Immune thrombocytopaenia in adults: a single-centre retrospective review of patients presenting over 7 years

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Abstract

Aim To compare the investigation and management of adult immune thrombocytopaenia in our institution with international guidelines.

Method Adults presenting with immune thrombocytopaenia over a 7-year period were identified from a database. Written and electronic case records were reviewed. Patient demographics, results of investigations and management were recorded and compared with international guidelines.

Results ITP was mild or asymptomatic in 57 of 67 patients (85%). Bone marrow aspiration was performed in 45 patients including 23 of 45 patients under 60 yrs. 15 patients (22%) were tested for HIV at presentation. 28 patients (42%) were inpatients including 18 patients who were asymptomatic or mildly symptomatic. 53 patients (79%) received first-line treatment with oral prednisone including 6 who were asymptomatic with platelets >30×10⁹/L. Splenectomy was performed in 17 patients at a median 7 months after diagnosis.

Conclusion Guidelines were followed in most cases although bone marrow aspirates were often performed unnecessarily in young patients. HIV testing was infrequently requested and should be considered in all new patients presenting with ITP. Asymptomatic patients have a low risk of serious or life-threatening bleeding and do not require admission to hospital. Most patients will eventually achieve a platelet count >30×10⁹/L off treatment.

Immune thrombocytopaenic purpura (ITP) is an autoimmune condition in which reduced production and increased peripheral destruction of platelets occurs. The incidence is between 1 per 1000 to 1 per 10,000 people and increases with increasing age.¹,² Approximately 30% of patients will have chronic thrombocytopaenia which is refractory to first and second-line treatments.³

Spontaneous remission in adult patients is less common than in children. The bleeding risk remains low even with a platelet count less than 30×10⁹/L. The fatal bleeding rate is 0.02–0.04 cases per patient year in those with a platelet count persistently less than 30×10⁹/L.⁴

There have been few randomised controlled trials to guide investigation and management. A review of UK practice in paediatric patients was published in 1997.⁵ Guidelines based on expert opinion have been published by the American Society of Haematology⁶ and the British Committee for Standards in Haematology⁷ with the aim of standardising investigation and treatment of this condition. We retrospectively reviewed a cohort of patients with ITP treated at our institution to compare local practice with these guidelines.
Methods

The institution database was searched for patients diagnosed with ITP between 2000 and 2007. We selected patients with idiopathic immune thrombocytopenia for whom no underlying or associated disease was found. A retrospective case record analysis was performed to record patient age, date of presentation, symptoms at presentation (categorised by type and severity of symptoms) and initial investigations. An investigation was considered as not performed if we were unable to find a result in either the clinical or electronic records.

The reason for performing a bone marrow was recorded if stated in the written clinical record. The numbers of inpatient days and platelet transfusions were recorded. Treatments were recorded as were the response, time to response and any treatment specific side-effects. We recorded the number of patients who continue to be followed-up and the most recent platelet count available.

Symptoms were graded as previously described in a paediatric population – asymptomatic, mild (bruising, petechiae, occasional minor epistaxis, very little or no interference with daily living), moderate (more severe skin manifestations with some mucosal lesions, and more troublesome epistaxis and menorrhagia) and severe (bleeding episodes requiring hospital admission and/or blood transfusion, symptoms interfering with quality of life). Hospital admission alone without significant symptoms was not considered as severe.

The response to treatment was graded as no response (NR); partial response (PR), platelet count rising to >50 or >100 but <150 in those patients whose platelet count was >50 at diagnosis; complete response (CR), platelet count > 150; or progressive disease. Time to response was taken as the number of days between the start of treatment and reaching a platelet count >30. The data was analysed using Microsoft Office Excel 2003.

The standards that we compared our practice to are taken from the British Committee for Standards in Haematology Guidelines on the investigation and management of ITP. We looked at the following recommendations:

- All adult patients with suspected ITP should have a full blood count and blood film to confirm the presence of thrombocytopenia and an autoimmune profile.
- No other routine blood investigations are recommended if the history is typical of ITP; platelet antibody testing is not advised.
- A bone marrow examination is not routinely required unless there are atypical features in the history or examination; the patient is over 60 years old; the patient is due to undergo a splenectomy; those who relapse, on or off treatment, after a complete remission.
- It is suggested that patients with a platelet count over 30 do not need treatment unless they have symptoms or signs.
- The first-line treatments are steroids and IVIG, with IVIG recommended if more urgent treatment is required.

Results

A total of 123 patients’ records were reviewed. Six patients were excluded from the analysis as records were incomplete or the initial diagnostic work-up had been completed at another centre. Sixty two patients were seen in the haematology outpatient clinic. Fifty five patients with suspected mild ITP were initially managed with written advice to the referring practitioner. Additional advice was requested for 15 of these 55 patients. Eight of the 15 patients were subsequently seen by a haematologist and 5 patients who were followed in the haematology clinic were included in the subsequent analysis. Data regarding the remaining 50 patients who were managed with written advice have been previously published. The remaining 67 patients were the subject of this report.

Figure 1 shows the frequency with which investigations were performed.
All patients had a full blood count (FBC). The most frequently requested investigations were anti-nuclear antibodies (74%), lupus anticoagulant (65%) and a coagulation screen (62%). All 15 patients (22%) who were tested for HIV at presentation were sero-negative. Of 51 patients not tested at diagnosis one was later found to be HIV positive (data not available for 1 patient).

Eight of 35 patients who received second-line treatment were tested for Helicobacter pylori and none were positive. Bone marrow aspiration was performed at presentation in 45 patients (67%); 23 of 45 patients were younger than 60 years; 18/23 had asymptomatic or mild disease at presentation. Three of 25 patients aged 60 years and over did not have bone marrow aspiration at presentation. One of the three patients had a bone marrow aspirate after presentation and before proceeding to splenectomy.

ITP was mild or asymptomatic in 57 of 67 patients (85%) including 22 patients with platelets <10×10^9/L. 7/67 patients had moderate symptoms; 2/67 patients presented with severe symptoms (1 patient with menorrhagia presented with a haemoglobin of 45 g/L; 1 patient had severe epistaxis); data was not available for 1 patient. There were no deaths attributable to thrombocytopenia and no cases of intracranial haemorrhage. Symptoms were more common when the platelet count was less than 10×10^9/L (Figure 2). One patient with severe symptoms and a platelet count between 50-99×10^9/L had significant underlying gynaecological pathology which contributed to the bleeding.
Figure 2. Severity of symptoms according to platelet count

Twenty-eight patients (42%) were admitted to hospital including 18 patients who were asymptomatic or mildly symptomatic. Twenty-one of 29 patients (72%) with platelets <10×10⁹/L were admitted, 8/29 (28%) were not. The proportion of patients admitted fell as the platelet count increased (Figure 3). The median length of stay was 3.5 days with a range of 1-13 days. One patient admitted for 13 days had non-medical problems preventing discharge.

1/67 patients received a platelet transfusion on a single occasion when the platelet count was 8×10⁹/L prior to cardioversion for supraventricular tachycardia. Twelve of 67 patients did not receive immediate treatment. Fifty-five of 67 patients (82%) received first-line treatment with either oral prednisone (n=53) or IVIG (n=2). Six of 55 patients who received treatment were asymptomatic with platelets >30. Forty-three of 53 patients receiving prednisone achieved a response (CR 18; PR 25; NR 9; PD 1) which occurred after a median 6 days. Both patients who received first-line treatment with IVIG had a complete response after one and two days. Patients requiring subsequent lines of treatment are summarised in Figure 4.
Figure 3. Inpatients according to platelet count

![Inpatients according to platelet count](image1)

Figure 4. Summary of treatment

![Summary of treatment](image2)
Splenectomy was performed in 17 patients (9 female, 8 male) and data was available for 14/17 patients. The median age at the time of splenectomy was 48 years (range 16–76). The operation was performed at median 7 months after diagnosis (range 2-36 months). The numbers of patients receiving first-, second-, and third-line treatment prior to surgery were 8, 6 and 1 respectively. These treatments included prednisone alone or prednisone and IVIG; the third-line treatment used was azathioprine.

Eight operations were performed prior to 2002 and 7 between 2003 and 2005. Eleven patients had a bone marrow examination at diagnosis; 2 patients did not have one at diagnosis but did so prior to splenectomy; 2 did not have a bone marrow examination at any stage. 12 patients achieved a CR; 3 patients received further treatment, of whom one did not achieve any response and has since been entered into the RAISE trial studying the effect of Eltrombopag.

Twenty one of 67 patients (31%) were followed-up in the haematology clinic for a median 21 months. 46 patients were followed up by their general practitioner. Figure 5 shows the platelet count for these patients at last follow-up. Six of 67 patients (9%) have a platelet count persistently <30x10⁹/L. The number of patients with platelet counts 30-49x10⁹/L, 50-99x10⁹/L and >100x10⁹/L were 4, 11 and 46 respectively.

Figure 5. Platelet count at follow up (median 21 months)
Discussion

The investigation of patients presenting with thrombocytopenia is directed towards excluding causes other than ITP. Bone marrow examination is recommended for selected patients: age over 60 years; before splenectomy; following relapse; and those with atypical features.\(^7\) In our institution bone marrow aspirates were performed without explanation in some younger patients for whom the likelihood of an alternative diagnosis was low. It is possible in these cases that the clinician felt the presentation was atypical for ITP although such no reason was recorded in the clinical notes and none was apparent on review of the data. HIV antibody screening was infrequently requested and should be considered in all new patients presenting with thrombocytopenia.

Asymptomatic patients have a low risk of serious or life-threatening bleeding and do not always require admission to hospital. No randomised trials have been performed to determine the clinical outcomes of treatment of adult ITP and published guidelines therefore reflect a wide variety opinion. In adult patients active treatment is rarely required if the platelet count is more than 30×10\(^9\)/L and there is no bleeding.

In line with current recommendations prednisone was used as first-line treatment with IVIG used in patients with significant bleeding where a more rapid response to treatment was required. In our patients the response to prednisone was seen after a median of 6 days (range 2 to 16 days). Second-line treatments do not need to be considered before this time unless the patient has bleeding complications. Six patients have platelet counts persistently <30×10\(^9\)/L consistent with published data showing that around 10% patients develop chronic, refractory ITP.\(^9\)

Splenectomy is the only treatment for adult ITP that is considered potentially curative but more than a third of patients will relapse and there is a risk of both immediate and long-term morbidity and mortality.\(^10\) The role of splenectomy in the management of ITP has been questioned with the emergence of new treatments and studies supporting the avoidance of aggressive strategies in patients with mild to moderate disease. It is unnecessary for a patient presenting with uncomplicated ITP to require a splenectomy as their second and probably even third-line of treatment in the absence of severe or life-threatening bleeding.

New agents e.g. anti-D immunoglobulin, anti-CD20 monoclonal antibody (Rituximab) and thrombopoietin receptor agonists (Eltrombopag) may eventually replace splenectomy although these agents need further evaluation in clinical trials and are not widely available in New Zealand. The low uptake of splenectomy-sparing strategies in our cohort of patients most likely reflects the high cost, lack of availability of these treatments in New Zealand during the study period and lack of randomised trials comparing these with traditional treatment options.

Conclusion

This audit found disparity between our practice and current recommendations for the investigation of ITP. It highlights that younger patients with typical features of ITP do not routinely require bone marrow biopsy at presentation but all patients should be tested for exposure to HIV. Most patients treated at our institution responded to first-
line therapy with oral corticosteroids but a minority developed chronic, refractory thrombocytopaenia consistent with previously published series.

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