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Platelets

Retrospective analysis of 472 Chinese children with chronic idiopathic thrombocytopenic purpura: a single center experience

We retrospectively analyzed the clinical characteristics and management of 472 Chinese children (age 1~14 years) with chronic idiopathic thrombocytopenic purpura (ITP). The distribution of cases by age showed a maximum at 4 years and more patients below 7 years old than between 7 and 14 years old had ITP (337, 71.4% vs. 135, 28.6%). Variable bleeding signs occurred in this series of patients. Steroids therapy was effective for Chinese children with chronic ITP whether as first- or second-line therapy. Traditional Chinese medicine was less effective than steroids.

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Idiopathic thrombocytopenic purpura (ITP) is a disorder characterized by platelet destruction caused by an anti-platelet antibody that results in platelet phagocytosis via the reticuloendothelial system.[1,2] Several papers involving children with chronic ITP have been reported,[3,4] however, a large-scale experience of Chinese children with chronic ITP has not been reported. To explore the clinical characteristics and management of Chinese children with this condition, we retrospectively analyzed 472 consecutive Chinese children (age 1-14 years) with chronic ITP diagnosed in our hospital from January 1980 to December 2000. The diagnosis of ITP was based on the previously reported criteria[5] except the cut-off age was 14 years in this study. The data were analyzed by SPSS10.0 statistical software. The response to therapy was calculated by the χ^2 test. A p value <0.05 was considered statistically significant. Of the 472 cases, we found a slight predominance of boys (256, 54.2%)over girls (216, 45.8%). The distribution of cases according to age (Figure 1) showed a maximum at 4 years old and more patients below 7 years old than between 7 and 14 years old had chronic ITP (337, 71.4% vs. 135, 28.6%). Our findings

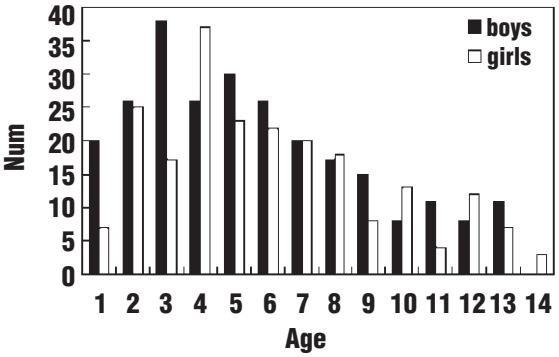

Figure 1. The distribution of chronic ITP in children of different gender and age.

are similar to those reported by Kuhne *et al.*[6] who compared Vietnamese and European cohorts of patients. However, our series showed that the frequency of boys with chronic ITP below one year of age (20 cases) was higher than that of girls (7 cases). This might be due to referral bias, because our hospital is the only one specialized in blood diseases in China, and those patients who were refractory to first-line therapy or who relapsed were usually referred to our hospital. Of the 382 patients for whom data were available, 117(30.6%), 96 (25.1%), 82 (21.5%) and 87 (22.8%) patients had the initial diagnosis made in spring, summer, fall, and winter respectively. At diagnosis, of the 277 patients for whom data were available, there were 147 (53.1%) boys and 130 (46.9%) girls with a mean platelet count of 32.93±21.56×10^9/L (range 2-90×10^9/L) and 34.35±21.15×10^9/L (range 1-90×10^9/L), respectively. Initial platelet counts of <20×10^9/L were found in 50 boys (34.0%) and in 45 girls (34.6%). The difference of platelet counts between boys and girls was not statistically significant (p>0.05). The vast majority of children had mild bleeding symptoms. Purpura and petechiae (430 cases, 91.1%), epistaxis (231 cases, 48.9%) as well as gum bleeding (79 cases, 16.7%) were often seen. No definitive statistical difference was found in the type of bleeding. Intracranial hemorrhage (ICH) occurred in two children (0.4%): one case in a boy 3 months after splenectomy (no platelet count recorded at that time; platelet count 26×10^9/L on the day he was referred to our hospital) who died from a recurrent ICH one year later; the other case in a girl with a platelet count of 6×10^9/L. Our data agree with Iyori's findings on the risk of ICH in Japanese children.[7]

Patients were treated with steroids, intravenous immunoglobulin (IVIG), immunosuppressive agents or traditional Chinese medicine (TCM). Patients who failed the initial therapy received open splenectomy, steroid and/or TCM as a second therapy. Treatment response was defined as follows: complete response (CR): a platelet count ≥100×10^9/L persisting for at least 2 months with no maintenance therapy; partial response (PR): a platelet count between 50-100×10^9/L; and no response (NR): a platelet count < 50×10^9/L. Three-hundred and twenty-four (68.6%) children received first-line therapy (Table 1). Two hundred and thirty-four (72.2%) had been followed up for more than 6 months and 167 (51.5%) for more than 12 months. There were significant differences between steroid treatment and TCM treatment (p<0.005)

Table 1. The response rate to the first- and second-line therapies.

	CR (%)	PR N (%)	NR N (%)	N
First line				
Steroids	48(32.9)	53(36.3)	45(30.8)	146
IVIG	3(30)	6(60)	1(10)	10
TCM	8(14.0)	19(33.3)	30(52.7)	57
S+T*	12(13.0)	35(38.0)	45(49.0)	92
Others**	4(21.1)	3(15.8)	12(63.1)	19
Total	75(23.1)	116(35.8)	133(41.1)	324
Second line				
Steroids	11(30.6)	13(36.1)	12(33.3)	36
IVIG	1(14.3)	5 (71.4)	1(14.3)	7
TCM	11(21.2)	12(23.1)	29(55.7)	52
S+T*	10(30.3)	12(36.4)	11(33.3)	33
Immunosuppressants	5(17.9)	11(39.3)	12(42.8)	28
Splenectomy	46(76.7)	3(5.0)	11(18.3)	60
Total	84(39.0))	56(25.6)	76(35.4)	216

S+T, steroids plus TCM; Others, vitamin C or any non-regulatory therapy.

and between steroid treatment and steroids plus TCM ($p<0.01$). However, there was not a significant difference between TCM and treatment with steroids plus TCM ($p>0.05$). Two hundred and sixteen of the regularly followed patients received second-line therapy because of a lack of improvement in response to the first-line therapy or because of a relapse after remission. Among these, CR rate obtained with open splenectomy (76.7%) was significantly higher than that with any other modality ($p<0.01$). Steroids as a second therapy was not significantly more effective (CR plus PR) than immunosuppressive therapy or steroids plus TCM ($p>0.05$) therapy. As anticipated, TCM therapy was the least effective of the treatments described above ($p<0.05$) compared to each other treatment. In addition, we note that the effect of steroids as second-line therapy was similar to that of steroids used as first-line therapy ($p>0.50$).

In conclusion, the data from our series revealed that the clinical characteristics of Chinese children with chronic ITP are similar to those of a European cohort of patients reported by Khune *et al.*[6] Steroid therapy is effective for chronic ITP whether used first- or second-line. TCM was much less effective than steroids.

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Key words: idiopathic thrombocytopenic purpura, children, steroids, splenectomy

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Stem Cell Transplantation

Bortezomib treatment followed by a second non-myeloablative allogeneic stem cell transplant in two previously autografted patients with multiple myeloma relapse

We report two cases of multiple myeloma relapse and progression following a combination of autologous stem cell transplantation and non-myeloablative allogeneic stem cell transplantation. After failure of donor lymphocyte infusions and thalidomide salvage therapy, the patients were treated successfully with bortezomib and eventually underwent a second non-myeloablative allogeneic stem cell transplantation.

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Patient #1. A 55-year old man was diagnosed with κ light chain multiple myeloma in stage IIIA in March 2001. Serum lactate dehydrogenase levels were elevated at diagnosis. After autologous stem cell transplantation (autoSCT) with melphalan 200 mg/m^2 in August 2001, he then underwent non-myeloablative allogeneic stem cell transplantation (alloSCT) with peripheral blood stem cells (PBSC) from his HLA-identical sister in November 2001 following conditioning with 2 Gy total body irradiation (TBI). Graft-versus-host-disease (GVHD) prophylaxis consisted of mycophenolate mofetil and cyclosporine A, discontinued on days +27 and +131, respectively. A study of chimerism showed full donor hematopoiesis at day +63. Complete remission (CR) was achieved after the establishment of limited chronic GVHD with cholestatic abnormalities of liver function tests requiring cyclosporine A treatment. Relapse occurred on day +567 and was unsuccessfully managed with cyclosporine A discontinuation and 2 donor lymphocyte infusions given on days +619 (1×10^7 CD3$^+$ cells/kg) and +645 (3.2×10^7 CD3$^+$ cells/kg). Thalidomide 100 mg once daily was started on day +763 but was discontinued one month later because of intolerable toxicity.