 % of patients with phlyctenular eye disease had *H. nana* ova in their stools. This incidence rises to 75 % among patients with multiple phlyctens. The eggs of other parasites were significantly fewer than those of *H. nana.* The ova of *H. nana* are not easily detected microscopically. Hence the most careful search should be done by a trained observer by both the direct and flotation methods (Belding, 1952). Phlyctenular eye disease is seen in the first two decades of life. The highest incidence was in the 5-15 year age group (80.0%), where the disease more commonly involved men (Sorsby, 1942; Thygeson, 1951). In the present study, sixteen cases (32%) of Phlyctenular keratoconjunctivitis were associated with parasitic infections and 34 Cases (68%) free of parasitic infections. But in controls, seven cases or14% (6 cases with single infection and one case with mixed infection) were associated with parasitic infections and 43 cases (86%) free of parasitic infections with P-value = 0.032* indicating statistically significance difference between cases and control group, with statistically significant increase in number of positive cases in patients with Phlyctenular keratoconjunctivitis can be explained by the fact that the parasitic infections play a great role in the aetiology of phlyctenuler eye diseases. Fourteen positive cases out of 32 cases (43.8%) in rural area and 2 positive cases out of 18 female cases (11.1%) in urban area, there is statistically significant increase in number of positive cases in rural area which can be explained by the fact that the parasites was more common in rural areas. This difference between urban and rural prevalence may be due to many factors which encourage the development and maintenance of parasites as well increased the risk of exposure including poor sanitation, usage of stools as fertilizers, availability of reservoirs through animal breeding and intermediate host e.g. snails in addition to lack of health hygiene. Habib *et al*. (2000) suggested that difference between urban and rural prevalence was contributed to the behavioral and environmental differences that provoked the increased exposure to parasitic infection. Regarding to age It was found that one case out of 15(6.7%) less than 6 years old were in-

fected , 13cases out of 25(52%)from 6-8 years old were infected , 2 cases out of 10(20%) more than 8 years old were infected, there is statistically significant increase in the number of parasites associated with phlyctenular keratoconjunctivitis in age from 6-8 years old which can be explained by the fact that the parasitic infections is more common in this age as children in this age are the most vulnerable group for parasitic infections due to their ignorance of personal hygienic habits and their high energy as they moved around too much and get more exposed to parasitic infections.

Crompton (1999) and El Badawy *et al*. (2001) agreed that the prevalence of parasites were widely varied from place to place, time to time and person to person even in endemic areas according to two main factors; the intensity of exposure to the parasites in one hand and the combating control measures in another hand, both these factors interact together to bring out the incidence and prevalence of parasitic infections. Regarding sex distribution of infection, It was found that 11cases out of 30 male cases (36.7%) were infected and 5 cases out of 20 female cases(25%) were infected ,there is statistically non-significant increase in the number of parasitic infections associated with Phlyctenular keratoconjunctivitis in male patients which can be explained by the fact that boys are more exposed to parasitic infections as they play outside the houses. Zuk and McKean, (1996) attributed sex differences to 1 or 2 causes: (1) ecological (sociological in humans); and (2) physiological, usually hormonal in origin. Examples of the first cause include differential exposure to pathogens because of sex-specific behavior or morphology. The second cause may stem from the well-documented association between testosterone and the immune system; sexually mature male vertebrates are often more susceptible to infection and carry higher parasite burdens. Researches focused on proximate mechanistic explanations for the sex difference in infection rates, but it is equally important to understand the generality of the patterns in an evolutionary context. Because boys potentially gain more than girls by taking risks and engaging in competition, sexual selection pressure has shaped male behavior and appearance to maximize competitive ability and attractiveness (Zuk and McKean, 1996). It was found that 12 cases out of 50 cases (24%) was infected with *Hymenolepis nana* and one case (2%) was infected with *Entamoeba histolytica*, one case (2%) was infected with *Enterobius vermicularis*, one case (2%) was infected with *Giardia lamblia*, one case (2%) was infected with *Taenia* species, there are marked increase in the number of patients infected with *Hymenolepis nana* in Phlyctenular keratoconjunctivitis cases. But in control group, There was only 2 cases (4.0%) infected with *Hymenolepis nana* with P-value = 0.004* indicating statistically significance difference between cases and control group. There was no significant difference between the incidence of other parasites in phlyctenular eye cases and controls. This can be explained by the fact that *Hymenolepis nana* has role in the etiology of Phlyctenular keratoconjunctivitis as it can produce a type of tissue hypersensitivity, phlyctenular eye disease may be partly referred to such an infection. Al-Hussaini *et al* (1979), examined stool samples of 471 patients suffering from phlyctenular eye disease and 157 controls and found that 295(62. 63 %), had *H. nana* ova in their stools as compared with 17 (10. 82%) out of 157 controls. Hussein and Nasr (1991): examined stool and urine analysis of 150 cases of phlyctenular eye disease, and revealed that 115 (76.67%) were positive for intestinal parasites. The most prevalent parasites were *Hymenolepis nana* (49.56%) followed by *Ascaris lumbricoides* (27.82%). Eosinophilia (5-10%) was detected in 90 phlycten cases (60%), 80 of them (88.8%) had parasitic infection. This results agreed with that of the present study but the ratio of infection of *Hymenolepis nana* was more, which

could be attributed to that the prevalence of parasitic infections in area of our study was differenced . The treatment of the phlyctenular eye diseases had been mainly by used of corticosteroids and other systemic biologic immunosuppressive therapy drugs such as infliximab and methotrexate (Joana *et al.,* 2014). Mohammad *et al*., 2008 found a severe recurrent unilateral corneal inflammation in a child whose stool was positive for *Hymenolepis nana*. Following treatment for the intestinal parasite, the child no longer suffered from recurrent ocular surface inflammation.

In conclusion: This study throw a light on the association between phlyctenular eye disease and parasitic infestation, especially *H. nana* which having an important role in the aetiology of the disease as detected by the present study. So any case that suffer from phlyctenular eye disease should be extremely examined parasitologically for excluding of parasitic infestation before starting any treatment which is usually corticosteroid and other systemic biologic immunosuppressive therapy drugs such as infliximab and methotrexate.

Conclusion

The repeated use of corticosteroid and other systemic biologic immunosuppressive drugs in the treatment of eye disease especially in children pave them to risky complications as viral infection, tension increase of eye or even glaucoma, repeated chest infections as well as other opportunistic infections. No doubt, depression of immunity which could be avoid by proper diagnosis of causative agent(s). Periodic surveys should be done to evaluate the problem, community health education especially in rural areas and sanitary disposable of human excreta would minimize the parasitosis.

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Explanation of figures

Figure 1: Distribution of infection according to residence
Figure 2: Direct saline wet mount shows egg of *Hymenolepis nana* (400 X).
Figure 3: Stool smear by formol-ether concentration technique shows egg of *Taenia* sp. (400 X).
Figure 4: Direct saline wet stool smear shows cyst of *G. lamblia* (400 X).
Figure 5: Direct saline wet stool smear shows egg of *E. vermicularis* (400 X).
Figure 6: Iodine stained wet stool smear showed cyst of *E. histolytica* (400 X).