SHORT REPORT

Extreme thrombocytosis in admissions to paediatric intensive care: no requirement for treatment

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Arch Dis Child 2007;**92**:515–516. doi: 10.1136/adc.2006.111484

Extreme thrombocytosis (ExtThr; platelet count $\geq 1000\times10^9$/l) is uncommon but may have an increased occurrence in critically ill children. The incidence of ExtThr for children on the Paediatric Intensive Care Unit at Bristol Royal Hospital for Children between January 2001 and December 2004 was calculated, and the notes of children identified with ExtThr were reviewed for possible common aetiological factors, potential treatment regimes and outcome.

Thrombocytosis is defined as an elevated platelet count. For healthy neonates, infants and children, the range of normal platelet counts is from 150×10^9/l to 450×10^9/l, with thrombocytosis usually being defined as a platelet count of $\geq 500\times10^9$/l. A further arbitrary classification has been chosen, in which extreme thrombocytosis (ExtThr) is defined as a platelet count of $\geq 1000\times10^9$/l.[1] Thrombocytosis can be classified as primary (essential) or secondary (reactive). Primary thrombocytosis is a myeloproliferative disease and is extremely rare in childhood. Secondary thrombocytosis results from increased megakaryocyte production and thrombopoiesis, and is a reactive process usually caused by infection, chronic inflammation, tissue damage or neoplasia.

METHODS

All children who had a full blood count examination performed while on the Paediatric Intensive Care Unit (PICU) between January 2001 and December 2004 were identified from the local pathology electronic records, which were crossed checked with the PICU admission records. The incidence of ExtThr was calculated, and for those children identified with ExtThr, the cases notes were retrospectively reviewed for possible common aetiological factors, other associations and outcome.

Local research ethics approval was not required as this study was considered to be a service evaluation and appropriate clearance was obtained from the trust Caldicott Guardian.

RESULTS

Incidence

During the study period there were 2749 admissions to the PICU. The incidence of ExtThr was 1.1% (31/2749). The maximum platelet count recorded during a PICU admission was 1659×10^9/l.

Age at admission

The age distribution of children with ExtThr is shown in table 1 and is in keeping with the age ranges of all children admitted to the PICU. The median admission age was 9 months. There was an excess of males in the group with ExtThr (M:F ratio, 1.6:1), which is above that seen for all admissions (M:F ratio 1.32:1).

Mortality

The incidence of death was 2/31 (6.5%) children with ExtThr, which was not markedly above that of the whole population of children admitted to the PICU (4.9%).

Length of stay

ExtThr was associated with a prolonged length of stay (median 16 days, range 2–425 days) compared to the PICU population as a whole during the same period (median 3 days). Six patients with ExtThr remained on the PICU for more than 30 days, of whom four stayed for more than 100 days. This prolonged length of stay appears to be a reflection of illness severity and disease processes rather than a consequence of thrombocytosis, with no child in the ExtThr group being noted to have any obvious sequelae secondary to their markedly raised platelet count.

Aetiology and sequelae

The possible aetiologies of thrombocytosis in children with ExtThr are shown in table 2. In many cases, due to their complexity, the aetiology appeared to be multifactorial. In the majority of cases there was a confirmed infection or episode of sepsis, of which 10 were due to *Staphylococcus aureus*. Respiratory infection appeared to be a particular risk, and in three infants viral bronchiolitis was the only risk factor identified. In eight children, ExtThr was associated with previous platelet consumption, secondary to bleeding or thrombus formation. No child underwent a bone marrow examination for investigation of their thrombocytosis. Thrombosis or the complications of thrombosis were not noted in any child secondary to ExtThr.

Treatment

Nineteen children with ExtThr received no antiplatelet treatment or anticoagulation during their PICU admission. Four children received low-dose aspirin (5 mg/kg) until their platelet counts fell below 500×10^9/l, while three others received aspirin as part of their post-operative cardiac surgical course. Two older children aged 12 and 14 received subcutaneous enoxaparin as part of DVT prophylaxis, while one child who presented with a clotted artificial valve received tissue plasminogen activator (tPA). One other child also received prostacyclin intravenously for pulmonary hypertension, in addition to receiving aspirin.

DISCUSSION

In this study we have found that during a 4 year period over 1% of children admitted to the PICU have an episode of ExtThr (platelet count $\geq 1000\times10^9$/l) during their PICU stay, compared to a reported incidence of just 0.5% for the occurrence of a platelet count $\geq 800\times10^9$/l in a UK children's hospital population.[2]

For all the children in our population, the cause of their elevated platelet count was secondary or reactive thrombocytosis (RT). The incidence of RT in childhood has previously been

Abbreviations: ExtThr, extreme thrombocytosis; PICU, Paediatric Intensive Care Unit; RT, reactive thrombocytosis

Table 1 Admission age distributions for children with extreme thrombocytosis on the PICU and all children admitted to the PICU

Age range	Extreme thrombocytosis (%)	All children admitted to the PICU (%)
Under 1 year	16/31 (51)	47
1–5 years	5/31 (16)	27
5–12 years	7/31 (23)	15
>12 years	3/31 (10)	11

Table 2 Contributing aetiologies for extreme thrombocytosis in children admitted to the PICU

Contributing aetiology	Numbers of children with extreme thrombocytosis (%)
Confirmed bacterial or viral infection	23/31 (74)
Respiratory infection	14/31 (45)
Inflammation/tissue damage	10/31 (32)
Platelet consumption (bleeding/thrombus)	8/31 (26)
Neoplasia	1/31 (3)

demonstrated to have an age-dependent pattern with the highest incidence being found in children of less than 2 years of age.[2–5] In a cohort of hospitalised Canadian children with at least severe thrombocytosis (platelet count $\geq 900\times10^9$/l), the median age was 9 months.[6] Within our population of children with ExtThr, the median age at admission was also 9 months, but as can be seen from table 1, the age distribution of these children closely matches that of all children admitted to the PICU during the study period, with no obvious decrease in incidence with age.

The most likely reason for the higher incidence of ExtThr in our study population, and the age distribution of those with ExtThr, is that it is a reflection of the greater severity of illness of children admitted to the PICU as compared to hospitalised children as a whole. This would appear to be borne out by the increased median length of stay of children with ExtThr as compared to that of all children admitted to the PICU during the study period (16 days vs 3 days). From our study there also appears to be a preponderance of males with ExtThr, as compared to the total population of children admitted to the PICU. The male:female ratio of 1.6:1 is in keeping with that reported in other studies of childhood RT,[4 5 7] although the reason for this excess of male cases is not clear.

Infections, either bacterial or viral, are the main cause of RT at any age during childhood, with previously reported rates of between 30% and 80%.[2–5 7] In our study, the incidence of confirmed bacterial or viral infection in children with ExtThr was 74%, although because of the complexity of the cases, a number of these children also had other possible aetiological factors during their PICU stay. This correlates closely with the previously reported proportion of cases of severe childhood RT (with platelet counts of $\geq 800\times10^9$/l or $>900\times10^9$/l) being due to infection.[2 7] *S aureus* was the most common infective pathogen isolated in our ExtThr group, with 10 out of 31 children having a confirmed infection. Respiratory infections have been particularly implicated as a cause of RT in children, especially those with pneumonia and empyema, in whom the incidence of a platelet count of $\geq 500\times10^9$/l has been reported as being over 90%.[8] In our study, 45% of children with ExtThr had a confirmed bacterial or viral respiratory infection.

Although multiple factors for RT were present in the majority of the children with ExtThr, the incidence of possible inflammation or tissue damage secondary to surgery or trauma is somewhat higher than that previously reported.[1 2] Likewise, the association of ExtThr with a previous episode of bleeding or thrombosis leading to a possible consumption of platelets was 26% in our group. This figure is nearly double the highest previously reported for rebound thrombocytosis alone as a cause of childhood RT,[7] but again is most likely just a reflection of the complicated nature of the most critically ill children admitted to the PICU.

In childhood, RT does not usually result in thromboembolic or haemorrhagic complications. No child in our group with ExtThr was noted to have had a thrombotic or embolic episode following the rise in their platelet count. Similarly, the mortality rate of children with ExtThr was not significantly different from that of the whole population of children admitted to our PICU during the study period.

The majority of children with ExtThr in our study (61%) did not receive any antiplatelet or anticoagulant therapy. Previously it has been suggested that antithrombotic prophylaxis is unnecessary unless other risk factors for thrombosis are present, such as vessel damage or immobilisation,[1] or for neonates and infants, the presence of a central venous catheter, septicaemia or a cardiac malformation.[9] More recent advice has suggested that childhood RT does not justify general prophylaxis with anticoagulants or platelet aggregation inhibitors, even if the platelet count is $\geq 1000\times10^9$/l.[10] The lack of thromboembolic complications in critically ill children with ExtThr and multiple risk factors in our study would seem to support this suggestion.

Conclusions

ExtThr occurs in over 1% of all children admitted to the PICU. Even in this group of at-risk critically ill children it does not appear to lead to thromboembolic complications or have an obvious influence on mortality, and therefore does not seem to need regular treatment.

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Competing interests: None.

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Accepted 22 January 2007

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