Aplastic anemia related to thymoma: a survey on behalf of the French reference center of aplastic anemia and a review of the literature

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Gendron et al.

Supplemental Methods

Patients from the literature

We searched via PubMed in the National Center for Biotechnology Information (NCBI) database for relevant articles using the keywords « thymoma » together with « aplastic anemia » or « pancytopenia ». References of all selected articles were reviewed for research of additional case reports. We screened a total of 52 patients from 42 articles published between 1958 and December 2018[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,3132,33,34,35,36,37,38,39,40,41,42]. All cases from literature were reviewed and confirmed by expert hematologists (RPL and FSF) and pathologist (AG) who established respectively final clinical AA diagnosis and thymic diagnosis. When available data were sufficient, thymic histology and staging were established according to the 2015 World Health Organization[43] classification and the Masaoka-Koga stage classification[44]. Cases were excluded if they had insufficient laboratory or pathology data to allow significant comparisons. Then, we selected 37 cases patient from 34 articles (**Supplemental Figure 1)** between 1958 and December 2018, with a diagnostic of AA and a previous or further diagnostic of thymoma with histological analysis (thymoma and/or BM or autopsy). Among the selected cases, 11 were reported between 1958 and 1972 and 26 after 1980s and are reported respectively in **Suppl. Table 1** and **Table 2**. Since the 1980s, survival in AA have drastically improved, likely due to immunosuppressive therapy (IST) with cyclosporine A (CsA) use in combination with anti-thymocyte globulin (ATG) increasing response rates of 60% to 70% and the advances in hematopoietic stem cell transplantation (HSCT) as well as better supportive care[45]. Furthermore, diagnosis criteria for AA and thymoma were less established at that time. Thus, the analysis of cases older than the 1980s had a high risk of bias since they were conducted more than 30 years ago and may not be applicable to the standard of care of today (**Supplemental Figure 3**).

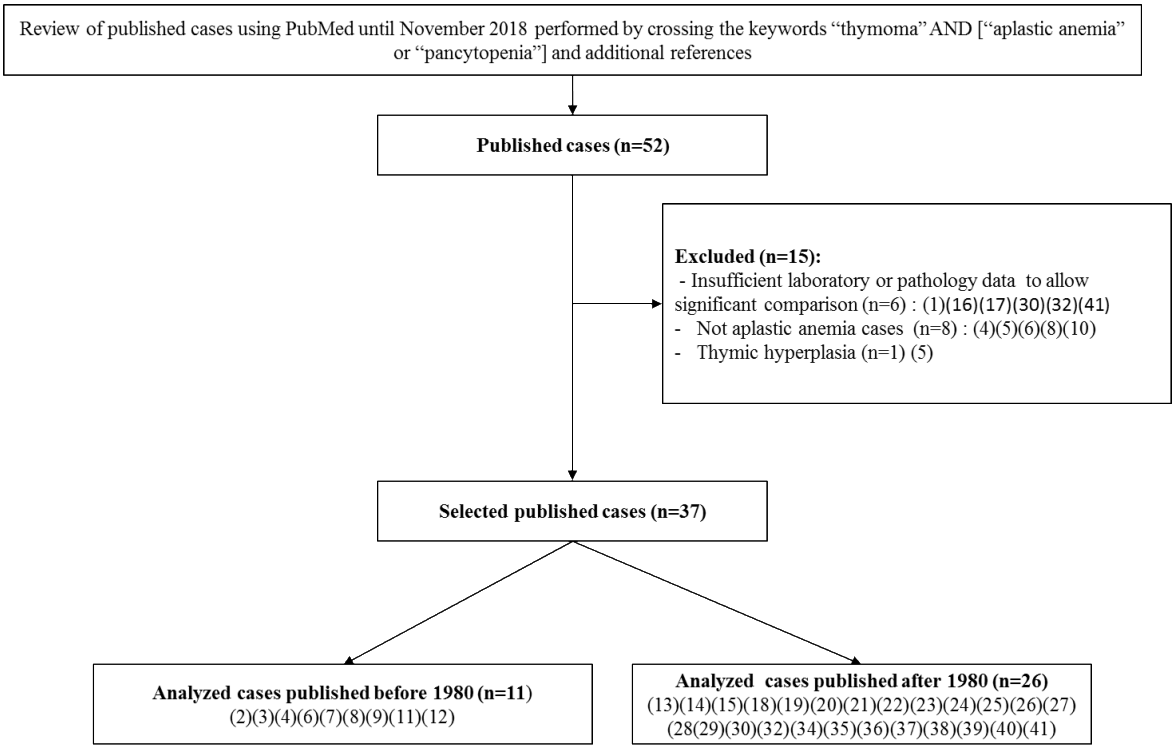
Hematologic response criteria

Hematologic improvements were assessed using the British Committee for Standards in Hematology response criteria[46]. Criteria responses for severe or very severe AA were as follow. A non-response (NR) was defined by a worse response of no achieving the criteria bellow. A complete response (CR) was defined by a platelet count >150 x 10^9/L and hemoglobin concentration normal for age and sex and neutrophils >1.0 x 10^9/L. A partial response (PR) was defined by transfusion independence and no criteria for severe AA. The criteria responses for non-severe AA were as follow. A NR was defined by a worse response of no achieving the criteria bellow. A CR was defined with the same criteria as for severe AA. A PR was defined by a transfusion independence (if previously dependent), or doubling or normalization of at least one cell line, or increase in baseline hemoglobin of >30 g/L (if initially <60 g/L), neutrophils of >0.5 x 10^9/L (if initially <0.5 x 10^9/L), platelets of >20 x 10^9/L (if initially <20 x 10^9/L).

Statistical analysis

Data are described as median and range for quantitative variables, and frequency and percentage for qualitative variables. Variables were compared using Fischer exact test. All statistical tests were 2-tailed with a significance level of 0.05. Survival curve was obtained using the Kaplan Meier estimator. Analyses were performed using GraphPad Prism 5 software (GraphPad Software Inc., San Diego, CA, USA).

Supplemental figure 1. Flow chart of method used for analysis cases reported from literature.



Supplemental figure 2. Patients' treatment lines, management and hematologic responses.

Among the entire cohort, 34 patients (one missing data) received 57 treatment lines. Patient's treatment and hematological response are reported in **Table 1** and **Supplemental table 3**.

Among the treated patient, 30 (88.2%) patients received IST. After first line of IST, the response rate was 60% but 12 (40.0%) patients were refractory. Thus, 18 patients responded to first line of IST: 9 (30.0%) CR and 9 (30.0%) PR. Patients with CR after first-line of IST received CsA alone (n=3), CsA plus ATG (n=4), CsA plus eltrombopag (n=1) and CsA plus predinisone (n=1). Patients with PR after first-line IST received CsA alone (n=5), CsA plus ATG (n=2), CsA plus eltrombopag (n=1) and CsA plus oxymetholone (n=1). Only one patient of 40 years-old had a first line HSCT with haplo-identical family donor and had a sustainable CR during 12 months of follow-up[35].

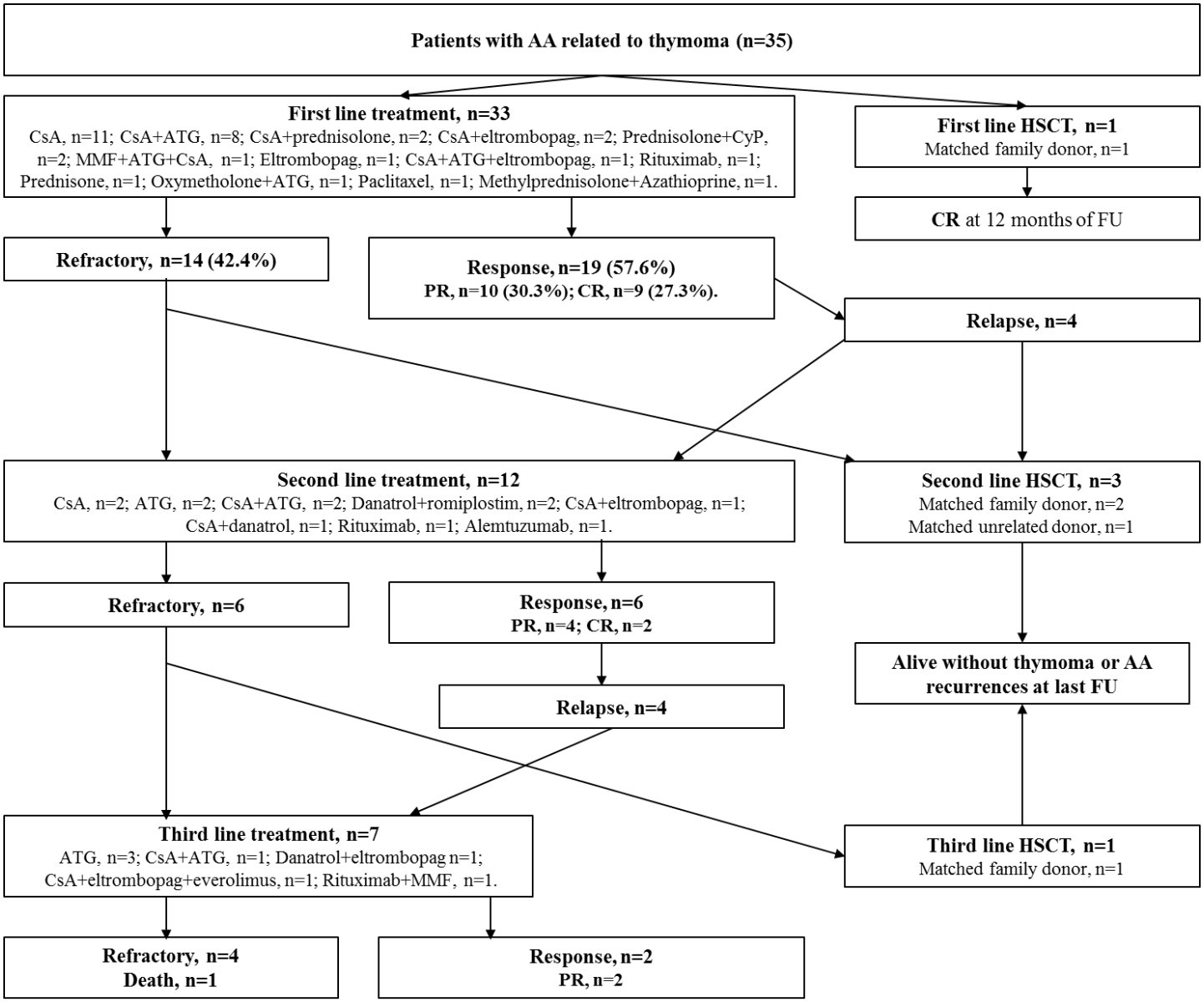
Among patients not responding to first line IST, 9 received a second course of IST. Five patients remained refractory, 2 had a PR and 2 had a CR.

Among the remaining patients refractory after the first line of IST, two underwent HSCT: one with haplo-identical family donor and one matched unrelated donor and both had engraftment and were alive without neither thymoma nor AA recurrences at last follow-up.

Among the 18 patients who respond to first line of IST, four patients (22.2%) with initial PR (n=3) or CR (n=1) had relapse. Among them, one underwent HSCT with a haplo-identical family donor and had a sustainable CR.

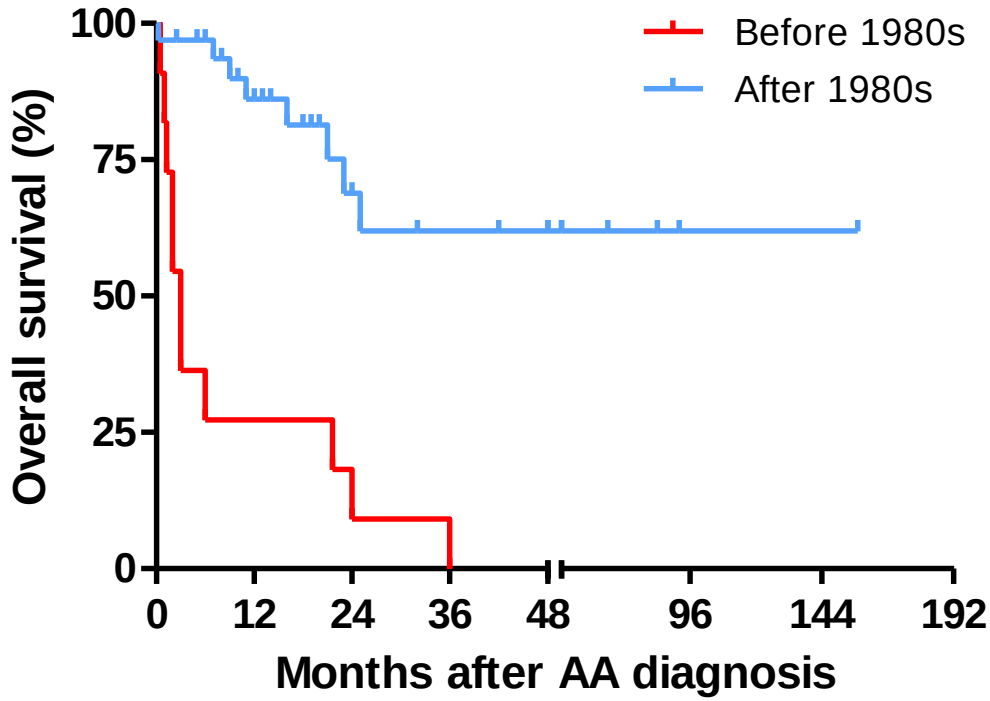
The overall response rate (ORR) was 72.7% with CsA plus ATG, 76.9% with CsA alone and 100% with HSCT. In this study only two reported cases had thymoma progression under IST but these patients had an inoperable thymoma[13,27].

Abbreviations: CsA, cyclosporine A; ATG, antithymocyte globulin; HSCT, hematopoietic stem cell transplantation; NR, non-response; PR, partial response; CR, complete response; CyP, cyclophosphamide; MMF, mycophenolate mofetil; FU, follow-up.


Patients with AA related to thymoma (n=35)
First line treatment, n=33
CsA, n=11; CsA+ATG, n=8; CsA+prednisolone, n=2; CsA+eltrombopag, n=2; Prednisolone+CyP, n=2; MMF+ATG+CsA, n=1; Eltrombopag, n=1; CsA+ATG+eltrombopag, n=1; Rituximab, n=1; Prednisone, n=1; Oxymetholone+ATG, n=1; Paclitaxel, n=1; Methylprednisolone+Azathioprine, n=1.
First line HSCT, n=1
Matched family donor, n=1
CR at 12 months of FU
Refractory, n=14 (42.4%)
Response, n=19 (57.6%)
PR, n=10 (30.3%); CR, n=9 (27.3%).
Relapse, n=4
Second line treatment, n=12
CsA, n=2; ATG, n=2; CsA+ATG, n=2; Danatrol+romiplostim, n=2; CsA+eltrombopag, n=1; CsA+danatrol, n=1; Rituximab, n=1; Alemtuzumab, n=1.
Second line HSCT, n=3
Matched family donor, n=2
Matched unrelated donor, n=1
Refractory, n=6
Response, n=6
PR, n=4; CR, n=2
Alive without thymoma or AA recurrences at last FU
Relapse, n=4
Third line treatment, n=7
ATG, n=3; CsA+ATG, n=1; Danatrol+eltrombopag n=1; CsA+eltrombopag+everolimus, n=1; Rituximab+MMF, n=1.
Third line HSCT, n=1
Matched family donor, n=1
Refractory, n=4
Death, n=1
Response, n=2
PR, n=2

Supplemental figure 3. Overall survival of patients after thymoma-associated aplastic anemia diagnosis. The survival curves of patients with thymoma-related aplastic anemia reported before (red line) and after the 1980s (blue line) were obtained using the Kaplan Meier estimator. Mortality rate of reported cases before 1980s was of 100% with a median survival of 3 months (range 0.5 to 36.0 months) compared to 26.5%and a median overall survival not reached at a median follow-up of 18 months (range 0.25 to 157.0 months; p<.0001).

Abbreviations: AA, aplastic anemia.



Supplemental table 1. Case reported in the literature before 1980 (n=11): patients' characteristics, aplastic anemia and thymoma presentation, management and outcomes.

Patient	Sex/Age at AA diagnosis	AA diagnosis bone marrow aspiration and/or biopsy, cytogenetic	AA Severity	Type of thymoma and stage*, time between AA diagnosis and thymoma resection	Good's syndrome Yes/no	PRCA Yes/No, time between PRCA and AA diagnosis	Other thymoma-related auto-immune disease	First line treatment and response	Second line treatment and response	Outcome, time from diagnosis to last FU and cause of death)
Josse (1958)	F/73	Biopsy alone, No	S	A, post-mortem	No	-	No	Prednisone, NR	Chlorampenicol+ hydrocortisone, NR	Deceased, 3 months
Green (1958)	F/70	BMA and biopsy (post-mortem), No	VS	NA, post-mortem	-	-	No	Chloramphenicol, NR	-	Deceased, 2 months, multiples hemorrhages
Green (1958)	F/78	BMA and biopsy (post-mortem), No	NS	NA, post-mortem	-	Yes, 1.8 years	No	No**	-	Deceased, 1.8 years, severe respiratory infection
Havard (1960)	F/49	BMA alone, No	NS	AB, post-mortem	-	Yes, 1 year	No	No**	-	Deceased, 2 years, severe respiratory infection
Schmid (1965)	M/62	BMA and biopsy (post-mortem), No	S	A, 3 years	-	Yes, 4 years	No	No**	-	Deceased, 3 years, NA

Korn (1967)	M/75	BMA and biopsy, No	M	NA, 4 months after AA diagnosis	-	-	Hypogammaglobulinemia	Testosterone, NR	-	Deceased, 6 months, pulmonary embolism
Hirst (1967)	M/62	BMA and biopsy (post-mortem), No	S	Stage III thymoma, 1 month (inoperable)	-	Yes, 9 months	No	Prednisone, NR	-	Deceased, 3 months, cerebral hemorrhage
Hirst (1967)	M/52	BMA and biopsy (post-mortem), No	S	AB stage I, post-mortem	-	No	No	No**	-	Deceased, 2 months, multiples hemorrhages
Rogers (1968)	F/60	BMA and biopsy, No	S	A, 0 month	-	No	Hypogammaglobulinemia	Prednisone+Testosterone, NR	-	Deceased, 1 month, severe respiratory infection
Talerman (1968)	M/5	BMA alone, No	VS	A stage I, 1 month	-	-	No	Prednisolone+Testosterone, NR	-	Deceased, 16 days, gastrointestinal bleeding
Dawson (1972)	F/20	BMA alone, No	S	Stage III thymoma, 11 months (inoperable)	No	-	Hashimoto's thyroiditis	Prednisone, NR	-	Deceased, 36 days, infectious complications

*Thymic histology and staging according to the World Health Organization classification[43] and the Masaoka-Koga stage classification[44].

**Supportive care only.

Abbreviations: F, female; M, male; AA, aplastic anemia; BMA, bone marrow aspiration; NS, non-severe; VS, very severe; S, severe; PRCA, pure red cell anemia; NR, non-response; PR, partial response; CR, complete response; NA, non-available.

Supplemental table 2. Case reported in the literature after 1980 (n=26): patients' characteristics, aplastic anemia and thymoma presentation.

Patient	Sex/Age at AA diagnosis	AA diagnosis bone marrow aspiration and/or biopsy, cytogenetic	AA Severity	Type of thymoma and stage*, time between AA diagnosis and thymoma resection	Good's syndrome Yes/no	PNH clone Yes/no	PRCA Yes/No, time between PRCA and AA diagnosis	Other thymoma-related auto-immune disease
Thomas (1987)	M/59	BM biopsy alone, No	S	Thymic carcinoma, (inoperable) 5.3 years after AA diagnosis	No	-	No	No
Lyonnais (1988)	M/38	BMA and biopsy, No	VS	NA, 0 month	-	-	No	No
Kobayashi (1993)	F/64	BMA and biopsy, Normal BM cytogenetic analysis	S	NA, 4 years	-	No (Ham-test and sugar water test negatives)	No	Immune thrombocytopenia
Liozon (1998)	M/65	BMA and biopsy, No	S	AB, 0 month	No	-	No	No
Späth-schwalbe (1998)	F/57	BMA alone, No	S	A, 3 years	-	-	Yes, 12 months	Hypogammaglobulinemia
Çöplü (2000)	F/39	BM biopsy alone, No	S	A stage I, 6 years after AA diagnosis	-	-	No	No
Dinçol (2000)	M/38	BM biopsy, Normal peripheral blood cytogenetic analysis	VS	AB, 3 months	-	No	No	No

Ritchie (2002)	M/50	BM biopsy, No mitoses evaluable for cytogenetic analysis	VS	B2 stage III, 1 year	-	No	No	Myasthenia gravis
Park (2003)	F/60	BMA and biopsy, No	VS	B1, 16 months	-	-	No	No
Kanat (2005)	M/43	BM biopsy alone, No	S	AB stage IVa, 2 years (inoperable)	No	-	No	No
Maslovsky (2005)	M/41	BMA and biopsy, No	VS	NA, 12 months (partial resection)	-	-	Yes, 12 months	Myasthenia gravis
Arcasoy (2007)	F/47	BM biopsy alone, No	NA	A, 0 month	-	-	No	No
Gaglia (2007)	M/75	BMA and biopsy, No	S	B2 stage IVa, 7 years (inoperable)	No	-	No	No
Trisal (2007)	M/44	BMA and biopsy, No	S	A, 0 months	-	-	No	Immune thrombocytopenia
Bajel (2009)	M/67	BM biopsy alone, No	S	A, 6 months	-	No	No	No
Escobosa Sanchez (2009)	M/12	BMA and biopsy, No	S	B2 stage III, 2 weeks	-	No	No	No
Migdady (2011)	M/37	BM biopsy, Normal BM cytogenetic analysis	S	B stage III, 0 month	-	-	No	No
de Castro (2011)	M/69	BM biopsy, No mitoses evaluable for cytogenetic analysis	S	NA, 3 years	-	No	No	No
de Castro (2011)	F/59	BM biopsy, No mitoses evaluable for cytogenetic analysis	S	NA, 2 years	-	No	No	No

Lu (2013)	F/40	BMA and biopsy, Normal BM cytogenetic analysis	VS	NA stage IVa, 0 months (inoperable)	-	-	No	No
Mirtavoos-Mahyari (2014)	M/56	BMA and biopsy, No	S	B2 stage IIb, 2 weeks	-	-	No	Coeliac disease
Chintakuntlawar (2015)	F/68	BM biopsy, Normal BM cytogenetic analysis	S	B2 stage I, 4 weeks after AA diagnosis	-	Yes, 0.05% of granulocytes	-	No
Osada (2016)	M/45	BM biopsy, Normal BM cytogenetic analysis	S	AB, 7 months	-	-	-	Myasthenia gravis
Dežmalj Grbelja (2017)	M/45	BMA alone, No	NS	B1, 5 months	-	-	No	Myasthenia gravis
Simkins (2018)	F/61	BM biopsy alone, No	S	B1, 12 weeks	-	-	Yes, 1 month	Amegakaryocytic thrombocytopenia
Toret (2018)	M/14	BMA and biopsy, No	VS	A stage 1, 0 month	No	No	No	No

* Thymic histology and staging according to the World Health Organization classification[43] and the Masaoka-Koga stage classification[44]

Abbreviations: F, female; M, male, AA, plastic anemia; BM, bone marrow; BMA, bone marrow aspiration; NS, non-severe; VS, very severe; S, severe; PRCA, pure red cell anemia; NA, non-available.

Supplemental table 3. Case reported in the literature after 1980s (n=26): thymoma-associated aplastic anemia treatment, response and evolution.

Patient	Sex/Age at AA diagnosis	AA Severity	First line treatment and response	Second line treatment and response	Third line treatment and response	Outcome, time from diagnosis to last FU and cause of death)
Thomas (1987)	M/59	S	Prednisone, PR	ATG, CR	ATG, NR	Alive, 5.5 years
Lyonnais (1988)	M/38	VS	Prednisolone+CyP, NR	ATG, CR	-	Alive, 1 year
Kobayashi (1993)	F/64	S	CsA, PR (+splenectomy)	-	-	Alive, 12 months
Liozon (1998)	M/65	S	Prednisolone+CyP, NR	CsA, PR	ATG, NR	Alive, 7 years
Späth-schwalbe (1998)	F/57	S	CsA, PR	-	-	Alive, 10 months
Çöplü (2000)	F/39	S	Oxymetholone+ATG, PR	CsA, PR	-	Alive, 7.7 years
Dinçol (2000)	M/38	VS	CsA+ATG, CR	-	-	Alive, 1.2 years
Ritchie (2002)	M/50	VS	CsA+ATG, PR	CsA+ATG,PR	CsA+ATG, PR	Alive, 1.6 years
Park (2003)	F/60	VS	CsA, CR	-	-	Alive, 8 months
Kanat (2005)	M/43	S	Placlitaxel, PR	-	-	Alive, 6 months
Maslovsky (2005)	M/41	VS	NA	-	-	NA
Arcasoy (2007)	F/47	NA	MMF+CsA+ATG, NR	Alemtuzumab, NR	-	Deceased, 7 months, infectious complications
Gaglia (2007)	M/75	S	CsA, PR	-	-	Deceased, 2 years, Thymoma progression

						in the mediastinum
Trisal (2007)	M/44	S	CsA, PR	HSCT (sibling), CR	-	Alive, 2.7 years
Bajel (2009)	M/67	S	CsA+ATG, CR	-	-	Alive, 10 weeks
Escobosa Sanchez (2009)	M/12	S	CsA, NR	-	-	Deceased, 6 days, pulmonary hemorrhage
Migdady (2011)	M/37	S	CsA+ATG, PR	-	-	Alive, 2 years developing PNH (PNH clone, 80% on erytrocytes and granulocytes) with arterial thrombosis
de Castro (2011)	M/69	S	CsA, CR	-	-	Alive, 49 months
de Castro (2011)	F/59	S	CsA+prednisone, NR	-	-	Deceased, NA, alveolar hemorrhage
Lu (2013)	F/40	VS	HSCT (sister), CR	-	-	Alive, 1 year
Mirtavoos-Mahyari (2014)	M/56	S	CsA, CR	-	-	Alive, 2 years
Chintakuntlawar (2015)	F/68	S	CsA+Prednisone, CR	-	-	Alive, 8 months
Osada (2016)	M/45	S	CsA, PR	-	-	Alive, 5 months
Dežmalj Grbelja (2017)	M/45	NS	MMF+Azathioprine, NR	Rituximab, NR	HSCT (sister), CR	Alive, 1.5 years
Simkins (2018)	F/61	S	CsA+ATG+eltrombopag, NR	HSCT (matched unrelated donor), CR	-	Alive, 1.7 years
Toret (2018)	M/14	VS	CsA+ATG, CR	-	-	Alive, 1.5 years

Abbreviations: F, female; M, male; AA, aplastic anemia; NS, non-severe; VS, very severe; S, severe; FU, follow-up; CsA, cyclosporine A; ATG, antithymocyte globulin; HSCT, hematopoietic stem cell transplantation; NR, non-response; PR, partial response; CR, complete response; CyP, cyclophosphamide; MMF, mycophenolate mofetil; NA for non-available.

Additional References

1. Weinbaum JG, Thompson RF. Erythroblastic hypoplasia associated with thymic tumor and myasthenia gravis; report of a case. Am J Clin Pathol 1955;25(7):761–769.
2. Josse JW, Zacks SI. Thymoma and pancytopenia; report of a case and review of the literature. N Engl J Med 1958;259(3):113–117.
3. Green P. Aplastic anaemia associated with thymoma; report of two cases. Can Med Assoc J 1958;78(6):419–421.
4. Havard CW, Scott RB. Thymic tumour and erythroblastic aplasia. Report of three cases and a review of the syndrome. Br J Haematol 1960;6178–190.
5. Barnes RD, O'gorman P. Two cases of aplastic anaemia associated with tumours of the thymus. J Clin Pathol 1962;15264–268.
6. Schmid JR, Kiely JM, Harrison EG, Bayrd ED, Pease GL. THYMOMA ASSOCIATED WITH PURE RED-CELL AGENESIS. REVIEW OF LITERATURE AND REPORT OF 4 CASES. Cancer 1965;18216–230.
7. Korn D, Gelderman A, Cage G, Nathanson D, Strauss AJ. Immune deficiencies, aplastic anemia and abnormalities of lymphoid tissue in thymoma. N Engl J Med 1967;276(24):1333–1339.
8. Hirst E, Robertson TI. The syndrome of thymoma and erythroblastopenic anemia. A review of 56 cases including 3 case reports. Medicine (Baltimore) 1967;46(3):225–264.
9. Rogers BH, Manligod JR, Blazek WV. Thymoma associated with pancytopenia and hypogammaglobulinemia. Report of a case and review of the literature. Am J Med 1968;44(1):154–164.
10. Safdar SH, Krantz SB, Brown EB. Successful immunosuppressive treatment of erythroid aplasia appearing after thymectomy. Br J Haematol 1970;19(4):435–443.
11. Talerman A, Amigo A. Thymoma associated with aregenerative and aplastic anemia in a five-year-old child. Cancer 1968;21(6):1212–1218.
12. Dawson MA. Thymoma associated with pancytopenia and Hashimoto's thyroiditis. Am J Med 1972;52(3):406–410.
13. Thomas CV, Manivel JC. Thymic carcinoma and aplastic anemia: report of a previously undocumented association. Am J Hematol 1987;25(3):333–335.
14. Lyonnais J. Thymoma and pancytopenia. Am J Hematol 1988;28(3):195–196.
15. Kobayashi H, Kitano K, Ishida F, et al. Aplastic anemia and idiopathic thrombocytopenic purpura with antibody to platelet glycoprotein IIb/IIIa following resection of malignant thymoma. Acta Haematol 1993;90(1):42–45.

16. King JA, Elkhalifa MY, Latour LF. Rapid progression of acquired amegakaryocytic thrombocytopenia to aplastic anemia. South Med J 1997;90(1):91–94.
17. Raschal S, Siegel JN, Huml J, Richmond GW. Hypogammaglobulinemia and anemia 18 years after thymoma resection. J Allergy Clin Immunol 1997;100(6 Pt 1):846–848.
18. Liozon E, Touati M, Allegraud A, et al. Thymoma-associated pancytopenia: effectiveness of cyclosporine A. Ann Hematol 1998;77(4):175–178.
19. Späth-Schwalbe E, Arnold R, Flath B, Possinger K. Red cell aplasia and megakaryocytic hypoplasia with elevated counts of CD8-positive lymphocytes after resection of a thymoma responding to cyclosporine. Ann Hematol 1998;76(1):51–52.
20. Cöplü L, Selçuk ZT, Haznedaroğlu IC, Doğan R, Güngen Y. Aplastic pancytopenia associated with thymoma. Ann Hematol 2000;79(11):648–650.
21. Dinçol G, Saka B, Aktan M, et al. Very severe aplastic anemia following resection of lymphocytic thymoma: effectiveness of antilymphocyte globulin, cyclosporin A, and granulocyte-colony stimulating factor. Am J Hematol 2000;64(1):78–79.
22. Ritchie DS, Underhill C, Grigg AP. Aplastic anemia as a late complication of thymoma in remission. Eur J Haematol 2002;68(6):389–391.
23. Park CY, Kim HJ, Kim YJ, et al. Very severe aplastic anemia appearing after thymectomy. Korean J Intern Med 2003;18(1):61–63.
24. Kanat O, Evrensel T, Kurt E, et al. Successful treatment of thymoma-associated erythroid hypoplasia and thrombocytopenia with paclitaxel. Clin Oncol R Coll Radiol G B 2005;17(1):68.
25. Maslovsky I, Gefel D, Uriev L, Ben Dor D, Lugassy G. Malignant thymoma complicated by amegakaryocytic thrombocytopenic purpura. Eur J Intern Med 2005;16(7):523–524.
26. Arcasoy MO, Gockerman JP. Aplastic anaemia as an autoimmune complication of thymoma. Br J Haematol 2007;137(4):272.
27. Gaglia A, Bobota A, Pectasides E, Kosmas C, Papaxoinis G, Pectasides D. Successful treatment with cyclosporine of thymoma-related aplastic anemia. Anticancer Res 2007;27(4C):3025–3028.
28. Trisal V, Nademanee A, Lau SK, Grannis FW. Thymoma-associated severe aplastic anemia treated with surgical resection followed by allogeneic stem-cell transplantation. J Clin Oncol Off J Am Soc Clin Oncol 2007;25(22):3374–3375.
29. Bajel A, Ryan A, Roy S, Opat SS. Aplastic anaemia: autoimmune sequel of thymoma. Br J Haematol 2009;147(5):591.

30. Escobosa Sánchez OM, Herrero Hernández A, Acha García T. [Malignant thymoma associated with severe aplastic anaemia]. An Pediatr Barc Spain 2003 2009;70(1):57–60.
31. Nakamura H, Miwa K, Adachi Y, Fujioka S, Haruki T, Taniguchi Y. Thoracoscopic extended thymothymectomy for myasthenia gravis with aplastic anemia. Ann Thorac Cardiovasc Surg Off J Assoc Thorac Cardiovasc Surg Asia 2009;15(5):328–331.
32. Migdady Y, Olszewski AJ. Paroxysmal Nocturnal Hemoglobinuria Presenting with a Left Intraventricular Thrombus in a Patient with Prior Thymoma and Aplastic Anemia. Clin Med Insights Oncol 2011;5343–348.
33. Sada E, Shiratsuchi M, Ohno H, et al. [Successful treatment with immunosuppressive therapy for aplastic anemia developed after resection of thymoma]. Rinsho Ketsueki 2011;52(5):293–298.
34. de Castro MA, de Castro MA, Arantes A de M, Roberti M do RF. Thymoma followed by aplastic anemia - two different responses to immunosuppressive therapy. Rev Bras Hematol E Hemoter 2011;33(6):476–477.
35. Lu C, He G, Jin S, et al. Haploidentical allogeneic hematopoietic stem cell transplantation for thymoma-associated severe aplastic anemia: a case report. Chin Med Sci J Chung-Kuo Hsueh Ko Hsueh Tsa Chih 2013;28(3):189–191.
36. Mirtavoos-Mahyari H, Khosravi A, Esfahani-Monfared Z, Shadmehr MB. Two thymus-related autoimmune disorders: a case report and review of the literature. OncoTargets Ther 2014;7633–636.
37. Chintakuntlawar AV, Rizvi SA, Cassivi SD, Pardanani A. Thymoma-associated pancytopenia: immunosuppressive therapy is the cornerstone for durable hematological remission. Ann Hematol 2015;94(3):453–458.
38. Osada O, Iwasaki A, Nakahashi H, Kim Y, Kaneko K. [A case of myasthenia gravis with transient taste disorders followed by aplastic anemia after thymectomy]. Rinsho Shinkeigaku 2016;56(3):200–203.
39. Dežmalj Grbelja L, Vrhovac R, Ulamec M. Myasthenia Gravis Associated With Thymoma And Aplastic Anemia: Case Report. Acta Clin Croat 2017;56(4):817–820.
40. Simkins A, Maiti A, Short NJ, et al. Acquired amegakaryocytic thrombocytopenia and red cell aplasia in a patient with thymoma progressing to aplastic anemia successfully treated with allogenic stem cell transplantation. Hematol Oncol Stem Cell Ther [Epub ahead of print].
41. Toret E, Demirag B, Köker SA, et al. Aplastic Anemia as an Immune-mediated Complication of Thymoma: A Case Report. J Pediatr Hematol Oncol 2018;40(7):e464–e466.

42. Mitsumune S, Manabe Y, Yunoki T, et al. Autologous Bone Marrow Transplantation for Polymyositis Combined with Myasthenia Gravis and Aplastic Anemia: A Case Report. Case Rep Neurol 2018;10(1):108–111.
43. Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. J Thorac Oncol 2015;10(9):1243–1260.
44. Detterbeck FC, Nicholson AG, Kondo K, Van Schil P, Moran C. The Masaoka-Koga stage classification for thymic malignancies: clarification and definition of terms. J Thorac Oncol Off Publ Int Assoc Study Lung Cancer 2011;6(7 Suppl 3):S1710-1716.
45. Scheinberg P, Young NS. How I treat acquired aplastic anemia. Blood 2012;120(6):1185–1196.
46. Marsh JCW, Ball SE, Darbyshire P, et al. Guidelines for the diagnosis and management of acquired aplastic anaemia. Br J Haematol 2003;123(5):782–801.