FILARIASIS: HEMATURIA AND CHYLURIA
With
REPORT OF 3 UNUSUAL CASES ★

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At the Shanta Bhawan Hospital, Kathmandu, Nepal we have many cases of Bancroftian filariasis, diagnosed clinically and usually confirmed by night blood specimens, for microfilaria, in the outpatient clinic and treated therein uneventfully with diethyl carbamzine.

Occasionally we admit such patients, either for obvious medical or surgical complications, or those presenting as diagnostic problem, such as fever whose cause is not initially apparent. We report herewith three such cases, each of which presented unusual aspects.

Case I

A 50-year old Nepalese was admitted to the hospital on June 8, 1970 because of pain in the left lower abdomen. This pain was burning in character and recurrent during the previous 3 to 4 months. Other complaints were dry cough of 8 months duration. 6 to 7 loose stools daily without blood for a few days one week prior to admission and mild swelling over the legs for one month before admission.

On physical examination the patient was thin and rather pale. The thyroid gland was moderately enlarged diffusely and soft. The eyes were normal and there was no tremor. Fine crepitant rales were audible over the base of the left lung. There was a grade II apical systolic murmur without radiation was normal. The abdomen was normal. There was moderate right inguinal adenopathy, with adjacent edema as well as mild pretibial edema. Pelvic examination showed a cystocele.

The temperature was 98.0°F, the pulse 90, the respirations 20, and the B. P. 100/60.

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Urinalysis showed a trace of albumin. 5—10 red cells and many white cells per high-power field, but a urine culture was sterile after 48 hours of incubation. The hematocrit was 40 per cent and the white-cell count 10,000 with 61% neutrophils, 21% lymphocytes, 4% monocytes and 14% eosinophils. A night blood examination was reported as "microfilariae positive (many)". A stool specimen showed ova of hookworm and ascaris. A postero-anterior roentgenogram of the chest revealed the trachea indented on its right side by a goitre, transverse diameter of the heart was enlarged (CTI-.6) and the main hilar shadows were prominent. No active lung lesion was seen.

During the first three days the patient was given Bendrofluazide 5 mg. daily; this resulted in diuresis amounting to a weight loss from 84 lbs. (39 kg) to 76 lbs. (35 kg). An initial evening fever of 101°F. was replaced by successively lower ones of 99.8 and 99.2 on the two following evenings. Daily blood pressures were 100/70, 100/70, 90/60 and 90/50.

On the fourth hospital day at 6:00 a. m. she was given 30 ml. of piperazine citrate. At 9:30 a. m. she was given promethazine Hcl (an antihistaminic) 25 mg. orally and diethyl carbamazone 100 mg. The latter was repeated at 1:00 p. m. At 1:50 p. m., she voided 90 ml. of urine on a bed pan. About 2:00 p. m., she was found flat in bed, pulseless and with unobtainable blood pressure. Attending physicians were at the scene a few minutes later and pronounced her dead.

Case 2

A 40 year old Nepalese man was admitted to the hospital in August, 1970, because of bloody urine with clots and sometimes milky urine 4-5 days duration. He also had epigastric pain mostly in the evening which appeared to be relieved by food, for 12 days prior to admission.

Ten years previously the patient had a similar, but transient, episode of bloody urine of unknown cause. He had also been treated for a purulent urethral discharge 7-8 years ago, as well as for positive serology.

Physical examination on admission disclosed only slight inguinal adenopathy. Vital signs were entirely normal. His weight was 94 lbs. (45 kg)

The urine was milky in color and had a heavy red sediment. This appearance was determined to be due to chyle and blood. Microscopic examination also revealed 15-20 WBC per high power field and microfilariae. A night blood specimen was also positive for microfilariae. Hematocrit was 42%. WBC: 7,850 with 86% neutrophils, 5% lymphocytes, eosinophils 4%. A urine culture was sterile. A stool specimen showed no ova or parasites. A Heaf Test was 3 and a VDRL was non-reactive. Postero-anterior roentgenogram of the chest and intravenous pyelography were not remarkable.

Except for an occasional slight elevation in temperature during the first week, the patient remained afebrile. He tolerated a 20-day course of diethyl carbamazine well, which began with 50 mg. once daily then twice daily, then thrice daily for the first three days respectively and 100 mg. thrice daily thereafter. Phenergan 25 mg. twice daily was given on the first 9 days. Daily inspection of the urine failed to show any change in its grossly chylous and bloody appearance, although microfilariae disappeared from both the urine and blood.

After this treatment a cystoscopy was performed. Chylous urine without blood or clots was obtained and the bladder was washed with warm normal saline solution. The mucosa appeared normal. At the upper border of the trigone and attached to the mucosa was a semicircular black thread-like structure with a transparent membrane and tapering ends. This was about 1mm. in diameter and 8-10 cm. in length. It was interpreted to be an adult female filaria.

On the following two days the bladder was irrigated through a catheter with a diethyl carbamazine solution (150 mg. in 50 ml. distilled H₂O). Each time stringy blood clots were passed, which might have contained disintegrated filaria, but no such worm could be definitely identified in this manner grossly. Microscopic examination of the second unfiltered specimen showed many RBC in the sediment and a few sluggish microfilariae even 2 hours after exposure to the diethyl carbamazine solution; 5 1/2 hours later, no motility was seen.

When seen in the Outpatient Department 2½ months after discharge he was asymptomatic: his urine was slightly opalescent, indicative of minimal chyluria; on microscopy there were about 10 RBC/HPF and moderate pyuria, for which he was treated with sulfasoxazole.

Case 3

A 26 year old Nepalese male was admitted to the hospital because of bloody urine and slight low backache of 3 weeks duration. There had been no dysuria or colic. Just before admission a urine specimen was very cloudy, with a reddish color, was packed with red cells, and revealed microfilariae.

One year ago the patient had noticed transient red color and clots in his urine.

Physical examination disclosed no noteworthy finding and specifically no adenopathy, localized swellings, abdominal or flank tenderness. Vital signs were normal.

Hematocrit was 45%, WBC — 13,600 with 62% neutrophils, 22% lymphocytes, 2% monocytes and 14% eosinophils. A night blood was also positive for microfilariae, the density of which was not stated. A stool specimen showed no parasites or ova. A postero-anterior roentgenogram of his chest and a plain film abdomen revealed no abnormalities.

The patient was given promethazine 25 mg. orally twice daily and then started cautiously on small doses of diethyl carbamazine 25mg. Once on first day, then 50 mg. once

daily, then twice daily then thrice daily, which he tolerated unequivocally well. However, one hour before his scheduled third dose of 100 mg. on the first day of this dosage schedule his blood pressure was 80/60 and his pulse 120/minute. He had never had a systolic pressure below 100 previously and usually it was 110-120; and he had never had a tachycardia. Even though he was asymptomatic, diethyl carbamazine was suspended. After an EKG proved normal, this drug was resumed cautiously until he received the maximum dosage of 100 mg. thrice daily, which was continued for a total of 3 weeks, two of which were completed as an outpatient. After initial disappearance of his hematuria and toward the end of the third week of treatment, his gross hematuria and milky urine recurred. An intravenous pyelogram revealed some irregularity in the left renal pelvis and in the bladder contour. On readmission a cystoscopy revealed nothing remarkable.

Discussion: Case 1 demonstrated microscopic hematuria, without chyluria or microfilariae in the urine but no detected cause other than filariasis. Such hematuria has been not uncommon in our experience, although it is not even mentioned in several texts consulted (Brown 1969; Edington et al 1969; Craig et al 1957; Chandler et al 1962) and in two (Adams et al 1966; Cambell 1954), in which it is, described only in association with gross chyluria.

Unfortunately, no necropsy could be performed to assist us in determining the cause of this patient's sudden death. One possible cause might have been a large pulmonary embolus from a thrombosed vein in the thigh, pelvic or retroperitoneal regions. Concurrent thrombopleditis has been described in a 52 page chapter on filariasis by Chatterjee in "Tropical Surgery" (Basu, 1965). He also describes one case of embolus to the heart from a clot extending from the spermatic cord to the inferior vena cava. He does not indicate however, how common such a complication may be. It must remain speculative, but several facts constitute circumstantial evidence that the cause might have been anaphylactic shock from sudden release of much foreign protein from rapid destruction of many microfilariae in the blood by diethylcarbamazine. This was the first known case here in which an experienced laboratory technician has reported "many" microfilariae in the blood. (A second such case had a of 100 mg diethylcarbamazine). Despite the customary concurrent antihistamin treatment this first patient received larger than our usual second dose by weight about 50 minutes before her sudden death, i.e. 100 mg. or about 3 mg/kg body weight although no larger than that recommended by Chandler and Read (1962). Because of frequent allergic reactions (Nrochni 1946; Meyler 1966) up to 29% in one large series (Patel et al 1958) which may be severe local or general one (Jopling 1968) ("Adams and Maegraith 1966) suggest no more than a total of 2 mg/kg body weight in one dose for the first day as well as an antihistaminic drug for the first 4-5 days. They give this dose twice daily on the second day and thrice daily thereafter for 21 days. We were unable to find any reports of sudden death proved to be due to diethylcarbamazine. Proof or not, we believe it is prudent to be cautious initially in such treatment, especially if the patient has many microfilariae in the blood, is dehydrated, malnourished, anemic, hypotensive or has a co-existing serious illness. Elective administration of other drugs, eg. piper-

zine, at the same time should be avoided, especially early in the course of diethylcarbamazine.

Case 2 is remarkable for persistent concurrent chyluria and gross hematuria, not mentioned in any of the texts consulted (Brown 1969; Edington et al 1969; Croig et al 1957; Chandler et al 1962; Adams et al 1966) except one (Campbell 1954). Surprisingly, the presence of microfilariae in the urine is specifically referred to in only two texts (Brown 1969; Adams 1966) and even here the pathogenetic mechanism (s) for this is not elucidated as can be presumed in this case to be this female worm producing microfilariae in the bladder. The latter discovery seems to be the first recorded since the texts repeatedly state the adult worms reside in the lymphatics and lymph nodes and have been reported in sections of the epididymis and testis (Campbell 1954). Until this finding by cystoscopy, it was assumed that microfilariae in the urine were coming from female worms somewhere in the lymphatics surrounding the genito-urinary system, which had ruptured into it, or perhaps even from large concentrations in the blood.

Brown (1969) has stated that diethylcarbamazine is quickly lethal to microfilariae and either kills adult females or permanently sterilizes them. He recommends a shorter course, for 7-14 days, than a commoner one of 21 days recommended by Adams and Maegraith (1966) and a smaller dose of 2 mg/kg body weight thrice daily than the 3 mg/kg suggested by Chandler et al (1962). Our experience in case 2 therefore was surprising in that microfilariae in the urine were still living even two hours after instillation of diethylcarbamazine in concentrated solution into the bladder. Unfortunately, it is still a matter of speculation how long the adult female survived, if indeed she is dead!

In view of his clinical course and appearance of the excretory urogram, we were naturally disappointed that we were unable to find another female worm in the bladder of the third patient (case 3). He was still in need of more than the usual three week course of diethylcarbamazine therapy at the time of cystoscopy, for his relief was transient. This result was contrary to the usual response of chyluria to rest alone, as stated by Adams and Maegraith (1966) and Braimerd et al (1969); however, Campbell (1954) has described the remarkable variability of in the duration of chyluria from days to years (rarely fatal from malnutrition) and the frequently unsatisfactory results with such surgical procedures as renal decapsulation.

Summary

Three unusual cases of filariasis are presented to illustrate:

- (1) the possibility of anaphylactic death from rapid destruction of many microfilariae by diethylcarbamazine;*

- (2) *the probability of frequent microhematuria, unassociated with chyluria, an important differential diagnostic feature in endemic areas, but generally not mentioned in pertinent texts;*
- (3) *the probably not infrequent co-existence of gross hematuria and chyluria;*
- (4) *the discovery of an adult female filarial worm in the bladder in a case of chyluria, hitherto unreported in the available literature.*

REFERENCES

- Adams, A.R.D. and Macgregair, B.G., 1966. Clinical Tropical Diseases 4th Ed., 61; 101. London, Blackwell Scientific Publications.
- Basu, A.K. 1965, Tropical Surgery/Clinical Surgery, 1st Ed., 51-103, London, Butterworths.
- Brainerd, H. et al, 1969, Current Diagnosis and Treatment, 2nd Ed, 853, Lange.
- Brown, H.W. 1969 Basic Clinical Parasitology, 3rd Ed., London, Butterworths.
- Campbell, M., 1954. Urology, 575; 577-580 Phila and London. W.B. Saunders Co.
- Chandlers, and Read, 1962, Introduction to Parasitology. 10th Ed., 480-481, New York and London, John Wiley and Sons, Inc.
- Craig and Faust 1957, Clinical Parasitology, 6th Ed., Philadelphia. 958, Lea and Febiger.
- Edington, G.M., and Giles, H.M., 1969, Pathology in the Tropics 1st Ed., London, Edward Arnold Publishers, Inc.,
- Extra Pharmacopeia, 1968, 25th Ed., London, Marthindale Press. quoting Trop. Dis. Bull 56751, 1959 and Patel, TB and Pamjpey. P.D. (1958) Indian J. Malar, 17, 171.
- Jopling, W. H. 1968, The Treatment of Tropical Disease, 2nd Ed., London, Johnwright and Sons, Ltd.,
- Meyler, L. 1966, Side Effects of Drugs, Vol, V, 361, Amsterdam Excerpta Medica Foundation.
- Nrochini, E., (1964) Trans, Roy, Soc., Trop, Med. Hyg. 58, 4313.