Evans' Syndrome Associated with Gastric Plasmacytoma: Case Report and a Review of the Literature

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We report a case of autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura (Evans' syndrome) associated with gastric plasmacytoma. Recognition of this rare entity is important because surgery and chemotherapy together may achieve a cure. Possible mechanisms causing the hemolytic anemia and thrombocytopenia are discussed.

Key words: Autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura, Extramedullary plasmacytosis

Evans' syndrome is the simultaneous occurrence of autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura. We report a case of Evans' syndrome associated with gastric plasmacytoma.

CASE REPORT

A 41-year-old woman presented in March 1982 with fatigue and general malaise. Physical examination revealed hepatosplenomegaly but no lymphadenopathy. Abdominal echography, gallium scanning, and liver-spleen scintigraphy showed no space occupying lesions in the liver or spleen. Hemoglobin was 3.9 g/dl, leukocyte count was $4.8 \times 10^3/\mu\text{l}$ with a normal differential, the platelet count as $2.6 \times 10^4/\mu\text{l}$, and the reticulocyte score was 127%. Thus, the peripheral blood showed anemia and thrombocytopenia. Bone marrow aspirate disclosed erythroid hyperplasia and an increased number of megakaryocytes. Both the direct and indirect Coombs' test were positive, and were characterized by anti-globulin activity to IgG and complement (IgG (2+), $\text{C}_3\text{d}-\text{C}_3\text{b}-\text{C}_4$ (+)). She

demonstrated only hypogammaglobulinemia, and there was no demonstrable monoclonal gammopathy. The above data indicated that autoimmune diseases such as systemic lupus erythematosus could be ruled out and that the cause of the thrombocytopenia might be idiopathic because anti-platelet antibody was positive and the other auto-antibodies were all negative (Table 1).

Autoimmune hemolytic anemia and thrombocytopenia (Evans' syndrome) was diagnosed, and she was treated with prednisolone at a dose of 30 mg daily. After one month, hemoglobin was 14.7 g/dl and the platelet count was $32.6 \times 10^4/\mu\text{l}$.

Four years later, an abdominal mass and splenomegaly were detected on physical examination. Laparotomy was performed, the lesion was biopsied, and a plasmacytoma was diagnosed from the presence of pleomorphic plasma cells with numerous mitotic figures (Fig. 1). Total gastrectomy and extended dissection with splenectomy were then performed. Lymph node, hepatic, and pancreatic metastases were evident, but there was no splenic or bone marrow plasmacytosis. Serum and urine

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Table 1. Laboratory findings on admission

			1st	2nd	
ESR (mm/h)		13	48		Anti-platelet Ab MPHA (−) (+)
Urinalysis protein	(+++)	(+)			LCT (+) (+)
sugar	(−)	(−)			Serology
blood	(+++)	(−)			CRP (±) (3+)
urobilinogen	(−)	(−)			RA (−) (−)
sediment	RBC many	n.p.			ASO (Todd) 80 80
Stool examination					HB-Ag (−) (−)
occult blood	(−)	(+)			HB-Ab (−) (−)
Blood chemistry					Wa-R (−) (−)
GOT (U/l)	15	65			ANF (−) (−)
GPT (U/l)	12	293			Coombs direct (2+) (±)
AIP (U/l)	30	124			Coombs indirect (2+) (−)
LDH (U/l)	179	265			Immunology
γ-GTP (U/l)	10	49			IgG (mg/dl) 623 621
T-Bil. (mg/dl)	0.4	0.3			IgA (mg/dl) 77 610
indirect (mg/dl)	0.4	0.2			IgM (mg/dl) 72 36
T-Ch (mg/dl)	162	193			PPD skin test (−)
FBS (mg/dl)	105	74			Peripheral blood
Na (mEq/l)	138	138			RBC ($\times 10^4/\mu\text{l}$) 228 468
K (mEq/l)	4.0	4.2			Hb (g/dl) 3.9 8.3
Cl (mEq/l)	107	105			Ht (%) 15.8 28.9
Ca (mEq/l)	4.2	4.1			Ret. (‰) 36 24
P (mg/dl)	3.5	2.5			Platelet ($\times 10^4/\mu\text{l}$) 2.6 16.6
BUN (mg/dl)	10	11			WBC (/ μl) 4800 11100
Cr. (mg/dl)	0.7	0.9			Seg 95 92
U. A. (mg/dl)	2.5	6.0			St 0 8
ChE (U/l)	1900	1100			Ly 4 8
Amylase (U/l)	35	208			Mo 1
T-P (g/dl)	3.7	2.7			Bone marrow
Alb (%)	70.3	46.7			NCC ($\times 10^4/\mu\text{l}$) 44.4 29.2
α_1 -gl. (%)	4.5	8.3			Mgk 90 315
α_2 -gl. (%)	7.1	15.9			Plasma (−)
β -gl. (%)	9.8	19.3			Erb. 74.4 1.7
γ -gl. (%)	8.2	9.7			
ZTT (KU)	2	1			
TTT (SHU)	1	1			(March (Oct.
Haptoglobin (ng/dl)	141	259			4.1985) 27.1987)

protein electrophoresis and immunoelectrophoresis were positive for IgA/k. One month after operation, her hemoglobin and platelet count improved markedly (Fig. 2).

The patient was treated with combination chemotherapy [K-18 (IgG-Melphalan), cyclophosphamide, prednisolone], and remission was achieved. Two months after surgery, the patient was discharged and she remains under continued follow-up observation.

Fig. 1. Gastric biopsy showing malignant plasmacytoma: proliferation of highly atypical plasmacytoid cells (H. & E. stain, original magnification $\times 1,000$).

Fig. 2. Clinical course after admission

DISCUSSION

This appears to be the first report of Evans' syndrome associated with gastric plasmacytoma.

Autoimmune hemolytic anemia and immune thrombocytopenia are increasingly reported in association with various neoplasms, but Evans' syndrome is rarely described. The gastric plasmacytoma in our

Fig. 2 Continued

patient was associated with multiple distant metastases. Plasmacytoma is an uncommon, rapidly growing tumor that occurs primarily in the elderly, and has to be differentiated from inflammatory pseudotumors, such as plasma cell granuloma. About 100 cases of gastric extramedullary plasmacytoma (EMP) have been reported, although EMP is most commonly found in the airways (1-5). An EMP may be an extramedullary manifestation of multiple myeloma, as is probable in this case because monoclonal gammopathy was present in the serum and urine, although the lack of other classical indicators and the absence of bone marrow plasmacytosis or bone lesions goes against this diagnosis (6-10). The prompt resolution of both the hemolytic anemia and thrombocytopenia following extirpation of the tumor and the chemotherapy treatment strongly suggests that these conditions were related.

There are several possible mechanisms for the development of Evans' syndrome; in an immunodeficient host the erythrocytes and platelets may produce a tumorigenic substance, or anti-erythrocyte and anti-platelet auto-antibodies may facilitate the development of a malignant tumor. Some antigens present on the patient's erythrocytes and platelets may cross-react with stimulation of the production of auto-antibodies, which may then allow a malignant tumor to develop or progress by initiating an immunodeficient environment.

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