Urinary Infection Presenting with Jaundice

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Urinary infection in infancy often presents a problem in diagnosis in the absence of the classical symptoms of loin pain, frequency of micturition, or dysuria. Rather, urinary infection enters the differential diagnosis of the unwell infant who vomits, fails to gain weight, and has few, if any, localizing signs on examination.

Occasionally the presenting symptoms may even be misleading. We report here the case histories of three infants in whom urinary infection presented with jaundice, the true diagnosis becoming apparent only on examination and culture of the urine. A case with similar features occurring in an older child is included as it may throw further light on the problem.

Case 1

A previously healthy 7-weeks-old male infant was admitted to hospital with history of jaundice, pale stools, and dark urine for "a few days." He was febrile (103° F. ; 39.4° C.) and appeared to have abdominal pain. Other than icterus, the only notable feature on examination was the presence of a tender liver palpable 3 cm. below the costal margin. The kidneys were not palpable and the external genitalia appeared to be normal. There was no superficial sepsis.

Investigations.—Serum bilirubin 4 mg./100 ml. ; thymol turbidity and zinc sulphate normal ; alkaline phosphatase 34 K.A. units ; urinalysis for bilirubin and urobilinogen was negative ; haemoglobin 54% ; white cell count 36,000/cu. mm. ; blood urea 43 mg./100 ml. with normal electrolytes. A urinary infection was clearly shown by the findings of organisms ++ on microscopy, with a white cell count of 1,045/cu. mm., and a heavy growth of paracolon bacilli on culture.

Treatment with ampicillin resulted in a rapid clearing of the urinary infection and a return of serum bilirubin to a normal level. Intravenous pyelography and micturating cystourethrography, performed after the infection had settled, were normal.

Case 2

A 3-weeks-old male Nigerian infant was admitted to hospital with one week's history of jaundice, pale stools, and dark urine. There had been occasional vomiting for 12 days, becoming increasingly severe during the previous 48 hours, and he had not gained weight in the week before admission. Examination revealed an afebrile baby with moderate icterus, minimal enlargement of the liver, and a large umbilical hernia but no signs of sepsis. The kidneys were not palpably enlarged and external genitalia appeared normal.

Investigations.—Serum bilirubin 5.5 mg./100 ml. ; thymol turbidity 2 units, zinc sulphate 3 units ; alkaline phosphatase 15 K.A. units ; and serum glutamic oxaloacetic transaminase (S.G.O.T.) 29 units (normal range 3–25) ; the urine contained bilirubin but no urobilinogen ; haemoglobin 78% ; white cell count 15,000/cu. mm. A urinary infection was apparent on finding protein ++, organisms + on microscopy, white cell count of 614/cu. mm., and a heavy growth of *Escherichia coli* on culture. Intravenous pyelography, performed later, showed no abnormality.

The urine became sterile after treatment with ampicillin and sulphadimidine, and the serum bilirubin returned to normal. Follow-up as an outpatient has shown no further urinary infection.

Case 3

A previously healthy female infant was admitted to hospital when aged 4 weeks. There was a history of anorexia, loss of weight, fever, and mild jaundice, with no localizing symptoms. On examination she was fretful, with a temperature rising to 103° F. (39.4° C.), anaemia, mild icterus, a palpable mass in the right loin, but no other abnormal signs.

Investigations.—Haemoglobin 60% ; white blood count 18,000/cu. mm. ; urea 145 mg./100 ml. ; serum bilirubin 2.7 mg./100 ml. ; thymol turbidity, zinc sulphate, and alkaline phosphatase normal ; S.G.O.T. 14 units ; urinalysis showed a trace of protein, 675 leucocytes/cu. mm. on microscopy, with a scanty pure growth of *E. coli* on culture.

The child was thought to have a urinary infection, with the presence of a right renal mass raising the question of a perinephric abscess. Treatment with cloxacillin and ampicillin resulted in the jaundice clearing, fever settling, urine becoming sterile, urea dropping to 43 mg./100 ml., and resolution of the mass. Intravenous pyelography 13 days after admission showed no abnormality.

Fifteen days after admission the child again became febrile, and urinalysis revealed 945 leucocytes/cu. mm. with a heavy mixed growth of *E. coli* and *Klebsiella aerogenes* on culture. There was no jaundice associated with this episode. After treatment with intramuscular Colomycin (colistin sulphomethate) the symptoms settled and the urine again became sterile. Follow-up as an outpatient showed no further urinary infections, and the haemoglobin rose spontaneously to 75% (having fallen to 50% during the acute illness).

Case 4

The following case is presented because it appears to us to be of considerable interest. The patient suffered from infectious hepatitis. Jaundice reappeared on two occasions after the initial remission ; each time it was apparently due to the presence of urinary infection.

A 12-year-old girl developed an illness characterized by slight jaundice, pale stools, dark urine, anorexia with vomiting, and malaise ; the symptoms settled during the next two to three weeks and were thought to be due to infectious hepatitis. On the day before admission to hospital she became febrile, vomited, and again was noted to be jaundiced. The principal examination findings were a temperature of 101° F. (38.3° C.), mild icterus, a palpable tender liver, and a palpable spleen. There had been no urinary symptoms or any renal tenderness.

Investigations.—Haemoglobin 74% ; white blood count 7,650/cu. mm. (neutrophils 73%) ; E.S.R. 97 mm./1 hr. ; serum bilirubin 2.2 mg./100 ml. ; alkaline phosphatase 22 K.A. units ; thymol turbidity 7 units ; zinc sulphate 9 units ; urine showed urobilinogen +++, bilirubin nil, protein +, pus cells +++ on microscopy, with a heavy growth of paracolon bacilli on culture.

Her temperature fluctuated up to 104° F. (40° C.) during the first 48 hours, but rapidly settled on treatment with ampicillin. She was discharged in apparent good health 11 days later on a maintenance dosage of ampicillin, the urine being sterile.

Three weeks later jaundice reappeared, though severe systemic symptoms were absent, and she was readmitted to hospital. Investigations now showed: serum bilirubin 6.4 mg./100 ml ; thymol turbidity 16 units ; zinc sulphate 18 units ; alkaline phosphatase 65 K.A. units with S.G.O.T. 585 units (normal range 3 to 25) ; urobilinogen and bilirubin were present in the urine ; L.E. cell preparation was negative ; two consecutive urine specimens contained protein with a pure growth of *E. coli* on culture. Treatment with tetracycline was associated with relief of the jaundice, and later urine specimens contained no protein and were sterile.

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Continued follow-up as an outpatient has shown no evidence of further urinary infection, and liver-function tests nine months later showed serum bilirubin 0.5 mg./100 ml., thymol turbidity 3 units, zinc sulphate 4 units, with a moderately elevated alkaline phosphatase of 34 K.A. units.

Discussion

The association between jaundice and urinary infection has previously been documented. Görter and Lignac (1928) described the cases of three infants with pyelitis complicated by jaundice, the one fatal case having necropsy evidence suggestive of pyaemia. Several series have been published since, notably those of Bernstein and Brown (1962) and Hamilton and Sass-Kortsak (1963). In these series the emphasis has been on jaundice as a feature of septicaemia associated with pyelitis—being primarily studies of infants in whom blood culture was positive.

Bernstein and Brown (1962) analysed 70 cases of infants with positive blood cultures (ante mortem or post mortem), all of whom came to necropsy. Of these, 14 (20%) were jaundiced and seven of the nine who presented with jaundice after the first week of life had evidence of pyelonephritis—five due to *E. coli* and two to paracolon bacilli. Six of the seven cases were jaundiced when first seen, jaundice being terminal in the seventh. The common histological lesions were bile stasis, intracellular pigment retention, and "toxic" cellular abnormalities. The authors felt that, in the absence of evidence of mechanical ductal obstruction, jaundice was due to inability of partially injured cells to excrete bile. Incidentally, none of the seven cases with pyelonephritis had underlying malformations of the genitourinary tract.

The series described by Hamilton and Sass-Kortsak (1963) consisted of 24 infants with septicaemia complicated by jaundice, which was the presenting symptom in 11 of the 24 cases. Among 18 infants in whom urine culture was performed 16 had urinary infections (13 due to *E. coli*) associated with gross pyuria. The nature of the jaundice was ill-defined, there being no evidence of actual infection of liver tissue in fatal cases coming to necropsy, and the authors felt that jaundice was initially due to red-cell haemolysis (Thurman, 1960), and, later, the result of toxic changes with hepatocellular dysfunction. Seven fatalities occurred in eight cases presenting in the first week of life, contrasting with four deaths among 16 cases presenting from the second week onwards. In a similar study of sepsis of obscure origin in the newborn Silverman and Homan (1949) reported jaundice as a feature in 14 out of 25 infants having positive blood cultures, pyuria being present in 9 of the 14 cases.

In our cases blood cultures were not undertaken. None of the infants had umbilical sepsis—a possible source of ascending infection leading to septic hepatitis or descending infection via the umbilical arteries leading to urinary infection—nor any signs of overt sepsis elsewhere. The mechanism whereby bacterial infection causes jaundice remains obscure. The low haemoglobin levels (78%, 60%, and 54% respectively in infants aged 3, 4, and 7 weeks) in the absence of overt loss of blood are suggestive of a haemolytic process. Absence of urobilinogen from the urine in Cases 1 and 2 is in keeping with an obstructive element which is almost certainly intrahepatic in origin, due to cellular injury. Zuelzer and Brown (1961) have postulated that a further factor in infection causing hyperbilirubinaemia, involving the immature liver, may be interference with the enzyme systems essential for conjugation of bilirubin.

The important feature of the cases described was the association of urinary infection with otherwise unexplained jaundice as the presenting symptom, the jaundice clearing with the cure of the infection. We would certainly support Hamilton and Sass-Kortsak (1963) in suggesting that any jaundice of sudden onset accompanied by leucocytosis raises suspicion of infection. In all cases of obscure jaundice in infancy urine culture is mandatory and blood culture desirable.

Summary

Jaundice was the presenting feature in four cases of urinary infection. The association is not uncommon, and its importance is stressed. Treatment of the urinary infection in each case resulted in disappearance of the jaundice.

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Squamous Carcinoma of the Thoracic Oesophagus in Malabsorption Syndrome

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This paper reports the occurrence of carcinoma of the oesophagus in four patients with malabsorption syndrome. In these cases the growth was situated in the lower two-thirds of the oesophagus, and anaemia was megaloblastic in three and normocytic in one. These features differ from the classical Patterson–Kelly association of postcricoid lesions and iron-deficiency anaemia.

The first case occurred in a man of 23, and his death was the only one recorded for oesophageal carcinoma in the age group (20–24) in England and Wales during the year 1957. Inevitably there appeared to be a connexion between his lifelong history of coeliac disease and the development of oesophageal carcinoma, particularly as the second case, admittedly in an older patient, occurred in this hospital during the same year, but it seemed wise to await further cases before reporting the association. The third and fourth cases occurred in 1962 and 1964 respectively, and it was the latter one, also in a comparatively young person, that determined this report.

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Case 1

This patient first attended the London Hospital in July 1952, at the age of 18. There was a story of diarrhoea since infancy with stunted growth noted from the age of 5. He had had severe discomfort from recurrent aphthous stomatitis for as long as he could remember and the second dentition was poor. His height was 4 ft.