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THE CARDINAL SIGNS AND DIFFERENTIAL DIAGNOSIS OF TRACHOMA AND OTHER ACUTE CONJUNCTIVITIS

by

Ibrahim Ahmed Mohamed, M.B., B.Ch., D.T.M.&H., D.O.M.S.*

In the following article I am not going to discuss the classical signs and the differential diagnosis of these inflammatory conditions of the conjunctiva, but I am going to discuss how, in recent years, we are facing in the Province of Egypt a necessity, when dealing with acute mucopurulent conjunctivitis, to consider seriously the possibility of such cases being viral and not bacterial or purely so in origin, as we used to take for granted in the last half century. The recent advances in the studies of the cytology of epithelial scrapings and discharge in such cases have accentuated the necessity of the considerations referred to above.

In discussing the present status of the epidemiology of ophthalmia in the Province of Egypt in the First Afro-Asian Congress (1) I concluded by saying: "I believe and predict that the country is going to face another type of ophthalmic epidemics whose aetiology is not clear, but all facts point towards viral origin". Professor Mitsui (2) of Japan made a similar statement by saying: "I would like to warn of the fact that the age of bacterial infection is being passed, as it can now be easily controlled by the new therapy. The age of trachoma will also pass away sooner or later as the virus of trachoma is not a true virus and it responds to some chemo-therapeutical agents presently available. Now the age of true virus

* Deputy Director
Memorial Institute for Ophthalmic Research
Giza
Province of Egypt (UAR)
United Arab Republic

infection is just around the corner, in Africa and Asia. We cannot be relaxed even if we eradicate bacterial ophthalmia and trachoma. In Japan, this situation has already been reached".

Dr. N.Haddad (3) of Saudi Arabia said also in this connection: "The virus of keratoconjunctivitis is prevalent in Saudi Arabia. Many of these cases were considered as trachoma without slit-lamp examination".

We can therefore say that in both the Near and Far East, the clinical picture of acute conjunctivitis, cannot conclusively be considered as bacterial in origin,as it used to be even in the presence of a negative bacteriological examination. The differential diagnosis between a bacterial, trachomatous or other viral origin, is getting necessary and even essential.

The intricate co-existence of an acute bacterial conjunctivitis in infants or children and the incipient stage of a trachomatous infection, is well known to all workers in this field in the Province of Egypt. A great number of acute ophthalmias, when kept under observation for a short time after the clearance of the ophthalmia, start to show the typical follicles of Tr. I. On the other hand, in cured trachoma cases, it has been observed if trachoma relapses in these cases, it is accompanied by acute conjunctivitis (Dolon's report 4).

Owing to the preponderance of its bacterial inflammatory manifestations, the trachomatous infection was masked clinically. Recently, as the severity and the incidence of acute ophthalmias are receding, the picture of incipient trachomatous infection is gradually ebbing on the surface. The question of an acute trachomatous conjunctivitis, or at least an acute incidence of trachoma, is being very cautiously discussed in the Eastern Mediterranean Region. The WHO Expert Committee on Trachoma states in the second report, 1956: "Item 2.3 - The Committee considers that trachoma may arise as an acute disease even in the absence of secondary bacterial or viral infection, but this acute onset is rare. Most cases of uncomplicated trachoma are of insidious onset. The term chronic should not be used in this connection".

Recent clinical observations and the great progress in laboratory and microscopic methods of diagnosis do not justify describing an acute onset of trachoma by the Expert Committee as rare. Perhaps if we refer to the same report specifying the clinical diagnosis of trachoma we can find an explanation. It says:

"Item 2.2 - In making the clinical diagnosis of trachoma two at least of the following should be present:

1. Follicles (conjunctival or limbal)
2. Epithelial keratitis most marked in the upper part of the cornea.
3. Pannus in the upper part of cornea.
4. Typical scars. "

Only the second finding can be considered as an indication of onset of trachoma, the other being relatively late manifestations of trachoma infection, even that second sign of epithelial keratitis is very difficult to demonstrate except by biomicroscopy which is not easy to use for infants and young children in whom the acute onset of trachoma is almost always seen. It is, therefore, if we limit ourselves to these criteria of diagnosis of trachoma, that we are apt to consider the incidence of trachoma as insidious because we are basing our diagnosis on relatively late signs in the process of trachoma infection. If the diagnosis is based on the laboratory findings, whether bacteriological, virological, or cytological, the trachoma process will be suspected in its acute phase.

In the Far East, especially Japan, an acute onset of trachoma is now the main current understanding. It may be noted that bacterial conjunctival infection is nothing like we get here. Still there is the other viral infection, particularly the E.K.C. group to be differentiated from acute trachoma. I believe we are approaching the same picture, especially in districts enjoying better hygiene and better standards of living, where both bacterial and trachomatous conjunctivitis is receding and other viral infections are taking the field.

Since the frequent adoption of the laboratory methods in elucidating the diagnosis of an acute conjunctivitis, previously taken for granted as seasonal bacterial, the diagnosis of acute trachoma has been seriously looked for in our countries. In the last few years, Professor Mitsui has paid repeated visits to various countries of the Region, conferring especially on the question of acute viral conjunctivitis, especially trachoma. Some of these were sponsored by the World Health Organization and reported upon (5) (6). He considers that acute onset of trachoma in the Middle East is just as common as in the Far East, although masked in the former by the seasonal bacterial infection. Seeing one or two cases of acute onset of trachoma is not considered by him as an indication of its rarity. On the contrary, (5) he considers it sufficient to be common. His explanation is as follows: "Suppose that trachoma lasts for fifty years on the average (600 months). Acute stage is for four to eight weeks in adults and for one to three weeks in infants. Roughly calculated, therefore, the probability of finding trachoma in its acute stage is one out of 400 to 1,200 cases of random samples. In other words, if we examine, for example, total inhabitants of a village of two or three thousand population where trachoma index is about five per cent, and if we find one or two cases of acute trachoma among them, this result is, from statistical standpoint, enough to prove the universal acute onset of trachoma. My experience in Middle Eastern countries indicates that trachoma starts acutely in these countries too, but most of these cases have been overlooked as a "seasonal conjunctivitis". Certain circumstances such as frequent bacterial invasions at the onset of trachoma in these countries, may give some difficulties in observing pure trachoma at onset; nevertheless, it does not indicate an insidious onset of trachoma".

To recognize the acute onset of trachoma as the rule and not as a rarity is very important in the modern science of trachomatology, because it will straighten the distorted picture of trachoma with its various MacCallan's stages, and will give it a more benign face that need not end in cellular proliferation and distorting scarring of both conjunctiva and cornea. In other words, as Prof. Mitsui says (5), "The classic trachomatologist emphasizes that trachoma is a disease hard to cure and cicatrization and pannus formation are signs characteristic for trachoma. The modern

trachomatologist indicates that an early trachoma is easy to cure; most of the early trachoma can be cured spontaneously without leaving any trace if patients are in good sanitary conditions; even a microscopic pannus can be absent in the earliest stages in some cases".

I believe that most of our colleagues, working on trachoma in this Region, are gradually adopting these views, although with a varying amount of caution, according to the routine methods of differential diagnosis followed. For example, from an article by Bietti and de Gaspare[7] : "The authors conclude that trachoma in all areas under consideration may begin with three different types: insidious onset and chronic course, acute bacterial onset, and pseudo-acute onset, actually following an acute bacterial or viral conjunctivitis, other than trachoma. The first type seems to be by far the most common". On the other hand, there are reports in the Region to the contrary. Z. Sherif [8] in a bacteriological and cytological survey of a group of cases concludes: "Inclusions are found in a high percentage of cases taken as acute conjunctivitis without any sign of trachomatous reaction. These patients were checked weeks later and all had developed trachoma". A very similar statement was made by Wilson of Giza Memorial Institute [9] reporting the very common observation of visible signs of trachoma a few weeks after a clinically typical acute conjunctivitis. In Wilson's case no examinations for the inclusion bodies were made in the acute stage. It can be very easily surmised that in Wilson and Sherif's cases, acute onset of trachoma was a possibility. The concomitant presence of bacterial infection does not exclude the simultaneous presence of acute trachoma, just as the presence of inclusion bodies does not exclude that of bacterial conjunctivitis. Either of the inclusion bodies or the bacteria might be relatively scarce in the specimens examined for the differential diagnosis. Only the great excessiveness of either while the latter is totally negative might be taken as a preliminary indication of the purity of the case. In countries, like ours, this is very rarely the case, especially so for what can be taken as acute trachoma. This has rendered the cytological differential diagnosis of great importance, and as a matter is rapidly being adopted as an imperative test for assurance of diagnosis in a given case of acute conjunctivitis. In such early cases, the cytological tests are based

on stained cell smear preparation from: (1) conjunctival epithelial scraping; (2) smears from conjunctival surface exudate. The first is based on the finding of the epithelial changes and reactions due to the viral infection, a process which can be demonstrated in vivo by corneal biomicroscopy in which the very early epithelial changes and punctate staining reactions are characteristic of early viral trachomatous infection, just as the cellular degeneration in cellular tissue culture of virus is indicative of its growth and transmission. In early established trachomatous infection, these epithelial scrapings will show the typical H.P. inclusion bodies, in their various stages. A recent prominence of such test is due to the striking development of the fluorescent antibody technique of microscopy, based on the immunocytochemical changes in virus infected epithelial cells.

The second method of cell smear preparation from surface conjunctival exudation is based on the result of different chemotactic response of blood cells to the invading organism. It is therefore necessary to take these smears from the part of the conjunctiva where vascular exudate will be at its maximum, e.g. at upper fornix taking layer of exudate next to surface of conjunctiva after gently swabbing upper degenerative accumulations of that exudate.

The type of cells present excessively in these smears is very helpful in making a differential diagnosis of the kind of conjunctivitis most probable. On the one hand, in cases of bacterial infection the polymorphonuclear cells almost monopolize the field, while in viral infection, e.g. E.K.C.s the mononuclears do so. As the trachoma virus stands in between, the cellular contact of a smear taken from the discharge of an acute case shows a mixture of the polymorphs and the mononuclears, with a preponderance of the first, early at the onset, and of the second a little later, provided, of course, the case has no secondary bacterial infection. In case of trachoma, of course, I am referring to the stage of acute inflammation before the appearance of follicles. When these form and do rupture or made to rupture, the cytological picture, as most ably studied by Thygeson, is very characteristic of trachoma, and is therefore used for differentiation between trachoma and other follicular diseases of the conjunctiva.

The series of cytological studies of acute conjunctivitis done lately at the Giza Memorial Institute, along with the frequent observations of negative bacteriological finding has led to the belief that the infantile type of E.K.C. must be investigated among the enormous amount of acute conjunctivitis we see yearly in Egypt. A thorough project of investigation is being carried out now conjointly by NAMRU 3 and the Giza Memorial Ophthalmic Institute. In April 1958, Prof. Mitsui had a tour in our clinic, and examined a great number of acute conjunctivitis in infants and children. He is definitely of the opinion that acute trachoma and the infantile type of E.K.C. are just as common in Egypt as it is in the Far East, although a pure condition is not easy to see, because of the preponderance of bacterial infection.

Clinically the type of acute conjunctivitis which we most suspect to be viral in origin is an acute mucopurulent conjunctivitis with a tendency or an attempt at an early formation of fibrinous milky coating of the conjunctival surface most marked on the fornical part. This fibrinous coating may be denser, giving the appearance of a pseudo-membrane. Both the suspected E.K.C. and acute trachoma show clinically this appearance as compared to the pure bacterial (K.W. - or rarely gonococcal) conjunctivitis. The clinical appearance of the conjunctival fornices helps also to make a preliminary differential diagnosis. In pure bacterial infection the local oedema seems to be affecting principally the conjunctival membrane, resulting in puckering of the fornices and formation of furrows full of mucopurulent discharge. In a suspected viral infection the oedema seems to be more of a subconjunctival bogginess which results in swollen, ballooned fornices, smeared with that milky fibrinous pseudo-membrane described above. It was an interesting observation that cases that proved later to be positive for H.P. inclusions, showed the same clinical picture described above, with the difference that the bogginess of the fornices are less marked and the tarsal conjunctiva shows an indication of an early subepithelial infiltration, which clinically shows most at the tarsal edge near the fornix as a slightly raised linear infiltration along this edge, very reminiscent of the early limbal epaulette of infiltration in the cornea at the incipient stage of trachoma. These are the clinical data by which we can make a preliminary or rapid differential diagnosis of a case of acute mucopurulent conjunctivitis.

They are very helpful observations, especially when dealing with hundreds of cases and in selecting suitable ones for observation or investigation. Of course the laboratory methods of diagnosis are imperative to make a final diagnosis.

In conclusion I may say that the tendency in Egypt now, is not to consider a case of acute mucopurulent conjunctivitis an ipso-facto case of K.W. or mild gonococcal conjunctivitis, as we used formerly to do. A mixed infection of bacterial, viral (E.K.C. and the like) and trachomatous is taken into consideration. The mere presence of K.W. in smear examination does not necessarily indicate a pure K.W. conjunctivitis.

In dealing with such a case from the clinical observation point of view a procedure of differential diagnosis such as follows seems sound:

1. A case showing a milky fibrinous film or a pseudo-membrane as described above is not common to be of bacterial origin in infants or young children. If bacteria are found in the smear in such cases they are mixed infection in most cases.

2. If a case of frank and typical catarrhal or mucopurulent conjunctivitis develops in a course of one week the appearance mentioned in the previous paragraph, a mixed active infection of bacteria and virus is highly suspected, because in a simultaneous infection the incubation period of bacterial conjunctivitis is a few days in general, while that of viral conjunctivitis, is about one week in most instances.

3. When an acute conjunctivitis is cured in a few days by antibiotics, a bacterial origin can be ondorsed. E.K.C. viruses and the like do not respond to antibiotics. Trachoma cases respond to tetracycline but the response is not so dramatic as bacterial ophthalmia.

When such cases are examined bacteriologically and cytologically on the basis discussed above the following procedure seems to be a sound method of differential diagnosis.

1. When K.W. or gonococcus are present in excess in a case of acute ophthalmia that shows no special feature, they are, in all probability, the causative agent. The almost exclusive presence of polymorphs in the smear is to be expected.

2. When K.W. or rarely, gonococcus, are seen in a smear taken from a case of acute conjunctivitis which shows a pseudo-membraneous formation, the following conditions are suspected:

(a) E.K.C. and the like + K.W. (or gonococcus) infection.

(b) Acute trachoma + K.W. (or gonococcus) infection.

In (a) the smear will be showing a reasonable number of monocytes in addition to the polymorphs. In (b) the same picture, but the polymorphs may overshadow the monocytes which should be looked for carefully. An epithelial scraping in these cases will definitely show the H.P. inclusion bodies, and other cells indicative of trachoma. The epithelium scraped and stained might also show the changes ascribed to trachoma infection.

In both (a) and (b) the bacteria will disappear from the smear after the proper antibiotic treatment, but the conjunctivitis remains, however, a little longer according to the therapeutic cure given to the case.

3. If the smear is negative for bacteria or positive only for a small number of staphylococci or xerosis bacillus, a viral conjunctivitis must be suspected, especially if the monocytes predominate in the smear. If H.P. inclusions are not present acute trachoma can be safely excluded.

I must again say that all details mentioned above in this paper refer only to the differential diagnosis of acute conjunctivitis as seen in infants and young children. In adults, however, the question is not so intricate because:

1. The adult E.K.C. is a different picture from acute mucopurulent conjunctivitis. The typical corneal lesions are diagnostic.

2. The age incidence of acute trachoma, in the great majority of cases, is in the early months of life.

3. Biomicroscopy, especially of the cornea, is easily applicable to older patient. This method of diagnosis is almost conclusive in establishing a diagnosis of acute or incipient trachoma.

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