OCCULT URINARY BLOOD IN EXUDATIVE TONSILLITIS

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"If circumstances lead me, I will find
Where truth is hid, though it were hid indeed
Within the centre"

Shakespeare, W (1602)

Definitions

By occult urinary blood I mean blood which cannot be seen with the naked eye in the urine (cf. haematuria) but blood or its components which can be detected by investigative methods as explained in this paper.

By exudative tonsillitis I mean those acute tonsillar infections which show evidence of exudate (patchy yellowish or dirty white areas of pus) in inflamed tonsils.

Introduction

This paper describes a most interesting finding I have come across by chance in recent months when dealing with feverish sore throats in older children and young adults. Pain in the throat is quite commonly caused by an inflammatory response in the lymphoid tissue of the pharynx, tonsils and soft palate to viruses, bacteria, mycoplasmae and fungi. By and large the commonest ones seen are those caused by viruses. The next common are those caused by bacteria, of which the first which usually comes to our mind, but which nowadays is very rare. is diphtheria. The present rarity of this is due to the mass immunization of infants. On the other hand we still have with us streptococcal sore throats, which are very common and whose eradication would perhaps be as important as has been that of diphtheria in view of the very well known medical facts that glomerulonephritis and rheumatic fever "follow" streptococcal infections, about 1 to 3 weeks after a feverish sore throat. Both these conditions are notorious in the medical field as the causes of considerable invalidism, morbidity and even sheer mortality. Thus, recognizing, a streptococcal throat infection from the start is very important, even more so because, penicillin and its newer derivatives (e.g. ampicillin) are bactericidal to the streptococcus. Haemolytic streptococci are still up to now sensitive to penicillin and its derivatives and these can usually be eradicated by at least a full week's course.

Differential Diagnosis of Sore throats

It is usually stressed in medical textbooks that ideally a throat swab should be taken from the start to find the causative organism of a sore throat. In practice however it is not always easy and practicable to carry out a bacteriological examination on every sore throat one encounters. In other words as Francis Bacon aptly puts it. "books must follow sciences, and not sciences books". However, there definite clinical characteristics in the various sore throats which allow one to make a presumptive diagnosis by the presenting symptoms and clinical signs. This paper principally deals with streptoccocal sore throats and a list has been drawn up of the important clinical characteristics all of which as explained later have to be fulfilled before a presumptive diagnosis of a streptococcal sore throat is reached.

Typically the patient gives some such history as this: "Doctor, since a few hours I have suddenly felt unwell. I have a severe pain in both sides of my neck (and here he will show the painful areas with his hand — see fig. 1 — usually grasping the neck with the thumb on one angle of the jaw and the fingers on the other.) Swallowing has become painful, I had rigors and I think I am running a temperature. Besides I have also developed pain in both my loins, which is worrying me, and, in fact, I have left you

a sample of urine should you want to examine it." With such a detailed history one need not be a medical Sherlock Holmes. to find that the patient is indeed running a temperature of at least 102°F (unless antipyretics have been taken). Looking with a good torch and using a tongue depressor one sees that the pharvnx and soft palate are fiery red. Both tonsils are enlarged and they show patchy yellowish or dirty white purulent exudate which may even be confluent in the severe cases. There is in addition anterior cervical glandular enlargement. The urine is usually clear, straw coloured and on examination with Albustix (Ames Co.) or the old boiling method one may find traces of albuminuria. Not to give straightaway to such patients penicillin or derivatives or a suitable alternative antibiotic, should known penicillin sensitivity exist, is, I am sure inviting trouble. Ideally penicillin or a derivative such as ampicillin should be given for a whole week (Gordon & Grant 1961). It is necessary to stress to the patient the importance of completing treatment. I usually tell them that I would like to re-examine their urine after a week to enquire whether they have in fact taken all the tablets presented and, as will be explained later, to see whether the urinary findings have really cleared completely. It is indeed surprising how much patients co-operate in this respect. I am saving this because on the exhibition of penicillin in streptoccocal sore throats there is such a dramatic improvement within 24-48 hours that there is a strong temptation on the part of the patient not to continue treatment for the time prescribed.

Urinary findings

Being short of Albustix (Ames Co.) one day, I decided to test the urine of a patient (patient No. 1) in a more expensive way by Labstix (Ames Co.) To my surprise I found that the patient had no albuminuria but he showed evidence of very considerable blood in his urine. I tried to blame the urine container for this finding and giving the patient's mother a cleaner container and repeating the test, found again a definitely marked positive reaction. I started the patient on a course of ampicillin straightaway and subsequent 'Labstix' tests began

to show a progressive diminution in the evidence of occult blood in his urine. This case gave me a lot of food for thought, and I decided to test the urine with Labstix in most of the cases of sore throat I have encountered recently, especially so when the patient complained of pain in both loins. This led me to discover further cases with similar histories, clinical symptoms and signs, showing occult blood with or without albuminuria. (see table 1).

Case Histories

Case No. I. This is the patient I have just mentioned. His sore throat and fever started the previous day and he was sent home from school because of very marked glandular swelling in his neck. On finding blood in his urine I was admittedly not one hundred per cent certain of the diagnosis and wanted to send the young boy hospital as I would have l'ked to have a white count carried out. However, his parents were against hospitalization, they would not even consider domiciliary consultation, but accepted my suggested treatment of a full course of ampicillin, bed rest, and a salt free diet. I always feel that innocent children should not suffer for their parents' ignorance and so I asked them if I could be allowed to visit the patient and keep an eye on his urine by testing it as I felt that their son was suffering from glomerulonephritis. This diagnosis they challenged as his father had had young when glomerulonephritis he distinctly remembered having frank haematuria and puffiness around his eyelids. I subsequently gained this family's confidence because within three days the big cervical swelling subsided dramatically after ampicillin, the Labstix test for blood showing also a complete clearing Ultimately, after ten days, the parents agreed at least to send the boy to Pediatric Out Patients where the consultant confirmed my diagnosis. To my relief the differential white count was within normal limits, and there was no evidence of abnormal white cells. Subsequent recovery was full and uneventful.

Case No. 2. A school teacher by profession, this young lady gave no history of previous past illnesses. She had marked patchy

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Labstix tfter 1 week Ampicillin	All neg.	All neg.	All neg.	All neg.	All neg.	All neg.
Ketone Blood	Severe	Moder.	Severe	Moder.	Moder.	Slight
Ketone	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
LABSTIX Protein Glucose	Neg.	Neg.	Neg.	Neg.	Trace Neg.	Neg.
LABSTIX Protein Gh	5 Neg.	Neg	+	Neg.	Trace	Neg.
Hd	rO	2	ß	9	9	5
URINE Naked eye characteristics	Smoky, straw coloured	Clear, straw coloured	Smoky, yellow coloured	Clear, straw coloured	Clear, straw coloured	Clear, straw coloured
Approximate Time of onset Naked of Sore Throat	24 hrs.	18 hrs.	48 hrs.	24 hrs.	8 hrs.	12 hrs.
Age	M 11 yrs.	27 yrs.	36 yrs.	29 yrs.	30 yrs.	24 yrs.
Sex	\mathbb{Z}	لثر	Z	ഥ	ഥ	ĪΤ
Patient Sex	MV	AC	FS	MP	CV	$\Gamma\Lambda$
Date	19/10/73	3/12/73	29/3/74	10/4/74	23/4/74	6/5/74
Case No.	-	2	က	4	22	9

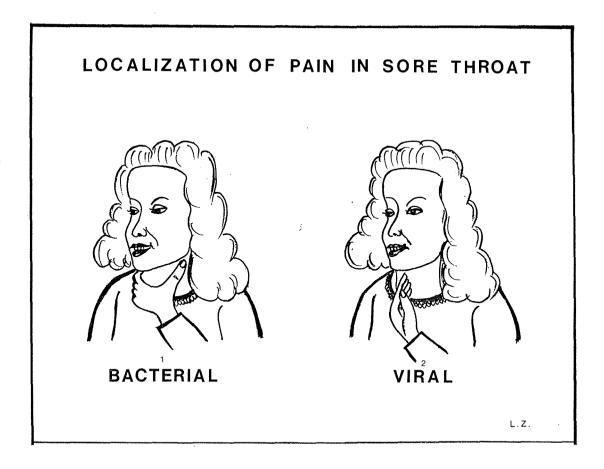
yellowish exudate in her enlarged tonsils and complained of moderately severe pain in both loins. She collected a urine sample for me to examine. On dipping a Labstix reagent strip I again found that this patient had moderate evidence of blood even though her urine was clear and lightly straw coloured. She had no other urinary tract symptoms in the form of pain on micturition, etc., and she was not menstruating. Ampicillin was given with dramatic improvement.

Case No. 3. This patient had no faith in doctors and he never saw one on a professional basis. He ultimately called me at his wife's insistence. His fever and sore throat had been present for about two days before examination and his urine was cloudy but still straw coloured. Labstix however revealed severe evidence of blood and one plus of protein.

Case No. 4. Again here there was no past history of illnesses in this patient but as her father had died of malignant hypertension with kidney failure she was worried about the pain in her loins. Again Labstix was positive for occult blood and she made a quick recovery as soon as ampicillin was started.

Case No. 5. This is perhaps the most interesting case because she was a secundigravida in her sixth month of gestation. I saw her on a routine ante-natal check up on 19.4.74 and found her doing well: the urine showed neither albumin nor glucose, BP was 120/80, and the foetal heart was audible. She called me four days later complaining of sore throat, feeling feverish, and had pain in both loins. Labstix showed a trace of albumin and moderate blood. Ampicillin was prescribed and produced full improvement. Her pregnancy continues satisfactorily otherwise. Her BP remained normal.

Case No. 6. The only important feature here was that two months before she came to me with her feverish sore throat she was being treated for "kidney trouble" with albuminuria. She admitted then to cutting short her penicillin treatment as soon as she was feeling better. Labstix on 6.5.74 showed slight blood but no protein.



Significance of Blood in the Urine

Urine which contains blood or haemoglobin contains also some albumin. Hutchinson and Hunter (1954) found that if human blood is added to normal urine in an amount sufficient to produce distinct smokiness, the quantity of albumin amounts to merely a trace. Even when the quantity of blood added is sufficient to render the urine distinctly red, the amount of albumin as shown by Esbach's method is only ½ per 1,000. It is not surprising therefore that though occult blood was found in the above cases albuminuria was either absent completely or present only in traces. I have recently tested the urine of at least 40 other cases of feverish sore throat and apart from the ones listed in table I no blood in the urine has been found. The negative cases however did not satisfy all the following criteria as the six cases in the table had done. Patients likely to show occult blood must satisfy all these criteria;

- 1 Acute onset of sore throat rendering swallowing painful.
- 2 Fever.
- 3 Pain felt bilaterally below the angle of the jaw. (fig. 1)
- 4 Pain in both loins.
- 5 Patchy yellowish or dirty white exudate in the tonsils.
- 6 Quick response to penicillin or derivatives (e.g. ampicillin).

The presumptive diagnosis in these cases is infection with group A haemolytic streptococcus which happens to have nephritogenic toxic properties besides haemolytic properties. Regrettably no throat swab examinations have been carried out. I feel that this pilot study should be further expanded and cases with the above criteria should be examined bacteriologically with throat swabs and perhaps blood cultures and urine microscopy and culture,

as well as serial measurements of antibody titre (ASO) over a period of 4-6 weeks. Renal biopsies if at all possible from some brave volunteers might give us a definite answer as to what is happening at the glomerulus in this acute phase. The CIBA Symposium in 1960 covered most aspects of the clinical use and value of renal biopsy. When frank haematuria, albuminuria, and oedemic puffiness occur 1-3 weeks after a sore throat there is already an advanced renal pathological condition as evidenced by the various histological findings in the different types of glomerulonephritis. It is sad to realise that these cases have either completely neglected their sore throat or treated it with simple methods of anaesthetic throat lozenges, etc. They usually have not received penicillin at the start. Symptoms of streptococcal infections disappear 3-5 days later even without antibiotic therapy (Davies and Quie, 1971). It seems that the average human is well equipped to deal defensively with pathological strains of streptococci. I think that immunologically maladjusted individuals glomerular damage can occur by the toxic products produced by the haemolytic streptococcus. It must also be remembered that besides haemolysins this micro-organism is known to produce other toxins namely leucocidin, fibrinolysin and erythrogenic toxins. Many strains also form a capsule the main constituent of which is hyaluronic acld which produces mucoid colonies (Fairbrother, 1953). It is in a way not surprising with all these chemical and toxic battles going on, to find occult blood in the urine of patients in the very acute phase of the infection. This is when the injury to the glomerulus starts. I have tried to check this finding in many well known medical textbooks and have not seen it mentioned in the texts relative to streptornical sore throats.

Differential Diognosis

When the soreness is felt in the centre of the neck, (see fig. 2) the most probable cause is a virus. These infections though clinically less severe can take longer, even up to 12 days, to clear. Vesicles and ulcerations but not exudate can be produced by certain viruses i.e. Coxsackie A (herpan-

gina) and herpes simplex. Cough and hoarseness are frequent associated symptoms as many viruses that cause upper respiratory disease also invade the respiratory tract. On the contrary respiratory symptoms are race in streptococcal infections. Pain in the muscles and glandular swellings are also more frequent in viral infections. Persistent smptoms even after ampicillin with pain in the left loin and left costal margin or frank splenomegaly should make one think of infectious mononucleosis Diphteria, which nowadays is rare, should be kept in mind. In Malta, sore throat with persistent undulant pyrexia which might be partially responsive to ampicillin, should make one suspect brucellosis.

Pain in Both Loins

Patients streptococcal with sore throats characteristically complain of pain in both loins and very often, as already mentioned, they collect a sample of their urine to be examined for albumin. In the past we checked such urines for albumin and very often the test was negative and the patient was reassured. Patients with other types of sore throats rarely complain of pain in both loins. I cannot understand why we attributed this pain to the fact that the patient has a fever and perhaps some urinary concentration with or without albuminuria. We at times also reassuringly explained to the patient that the pain might be due to the fact that he has been lying for some hours in bed as we put it in Maltese "tas-sodda". The true fact seems to be that this pain in both loins is in fact kidney pain.

Labstix

According to the information supplied by the makers (Ames Co.) who manufacture these reagent strips, "the blood test area is more sensitive to free haemoglobin and myoglobin than to intact erythrocytes. The chemical test for haemoglobin is designed to complement microscopic examination for erythrocytes. The test gives an indication of the amount of haemoglobin present . . . False positive reactions are found only in urines collected in containers contaminated by strong oxidizing agents such as hypochlorites; iodides are not sufficiently

strong. A negative result for protein does not preclude a true positive result for blood because of the different sensitivities of the two tests"

Conclusions

I firmly belief that one must kill the streptococcus immediately it is suspected. Thanks to Fleming we have a very useful bactericidal drug to do so. The quicker one eradicates the haemolytic streptococcus the less chance it is given to play havoc with kidney glomeruli and perhaps also heart valves. In this instance it is not a question of prevention being better than cure but of complete cure being better than chronic invalidism with pathologic kidney glomerular lesions and rheumatic heart valve disease. It is my conviction that glomerulonephritis arises de novo and concomitantly with an acute streptococcal sore throat rather than "following" such a sore throat infection after one to three weeks, as is generally believed.

Acknowledgements

I wish to thank all my patients who always co-operated and never hesitated to bring me their urine samples when called upon to do so.

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'Albustix' and 'Labstix' are trade marks of Ames Company, Division of Miles Laboratories Ltd., Slough, Bucks, England.