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Case Report

Thrombotic Thrombocytopenic Purpura in a Patient with Klinefelter Syndrome

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Abstract

Thrombotic thrombocytopenic purpura (TTP) is a rare disease associated with microangiopathic hemolytic anemia, thrombocytopenia, fever, neurological disorders, and renal insufficiency pentad. It is a fatal hematologic emergency if left untreated. If plasma exchange is feasible, treatment is easy and comfortable. It should be kept in mind that such as in our patient may be acquired at all congenital illnesses.

Keywords: Klinefelter syndrome, thrombotic thrombocytopenic purpura, plasma exchange

Introduction

Klinefelter syndrome is the most common congenital anomaly, which causes primary hypogonadism. This syndrome affects 1 in 1,000 newborn males (1). The most common genotype is 46,XXY. However, more and less X chromosomes have also been reported, leading to karyotypes such as 48,XXXY and 46,XY/46,XXY mosaic (2). A decrease in the testosterone level and an increase in the FSH-LH levels lead to testis atrophy, infertility, and decreased virilization (3). In later life stages, it may cause morbidity unrelated to testosterone deficiency (4), such as lung diseases (chronic bronchitis, bronchiectasis, and emphysema), cancers (germ cell tumors, breast cancer, and non-Hodgkin's lymphoma), varicose veins leading to leg ulcers, systemic lupus erythematosus (SLE), and diabetes mellitus due to extra X chromosome (5-9). Herein, we report the development of acquired thrombotic thrombocytopenic purpura (TTP) in a patient with Klinefelter syndrome.

Case Presentation

A 36-year-old male with Klinefelter syndrome was admitted to the emergency service with a week-long history of headache, which increased in severity and changes in consciousness. The patient was assessed in the emergency department; he was unconscious and nonresponsive to the painful stimulus. His blood pressure was 90/60 mmHg, pulse rate was 116/min, and fever was 36.7°C. In the tests performed, his WBC was 10900/µL (range, 4000-10000), hemoglobin was 6.2 g/dL (range, 13-17), platelet count was 7000/µL (range, 150000-450000), reticulocyte percentage was 17.2% (range, 0.5%-2%), creatinine was 1.39 mg/dL (range, 0.7-1.2), LDH was 1749 U/L (range, 125-220), total bilirubin was 1.99 mg/dL (range, 0.2-1.2), indirect bilirubin was 1.33 mg/dL (range, 0.1-0.7), SGPT was 33 U/L (range, 0-55), and SGOT was 68 U/L (range, 5-34). Direct and indirect Coombs tests were negative, and haptoglobulin was <9 mg/dL (range, 40-240), B12 was 291 pg/mL (range, 195-961), and folic acid was 3.51 ng/mL (range, 3.1-19.9). Antinuclear antibody was detected as negative. In a peripheral smear spread, extensive schistocytes and thrombocytopenia were observed in each region (Figure-1).

The case report was presented after obtaining informed consent from the patient.

Considering thrombotic thrombocytopenic purpura (TTP), a blood sample for ADAMTS13 was taken, and methylprednisolone 1 mg/kg/day was initiated; in addition, 1 plasma volume of plasma exchange was performed. After the first plasmapheresis, the patient gained consciousness, LDH dropped to 377 U/L, and platelet count increased to 47000/µL. Plasma exchange was continued. After the third plasmapheresis, the platelet count was 164000/µL. Treatment was supplemented with acetylsalicylic acid 100 mg/day. ADAMTS13 activity was <0.2% (range, 40%-1330%), ADAMTS13 antigen was 0.06 µg/mL (range, 0.6-1.6), and ADAMTS13 inhibitor level was 60.90 U/mL (<12). The patient was diagnosed as having acquired TTP. Plasma exchange

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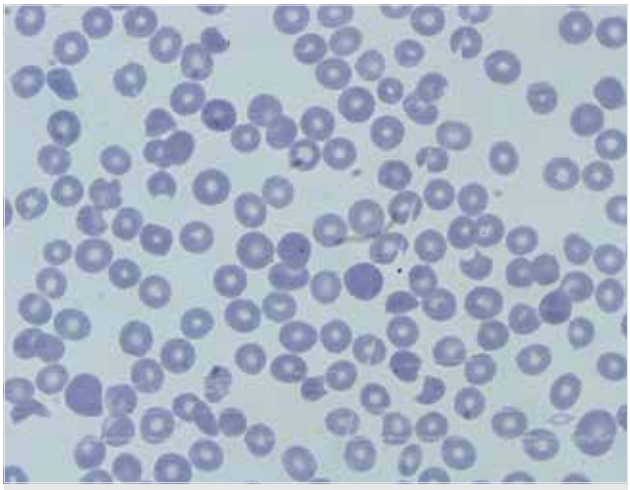

Figure 1. Common schistocytes and thrombocytopenia

was performed 11 times in total, and methylprednisolone was decreased and then cut off within 3 months. The patient is still in remission. The patient`s consent was obtained.

Discussion

Thrombotic thrombocytopenic purpura is a thrombotic microangiopathy caused by severely reduced activity of ADAMTS13, which disrupts the von Willebrand factor (10). Thrombocytopenia is characterized by microangiopathic hemolytic anemia and thrombus occlusion of small vessels causing organ damage. TTP is a medical emergency that is almost always fatal if appropriate treatment is not initiated immediately (11). Survival rates above 90% are possible with appropriate treatment. The incidence is approximately 3 in 1,000,000 a year. More than 95% of TTP cases are acquired cases with inhibitors against ADAMTS13, whereas hereditary cases characterized by the absence of ADAMTS13 constitute <5% of all TTP cases (12). With plasma exchange performed during the treatment, the donor-derived ADAMTS13 is provided to the patient and the autoantibodies against ADAMTS13 are removed. As with our patient, the responses after plasma exchange are usually satisfactory, even with a few sessions (12). Acquired TTP may also develop in patients with other autoimmune disorders, such as SLE. It is believed that this relationship may be due to a combination of similar demographics and/or similar pathophysiology.

We did not find any association between Klinefelter syndrome and TTP in the literature. However, there is evidence that the incidence of SLE is increased among patients with Klinefelter syndrome. Scofield et al. showed that SLE is 14 times more common among patients with Klinefelter syndrome with 46,XXY karyotype than 46,XY males with normal karyotypes. It is argued that this increase may be due to the extra X chromosome because autoimmune diseases are more frequently seen among women (9). The increased frequency of acquired TTP among patients with SLE and the more frequent occurrence of SLE among patients with Klinefelter syndrome compared with normal men suggest that acquired TTP among patients with Klinefelter syndrome is associated with autoimmunity. However, due to the lack of such studies or case presentations in the literature, there is insufficient data in this regard. In our case, there was no clinical or laboratory finding supporting this hypothesis that suggested the presence of an autoimmune disease, such as SLE. Randomized controlled studies are required to establish this relationship. To the best of our knowledge, this is the first reported case in the literature with Klinefelter syndrome wherein the patient developed acquired TTP.

Conclusion

TTP is rarely congenital and often acquired. Congenital diseases or other comorbid conditions of patients may delay diagnosis. If it is untreated, it is fatal; therefore, all patients with microangiopathic hemolytic anemia and thrombocytopenia should be approached as a TTP case until proven otherwise.

Informed Consent: Informed consent was obtained from the patients who participated in this study.

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