*Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 23 (3), pp. 349—355 (1982)*

# Use of thrombocytopenia for the early identification of sepsis in critically ill newborns

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The detection of thrombocytopenia seems to have gained widespread use as an early sign of neonatal septicaemia. A prospective study of 78 full term and preterm babies was done to clarify the significance of serial platelet counts for early sepsis identification in critically ill and ventilated newborns. The results show that thrombocytopenia in this special patient group is too unspecific to be associated with septicaemia. Neither sporadic nor serial platelet counts are suitable as a reliable diagnostic test for the early detection of neonatal septicaemia.

The diagnosis of neonatal septicaemia is based on finding a bacteraemia with pathogenic organisms correlated with corresponding clinical symptoms. Because it usually takes at least one to two days for the microbiological detection of bacteria and because of the non-specific clinical manifestations in full term and premature babies [5, 13], simple and rapid auxiliary diagnostic tests have been devised for the early identification of neonatal sepsis. The platelet count seems to have gained widespread use in routine clinical work as a screening test for the early detection of septicaemia [1, 2, 3, 9, 10, 12, 14, 16]. Although the usefulness of this sign is somewhat questionable in non-critically ill newborns [7, 11], more reservations seem to arise in relation to critically ill and ventilated babies [13]. The following prospective study was done in order to clarify the significance of serial platelet counts for early sepsis identification in critically ill newborns.

## SUBJECTS AND METHODS

Seventyeight full term and preterm babies with birth weights from 900 g to 4410 g who were admitted to the Intensive Care Unit of the University Children's Hospital Düsseldorf from January to October, 1978, were studied. On a flow sheet clinical data (symptomatology, endotracheal intubation, intravascular catheters, antibiotic therapy), laboratory and microbiological culture results were documented over the two to fifty-two days period of treatment in the Unit. As a routine test, on all babies serial platelet counts were performed daily in a counting chamber according to the method of Feissly—Lüdin [4], and from a peripheral vein 0.5 ml blood was drawn every second day and sent for bacteriological investigation. In case of suspected septicaemia additional cerebrospinal fluid and urine specimens were examined for pathogenic organisms. The diagnosis of sepsis was established according to the following findings [14]:

1. Bacteraemia with an organism considered pathogenic.

2. The same germ was detected in all blood samples and (if examined) in the cerebrospinal fluid and urine cultures.

3. Appropriate clinical manifestations

TABLE I

Clinical data of the 78 children in the study

| Patient No. | Normal platelet counts | Chronic thrombocytopenia | Sudden drop in platelet count | Endotracheal tube | Bacteraemia | Adequate clinical symptoms | Other diagnoses | Antibiotic therapy |
|---|---|---|---|---|---|---|---|---|
| 1 | + | | | + | E. coli | + | HMS | + |
| 2 | + | | (+) | + | Streptococcus | + | HMS | + |
| 3 | + | | (+) | + | Listeria | + | AS | + |
| 4 | | + | | + | Serratia | + | HMS | + |
| 5 | + | | (+) | + | Listeria | + | AS | + |
| 6 | + | | (+) | + | Serratia | + | AS | + |
| 7 | + | | | + | Staph. aureus | + | AS | + |
| 8 | + | | | + | Staph. aureus | + | HMS | + |
| 9 | | + | | + | E. coli | + | AS | + |
| 10 | + | | | + | E. coli | — | A. S. | — |
| 11 | | | + | + | Ps. aeruginosa (terminal) | — | HMS, IVH | — |
| 12 | + | | | + | Ps. aeruginosa (terminal) | — | HMS, IVH | + |
| 13 | + | | | + | Staph. epiderm. | — | HMS | — |
| 14 | | + | | + | Staph. epiderm. | — | HMS | — |
| 15 | | | + | + | Staph. epiderm. | — | HMS | — |
| 16 | | + | | + | Staph. epiderm. | — | HMS | + |
| 17 | + | | | + | Staph. epiderm. | — | HMS | — |
| 18 | + | | | + | Staph. aureus | — | HMS | — |
| 19 | | + | | + | Staph. aureus | — | HMS | — |
| 20 | | + | | + | — | — | HMS | — |
| 21 | | + | | + | — | — | HMS | — |
| 22 | + | | | + | — | — | AS | + |
| 23 | | + | | + | — | — | HMS | + |
| 24 | | + | | + | — | + | AS | + |
| 25 | + | | | + | — | — | Pneumonia | + |
| 26 | | + | | + | — | — | AS | — |
| 27 | | + | | — | — | — | Ileus operation | + |
| 28 | | + | | + | — | — | Heart disease | + |
| 29 | | + | | + | — | — | Pneumonia | + |
| 30 | | | + | + | — | — | HMS | — |
| 31 | | + | | + | — | — | AS | — |
| 32 | | + | | + | — | | HMS | — |
| 33 | | + | | + | — | — | Paroxysmal tachycardia | — |
| 34 | | + | | + | — | — | Meconium aspiration | + |
| 35 | + | | | + | — | — | AS | + |
| 36 | + | | | + | — | — | HMS | — |
| 37 | + | | | + | — | — | AS | + |
| 38 | | | + | + | — | — | HMS | — |
| 39 | + | | | + | — | — | HMS | — |
| 40 | + | | | + | — | — | Heart disease | — |
| 41 | + | | | + | — | — | HMS | — |
| 42 | + | | | + | — | — | HMS | — |
| 43 | | + | | + | — | — | Rh-Erythroblastosis | + |
| 44 | | | + | + | — | — | HMS | — |
| 45 | | | + | + | — | — | HMS | + |
| 46 | + | | | + | — | — | HMS | — |
| 47 | | | + | + | — | — | HMS, IVH | — |

TABLE I (cont.)

| Patient No. | Normal platelet counts | Chronic thrombocytopenia | Sudden drop in platelet count | Endotracheal tube | Bacteraemia | Adequate clinical symptoms | Other diagnoses | Antibiotic therapy |
|---|---|---|---|---|---|---|---|---|
| 48 | | + | | + | — | — | HMS | — |
| 49 | + | | | + | — | — | HMS | — |
| 50 | | + | | + | — | — | HMS | — |
| 51 | + | | | + | — | — | HMS, IVH | + |
| 52 | | | + | + | — | — | Diaphragmatic hernia | — |
| 53 | | | + | + | — | — | HMS | — |
| 54 | | | + | + | — | — | HMS | — |
| 55 | + | | | + | — | — | HMS | — |
| 56 | | + | | + | — | — | HMS | — |
| 57 | + | | | + | — | — | AS | — |
| 58 | | | + | + | — | — | HMS | + |
| 59 | | + | | + | — | — | PFC | — |
| 60 | | + | | + | — | — | Heart disease | — |
| 61 | + | | | + | — | — | Heart disease | — |
| 62 | | | + | + | — | — | AS | — |
| 63 | + | | | + | — | — | HMS | — |
| 64 | | | + | + | — | — | AS | — |
| 65 | | + | | + | — | — | HMS | — |
| 66 | + | | | + | — | — | HMS | + |
| 67 | | + | | + | — | — | HMS | — |
| 68 | | + | | + | — | — | HMS | — |
| 69 | | + | | + | — | — | HMS | — |
| 70 | | | + | + | — | — | AS, IVH | — |
| 71 | + | | | + | — | — | HMS | + |
| 72 | | + | | + | — | — | HMS | + |
| 73 | | + | | + | — | — | HMS | — |
| 74 | + | | | — | — | — | Oesophageal atresia | + |
| 75 | | + | | — | — | — | Small-for-dates | — |
| 76 | | + | | + | — | — | HMS | — |
| 77 | | + | | + | — | — | HMS | — |
| 78 | + | | | — | — | — | Ileum resection | + |

Abbreviations:
HMS = Hyaline membrane syndrome; AS = Aspiration syndrome; IVH = Intraventricular haemorrhage; PFC = Persistent fetal circulation; Adequate clinical symptoms = clinical manifestations pointing to septicaemia

after exclusion of other, quickly determined causes (i.e. complications of respiratory therapy, anaemia, hypovolaemia, congestive heart failure, hypoglycaemia, acidosis, hyponatraemia).

## RESULTS

The main indication for transfer of the 74 babies to the Intensive Care Unit was respiratory failure calling for endotracheal intubation and ventilation. Only 4 of the newborns were treated without any sign of ventilatory disturbance (postoperatively after an ileus operation,; oesophageal atresia; ileum resection; small for date baby of a mother with toxaemia). Sixty-seven babies had an intravascular catheter (umbilical artery, umbilical vein, cutdown) some time during

the observation period, 11 had scalp needles for intravenous fluid therapy. According to the above definition there were 9 full term and preterm babies considered to have sepsis (Nos 1—9). Another 10 (Nos 10—19) had positive blood cultures some time during the treatment, but these were regarded either as contamination or transient bacteraemia. The results of the daily platelet counts could be subdivided into three groups.

1. Normal platelet count (>150,000/mm$^3$).

2. Chronic thrombocytopenia (<150,000/mm$^3$) during a period of several days.

3. Sudden drop in platelet count (<100,000/mm$^3$) within 24 hours.

Table I shows some relevant data of the babies in the study.

The use of antibiotics did not alter the potential diagnostic value of serial platelet counts as can be seen in Table II of the temporal correlations of platelet counts with positive blood cultures, the first observation of clinical manifestations and the first day of antibiotic therapy in the septic babies.

Among the 69 non-septic patients there were only 2 (Nos 25 and 29) with assumed focal bacterial infection (pneumonias). The liberal use of antibiotics in numerous patients without signs of any bacterial infection can only partly be explained by the prophylaxis; it was rather the result of a diagnostic uncertainty in regard to the unspecific clinical manifestations of infections in critically ill newborns.

Besides the chronic thrombocytopenia in 2 cases and the sudden drop in platelet count in 4 cases, another 30 patients with chronic thrombocytopenia and further 14 patients with a sudden drop in platelet count could be observed without any sign of septicaemia. Except patients Nos 45 and 58, all the other 12 babies with a sudden drop were not treated with antibiotics, so that an alteration of the platelet count by antimicrobial therapy could be excluded. In addition, 20 of the patients with chronic thrombocytopenia did not get antibiotics and were not assumed to have any focal bacterial infection.

No further diagnostic tests were performed for the evaluation of thrombocytopenia not associated with septicaemia.

## Discussion

Looking at the efforts to find a simple and rapid auxiliary laboratory test for the early detection of septicaemia, one cannot miss to encounter thrombocytopenia [1, 2, 3, 9, 10, 12, 14, 16] especially in relation to Gram negative septicaemias [1, 2, 12]. In a study of postoperative paediatric surgical patients Rowe et al. [12] emphasized the significance of a drop in the platelet count as an early sign of Gram negative sepsis. In their series, 100% of the children with Gram negative septicaemia had platelet counts <150,000/mm$^3$, 71% had values <100,000/mm$^3$. A similar optimistic opinion was expressed by Modanlou and Ortiz [10].

TABLE II

Temporal correlation of thrombocytopenia with positive blood culture, the appearance of clinical manifestations and the start of antibiotic therapy

| Patient No. (birth date) | Date | Blood culture | Platelet count mm³ | First observation of clinical manifestations | Antibiotic therapy |
|---|---|---|---|---|---|
| 2 | 7—5 | Streptococcus | 187,000 | | — |
| (7—5—78) | 7—6 | | 174,000 | ++ | + |
| | 7—7 | — | 135,000 | | + |
| | 7—8 | | 210,000 | | + |
| | 7—9 | — | 34,000 | | + |
| | 7—10 | | 85,000 | | + |
| | 7—11 | — | 177,000 | | + |
| 3 | 1—13 | Listeria | 148,000 | ++ | — |
| (1—13—78) | 1—14 | | 151,000 | | — |
| | 1—15 | — | 18,000 | | + |
| 4 | 1—19 | — | 74,000 | | — |
| (1—19—78) | 1—20 | | 76,000 | | — |
| | 1—21 | — | 80,000 | | + |
| | 1—22 | | 83,000 | | + |
| | 1—23 | Serratia | 100,000 | ++ | + |
| | 1—24 | | 45,000 | | + |
| 5 | 3—17 | Listeria | 200,000 | ++ | + |
| (3—17—78) | 3—18 | | 115,000 | | + |
| | 3—19 | — | 100,000 | | + |
| | 3—20 | — | 118,000 | | + |
| | 3—21 | — | 98,000 | | + |
| | 3—22 | | 141,000 | | + |
| 6 | 3—26 | — | 180,000 | | — |
| (3—26—78) | 3—27 | | 220,000 | | — |
| | 3—28 | — | 200,000 | | — |
| | 3—29 | | 230,000 | | — |
| | 3—30 | Serratia | 210,000 | | — |
| | 3—31 | Serratia | 120,000 | | + |
| | 4—1 | — | 114,000 | ++ | + |
| | 4—2 | — | 93,000 | | + |
| 9 | 9—19 | — | 82,000 | | — |
| (9—19—78) | 9—20 | | 54,000 | | — |
| | 9—21 | E. coli | 15,000 | ++ | + |
| | 9—22 | | 18,000 | | + |
| | 9—22 | | 18,000 | | + |

For the often difficult diagnosis of sepsis in critically ill and ventilated newborns [13], such a simple and rapid test would be of great value. There are, however, some theoretical reservations concerning its usefulness. Although there is a pathophysiological association of septicaemia and thrombocytopenia without disseminated intravascular coagulation (DIC), the authors emphasize the combination of thrombocytopenia — DIC and septicaemia [3, 9, 12, 16]. In any case, thrombocytopenia is a criterion of the diagnosis of DIC, so that a drop in platelet count may be considered a sign of DIC, irrespective of the presence of septicaemia. Considering that asphyxia, hypoxia, acidosis and respiratory distress syndrome may also be associated with DIC in the newborn under intensive care [6], the usefulness of the test for the early identification of septicaemia becomes questionable. Another argument for the unreliability of thrombocytopenia in these special patients is the observation of a drop in platelet count in premature babies treated with phototherapy for hyperbilirubinaemia [8]. Finally, thrombocytopenia may also occur in association with intravascular catheterization. The tip of the catheter is always covered with a thrombus. During the procedure of drawing blood from an artery, platelets can be trapped at the tip and dissimulate the real platelet count [15].

These theoretical reservations are supported by practical experience. Serial platelet counts were done in 50 (64%) of the 78 studied patients. An association with septicæmia could be documented in six cases only.

As to the temporal correlation of thrombocytopenia with positive blood cultures and the appearance of clinical manifestations (Table II), one sometimes finds a chronic thrombocytopenia from the beginning (Patients 4 and 9) while in other instances the drop in platelet count occurs late, two to four days after the positive blood culture and the clinical manifestation (Patients 2, 3, 5, 6), an observation already described by other authors [7, 11]. It is therefore concluded that 1) neither sporadic nor serial platelet counts are suitable for use as a diagnostic test for the early detection of neonatal septicaemia; 2) a thrombocytopenia occurring in critically ill and ventilated newborns is too unspecific to be associated with septicaemia; 3) normal platelet counts do not exclude septicaemia.

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*Received October 29, 1981*

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