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DIAGNOSIS AND TREATMENT

Neonatal Gonococcal Arthritis: Three Cases and Review of the Literature

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It is well known that gonorrhea is presently out of control, in fact pandemic, in many areas including many in the United States. On the Navajo Indian Reservation in Arizona and Western New Mexico, the incidence of gonorrhea is statistically higher than it is elsewhere in this country. For a population of 101,200 in 1970, the incidence of gonorrhea on the Reservation for fiscal 1970 was 2,480 per 100,000.¹ In 1971 there were 2,564 new cases reported and on a revised population of 188,123, this is an incidence of 1,363 per 100,000 for fiscal 1971.^{2*}

The Fort Defiance, Arizona Indian Hospital provides health services for an estimated 25,000 Navajos. In calendar year 1971 there were 363 new cases of gonorrhea reported there, an incidence of 1,452 per 100,000. With the resurgence of gonorrhea there has been increased reporting of pediatric gonococcal infections.³⁻⁷ In the year August 1971 to August 1972 three proven cases and one presumptive case of neonatal disseminated gonococcal infection were treated at the U.S. Public Health Service Indian Hospital in Fort Defiance. The three proven cases presented as neonatal gonococcal arthritis. A fourth case with a positive blood culture (cord blood) for *Neisseria gonorrhoeae* was also treated. The paucity of information on this disease, and its apparent rarity, stimulated this report.

CASE REPORTS

Case 1

V. K., a healthy, Apgar 10, 3,827-gm (8 lb, 7 oz) male infant was born on August 16, 1971, to a 20-year-old G2P1 Navajo woman after 40 weeks' gestation. Labor and

delivery were complicated by PROM of 36 hours. The mother had a postpartum fever of 37.8 C and was treated with orally administered ampicillin. The infant was normal and left the nursery at 2 days of age. At 3 days of age he developed a purulent conjunctivitis which was treated empirically with topically administered Neosporin. At 9 days of age he was admitted to the Fort Defiance Indian Hospital (FDIH) with a history of irritability and three days of not moving the left leg. Examination showed an irritable infant with severe bilateral exudative conjunctivitis. Other positive findings included edema erythema, and tenderness of the left knee, right great toe, and right fifth finger. There were no skin lesions, and all other joints were normal. A left-knee arthrocentesis revealed purulent synovial fluid. Gram-stained smears and cultures of the synovial fluid and conjunctival exudates revealed *N. gonorrhoeae*, confirmed by sugar fermentation studies. All other cultures were sterile. Treatment consisted of parenteral aqueous penicillin G (see Table I). The infant responded well to therapy and was discharged after 23 days. He was entirely normal at 6 weeks of age.

Case 2

On January 20, 1972, a normal, Apgar 9, 2,667-gm (5 lb, 14 oz) female infant (V.F.) was born to a 20-year-old G2P1 Navajo female after 38 weeks' gestation. Labor and delivery were normal. Immediately postpartum the mother developed sudden gross hematuria and fever of 40 C. Gram stain and culture of the urine revealed *N. gonorrhoeae*. She was treated with 1 gm of probenecid (Benemid), 4.8 mμ penicillin G procaine intramuscularly, and ampicillin orally. The infant was well on repeated physical examinations, and cultures of her blood, urine, and stool were sterile. She was discharged from the nursery well at 5 days of age. At 15 days she was brought to the FDIH night clinic with a two-day history of fever and irritability. Examination showed mild rhinorrhea and a rectal temperature of 37.8 C. She was given antipyretics and nose drops. At 18 days of age she was admitted to FDIH with a history of continuing irritability and a swollen ankle for two days. Positive findings included irritability and obvious arthritis of the left ankle which was held motionless and showed erythema and tenderness over an obvious lateral malleolar

* Although the reported incidence of gonorrhea is higher here than reported nationally, it is believed that this difference reflects better reporting (nearly 100%) in the Navajo Area, and not a higher incidence of gonorrhea in Navajo people.

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effusion. All other joints were normal, there was no conjunctivitis, and there were no skin lesions. Arthrocentesis of the left ankle yielded 5 to 7 cc of purulent synovial fluid, culture of which confirmed the presence of *N. gonorrhoeae*, as substantiated by sugar fermentation reactions. All other cultures were sterile. Treatment consisted of two weeks of parenteral aqueous penicillin G to which she responded promptly. She was discharged on the 15th hospital day and at 2 months of age was perfectly well.

Case 3

On April 15, 1972, a normal, Apgar 9, 3,402-gm (7 lb, 8 oz) female infant (L.S.) was born to a 35-year-old G9P8 Navajo woman after 39 to 40 weeks' gestation and a normal labor and delivery. Three days later both infant and mother were well and accordingly discharged. At 14 days of age the infant was brought to the night clinic with a six-day history of diaphoresis. Physical examination revealed an irritable infant with no fever or identifiable abnormalities. At 18 days of age she was admitted to the FDIH with a history of swelling and redness of the left ankle for two days and of the right ankle for one day. Examination revealed a very irritable infant whose ankles were held motionless and showed discoloration over the medial malleoli, with the left showing more erythema and obvious effusion. Arthrocentesis of the left ankle yielded grossly purulent synovial fluid, and culture and Gram stain showed *N. gonorrhoeae* as confirmed by sugar fermentation. Cultures of the clinically normal rectum and conjunctivae also showed *N. gonorrhoeae*. Treatment consisted of parenteral aqueous penicillin G for two weeks. The patient responded promptly to therapy and was discharged after the 15th hospital day. At 6 weeks of age she was entirely normal. The mother was treated for gonococcal cervicitis on the 20th postpartum day, receiving 1 gm of probenecid and 4.8 mμ of penicillin G procaine intramuscularly.

Case 4

On August 29, 1972, a full-term male infant (B.B.) with Apgar 10 was born to a 33-year-old G6P4Abl Navajo woman after 42 weeks' gestation and 32 hours PROM. The mother developed a fever of 38.3 C five hours postpartum and was treated with penicillin and kanamycin. At birth the infant was perfectly normal. Cultures of the pharynx, rectum, conjunctiva, orogastric aspirate, and cord blood were performed at birth due to the PROM. Four hours later the cord blood culture showed abundant growth of *N. gonorrhoeae* confirmed by sugar fermentation.† The infant was treated with aqueous penicillin G for seven days and kanamycin for five days. All other cultures were sterile and examination remained normal except for mild physiologic jaundice. He fed well, had no temperature irregularity, and no evidence of skin lesions, arthritis, or conjunctivitis. He left the hospital well at 8 days of age, and follow-up examinations at one and three months showed sterile blood cultures and no abnormalities.

DISCUSSION

A summary and comparison of the now ten reported cases of disseminated gonococcal infection in newborns in the postantibiotic era are in Table I.

In the preantibiotic era gonococcal disease would hardly have been considered uncommon. In 1905

Holt⁸ reviewed several hundred cases of gonococcal disease, among whom were two neonates with arthritis. In 1927 Cooperman⁹ reported an epidemic of 53 cases of neonatal gonococcal arthritis which had occurred in a month's time in a nursery in Philadelphia in 1924. Once introduced, the disease was presumably disseminated by fomite passage.⁹ Since these works only occasional single case reports of neonatal gonococcal arthritis have appeared.¹⁰⁻¹⁴

It is clear that as the newborn infant passes through the birth canal, any of its orifices may act as a portal of entry for the gonococcus. The conjunctiva is a well known and oft-reported site for invasion and infection.¹⁵⁻²⁰ However, the anogenital, oropharyngeal, and umbilical orifices are also easily accessible to the organism and recent work⁷ has documented the presence of the gonococcus in the rectum, throat, and orogastric aspirate. In the cases reported here and those reviewed, the portal of entry is not definitely known, though in two of our cases (7, 9; Table I), the conjunctiva and rectum are strongly implicated as primary sites of invasion.

Earlier reviews^{8,9} have adequately described the clinical features usually seen in neonatal gonococcal arthritis and typified by those presented herein. Usually nonspecific prodromal symptoms do occur in neonates. In all of our cases and in most previously reported^{9,11,13,14} there was a history of generalized irritability, poor feeding, and temperature elevation for several days prior to the onset of joint sepsis. Symptoms such as these should lead the clinician to be sufficiently suspicious to investigate further. Fever and/or irritability of unexplained origin in a neonate particularly is indication for at least a lumbar puncture, if not more extensive diagnostic evaluation.

In adults with gonococcal arthritis the course of the disease has been divided into two fairly distinct stages with polytenosynovitis, arthralgias, and skin manifestations representing the early bacteremic phase of the disease; and classical signs and symptoms of septic arthritis becoming apparent in the so-called late, septic joint stage when gonococcal disease is usually easier to substantiate.^{21,22} The early, bacteremic form has never been diagnosed *per se* in neonates. Superficial abscesses, tenosynovitis, bursitis, and subperiosteal abscesses were described in early studies,⁹ but not specifically ascribed to the gonococcus. In adults, skin lesions typical for *N. gonorrhoeae* have been described.²² Cooperman briefly mentions skin lesions in some pediatric patients in the prearthritis stage of their illness, but makes no mention of whether the gonococcus was ever isolated from these lesions. These

† Culture of the cord blood was obtained by the following method: (1) the cord was clamped and cut at delivery; (2) the cord on the placenta was swabbed with povidone-iodine (Betadine) and re-cut with sterile scissors, (3) as the cord was re-cut, blood was allowed to drip freely into a blood culture medium which was then tightly resealed and incubated in a 10% CO₂ atmosphere.

TABLE I
CLINICAL AND LABORATORY FEATURES OF DISSEMINATED GONOCOCCAL INFECTION IN TEN NEONATES

Case	Age		Maternal Gonorrhea	Joint(s) Affected	Max Temp.	WBC	Synovial Fl.		Other Cultures For <i>N. Gonorrhea</i>	Treatment	Days Symptoms After Therapy
	Symp Onset	Hosp Adm					Gm. Sin	Cult.			
1 ¹⁰	21 d	24 d	Presumptive: Mig. jt. pain; Pat. urethra cult. + GC; vag. discharge	L. Knee	?	21000	Pos.	Neg.	Eye, ear, nose, throat, rectum, urethra all Negative	Sulfanilamide for 16 days	14 days
2 ¹³	?	21 d	???	L. Knee	1° ↑	14900	Pos.	Neg.	??	??	27 days
3 ²³	14 d	21 d	Proven: Ureth Smear + GC 3 wks pp	Both Hips esp. R.	1° ↑	17150	Pos.	?	??	Proc. Pen. 300,000 bid for 3d, then q d x 8d & intraarticular pen hip	12 days
4 ¹¹	8 d	13 d	Proven: Cerv cult. + GC at deliv.	L. Hand, L. wrist, L. Knee, R. Ankle	100.4°	30350	Pos.	Pos.	"Negative"	Proc. Pen. 300,000 bid for 3 wks., then intraarticular pen to knee	4 days
5 ¹³	10 d	16 d	Proven: Cerv cult. + GC 2nd pp day	L. Ankle, R. Knee	No inc	18000	Pos.	Pos.	"Negative"	Cryst. Pen q4h 5d, then Proc. Pen. q12h 13 d, then Benz. Pen and in- traarticular pen ankle	1 day
6 ¹⁴	18 d	28 d	Proven: Cerv cult. + GC 28th pp day	Both Ank. & Wrists Esp. L. Ank.	Afeb.	19100	Pos.	Pos.	Blood cultures negative	Aq. Pen. 750,000 u IV x 2 wks (1 million units/ kg/day) + intraarticular pen to ankle	5 days
7	3 d	9 d	Presumptive: PROM 36 h, Fever pp, Cerv cult. "Non-GC Neisseria"	R. 5th Fing. R. 1st Toe L. Knee	102° (38.9)	26500	Pos.	Pos.	Conjunctiva Pos. Blood, rectum, throat, urine all Neg.	Aq. Pen. G 100,000 u per kg/day IV x 9d q12h, then IM q12h x 14 d	21 days
8	13 d	18 d	Proven: Urine cult. + GC 4h pp T = 104 Sterile Cerv cult. 2 wks before deliv.	L. Ankle	100.6° (38.1)	10200	Pos.	Pos.	Two each blood, throat, urine, conjunctiva, rectum all Nega- tive. Maternal blood, throat, lochia Neg.	Aq. Pen G 100,000 u per kg/day IV x 10d q12h, then IM x 4 d q12h	4 days
9	8 d	18 d	Proven: Cerv cult. + GC 20th pp day	Both Ankles	100.4° (38.0)	19700	Pos.	Pos.	Conjunct. Positive Rectum Posi- tive Blood, throat, urine all Negative	Aq. Pen G 100,000 u per kg/day IV x 7d q12h, then IM x 7 d q12h	6 days
10	Onset Birth		Presumptive: Neg. Cerv. Cult. 4, 7 mes. pid but PROM 32h pp T = 38.3°	None	99.2°	—	No arthritis		Blood culture (Cord) Positive Conjunct. orogast. asp., pharynx rectum all Negative Maternal cervical, urine, blood cultures all sterile (done at delivery)	Aq. Pen G 100,000 u per kg/day IM x 7 d q12h; Kanamycin 15 mg/kg/d x 5 d	Never symptom.

were described as "toxic rashes distributed over the body or extremities . . . and superficial abscesses in various parts of the body."⁹ In contrast none of the patients in Table I displayed skin lesions of any kind.

Laboratory investigation of the synovial fluid will usually establish the diagnosis. In the past, cultures of joint fluid have not been positive where clinical signs and gram stains have been suggestive for *N. gonorrhoeae*.^{13,23} By means of chocolate agar, and more recently Thayer-Martin, the sensitivity of the cultural diagnosis of gonococcal disease has greatly increased.

TREATMENT

In previously reported cases, treatment with penicillin for a minimum of three weeks and in excess of 4 million units has been recommended. In addition, local therapy with intra-articular penicillin was an accepted mode of therapy (Table I).^{13,14} It has been shown recently that there is usually no need for intra-articular penicillin therapy in the treatment of septic arthritis.²⁴ Different modes of systemic therapy have been successfully employed in the treatment of neonatal gonococcal arthritis. In each of our patients, treatment consisted of aqueous crystalline penicillin G in doses of 100,000 units/kg/day in two divided doses, intravenously for at least one week, and for a total of at least two weeks of parenteral therapy. In the patient with the positive cord blood culture treatment was limited to one week of intramuscular therapy with the identical dose of penicillin.† There were no complications of any kind with this therapy, and all patients were normal at this writing. Although the doses of penicillin were certainly adequate (i.e., sufficient to effect cure), administration should have been on either a q six-hour or q four-hour basis for those infants over 5 to 7 days old in order to account for the increased renal excretion of penicillin at this age. With this alteration the aforementioned regimen should be considered in the treatment of disseminated gonococcal infection of the newborn.

Although identification and management of neonatal gonococcal disease is clearly important, a consideration of much greater priority should be toward prevention of these states. It is generally accepted that neonatal gonococcal infection originates in the mother infected with *N. gonorrhoeae* and that the infant acquires this infection during passage through a birth canal that harbors the or-

ganism. Intrauterine infection of the fetus from a mother who has had asymptomatic disease during pregnancy is well recognized for diseases such as cytomegalic inclusion disease, rubella, syphilis, and toxoplasmosis. However, intrauterine infection from the far more common, asymptomatic maternal gonorrhea has not been seriously considered. The possibility of intrauterine infection of the fetus with *N. gonorrhoeae* was mentioned as early as 1905.^{8,15} More recently, Handsfield has described a case with orogastric contamination with *N. gonorrhoeae* in an infant born by cesarean section following PROM, thereby proving intrauterine acquisition of the gonococcus.⁷

It is suggested that this is a much more common occurrence than previously recognized. In the cases discussed here, seven of ten mothers had positive evidence of gonorrhea, and ten were treated for gonococcal disease in the perinatal period. In all of their infants, infection could conceivably have been acquired *in utero* as well as during passage through the birth canal. Though all infants described received 1% silver nitrate prophylaxis at birth, two subsequently proved to have gonococcal ophthalmia. The other case of gonococcal arthritis displayed no other positive cultures, and here too infection could conceivably have occurred *in utero* as well as at delivery. Similarly, the positive cord blood culture could represent *in utero* acquisition of the organism as well as contamination at delivery.

It is this concept of intrauterine acquisition of *N. gonorrhoeae* that fosters the idea that disseminated neonatal gonococcal infection is preventable. The incidence of asymptomatic gonorrhea in pregnancy ranges from 5% to 10%.²⁹⁻³¹ Because of the potential in neonates for not only ophthalmia, but also for disseminated gonococcal disease such as joint sepsis, and because of the possible increased morbidity in pregnancy and its attendant neonatal morbidity,⁷ it is strongly recommended that endocervical and rectal cultures for *N. gonorrhoeae* should become routine in all prenatal care.

Until such time as future studies further delineate the incidence and pathogenesis of gonococemia in newborns, consideration should be given to an investigative and preventive approach to management of infants whose mothers have proven or suspected gonococcal disease. Our current regimen toward this end includes (1) thorough bacteriologic investigation for *N. gonorrhoeae* in all prenatal patients, with cervical and rectal cultures being done at the first prenatal visit and the last visit before delivery; (2) treatment with 1 gm of probenecid and 4.8 mμ of penicillin G procaine intramuscularly for all positive cultures, and subse-

† This patient also received kanamycin for five days though this should have been discontinued as soon as the remaining cultures proved to be sterile.

quent follow-up cultures after therapy; (3) continuing use of silver nitrate prophylaxis with the understanding and suspicion that failures can and do occur; (4) thorough bacteriologic investigation of the neonate at delivery, including cultures of the orogastric aspirate, pharynx, rectum, conjunctiva, cord blood, and peripheral blood, with specific culturing for *N. gonorrhoeae* (Thayer-Martin) as well as routine investigations; (5) consideration of any positive (gonococcal) culture as at least presumptive evidence of disseminated gonococcal infection, and institution of systemic penicillin therapy as outlined earlier; and (6) in the absence of positive cultures, close follow-up on several occasions during the infant's first month following discharge from the nursery. In addition, mothers of these asymptomatic, culture-negative infants are instructed to observe closely for the signs of arthritis as well as for general signs and symptoms suggesting illness in newborn infants.

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