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CASE REPORT

Extreme thrombocytosis under the treatment by amoxicillin/clavulanate

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Abstract Amoxicillin/Clavulanate related extreme thrombocytosis during the treatment of pneumonia has never been reported. We present a 54-year-old patient who was admitted due to pneumonia, and was treated with amoxicillin/clavulanate IV and 3-day course of 500 mg azithromycin. Despite clinical and radiological evidence showing that pneumonia improved, thrombocytes increased rapidly. After stopping the antibiotic, the thrombocytes returned gradually to normal. Considering the clinical course, we propose that this extreme thrombocytosis was caused by the administration of amoxicillin/clavulanate. We describe this rare and unique patient and review the literature.

Keywords Thrombocytosis · Amoxicillin/clavulanate · Adverse events

Introduction

Reactive thrombocytosis is usually benign and transient, caused by systemic inflammation, tumors, bleeding, and trauma or iron deficiency anemia. Antibiotics inducing reactive thrombocytosis is relative uncommon [1–4] and extreme thrombocytosis is very rare. Herein we present a patient who had community acquired pneumonia and received empiric antibiotics—amoxicillin/clavulanate, extreme thrombocytosis developed in the improvement course of pneumonia and persisted until amoxicillin/clavulanate was discontinued. We present the patient and review the associated literature.

Case report

We report a 54-year-old patient who was healthy before this hospitalization. The patient suffered from a cough with copious yellowish sputum, high fever and hypoxemia for 3 days. The chest X-ray revealed pneumonia in the right upper lobe and left lower lobe. Admission laboratory data showed white blood cell count 17.32×10^3/ul, hemoglobin 7.94 mmol/l, platelet 122×10^9/l, blood urea nitrogen 7.53 mmol/l, creatinine 117.57 μmol/l. GOT/GPT = 1.45/1.02 μkat/l, Total/Direct Bilirubine = 57.63/37.79 μmol/l. Abdominal sonography showed some sludge in the gall bladder without obstruction. Physical examination revealed crackles over both lung fields. SpO2 = 86% in room air. The sputum smear showed many gram positive coccus in chain. Because community acquired pneumonia was diagnosed, we prescribed intravenous Augmentin (1 vial containing amoxicillin 500 mg + clavulanate 100 mg) 2 vials every 8 h and a 3-day course of 500 mg oral azithromycin as the initial empiric antibiotics. Fever and shortness of breath caused by pneumonia improved after a 5-day treatment course. SpO2 equaled to 93% in room air in day 5.

However, increased thrombocyte developed. Platelet count was up to 740×10^9/l on day 5 and the counts

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steadily increased to an extremely high level— 1420×10^9/l on day 10 despite no fever or dyspnea being monitored at that time. The patient was discharged on day 15 in stable condition. However, his thrombocyte count was still at a high level—1206×10^9/l at that day (D15). His thrombocyte count returned to 565×10^9/l on day 22 and spontaneous went back to the normal limit—350×10^9/l on day 43 (Fig. 1).

Fortunately, despite the marked thrombocytosis, no clinical consequences included neurological, cardiovascular or hematological complications were noted during this period.

Discussion

We believe that this is may be the first report associated with amoxicillin/clavulanate causing extreme thrombocytosis in the English literature according to a Medline search. ''Thrombocytosis'', ''antibiotics'', ''amoxicillin'', ''clavulanic acid'' that were used as search terms.

Thrombocytosis is generally defined as platelets counts $>400 \times 10^9/l^1$. Patients with systemic inflammation, tumors, bleeding, drugs, trauma, stress, iron deficiency anemia may have an increased platelet count, a benign condition called secondary or reactive thrombocytosis. On the other hand, the increase in platelet count that is characteristic of myeloproliferative disorders such as polycythemia vera, chronic myeloid leukemia, myeloid metaplasia, and essential thrombocytosis can be much higher and cause either severe bleeding or thrombosis [5]. The patient we present had no history of essential thrombocytosis and no other hematological disorder in the past.

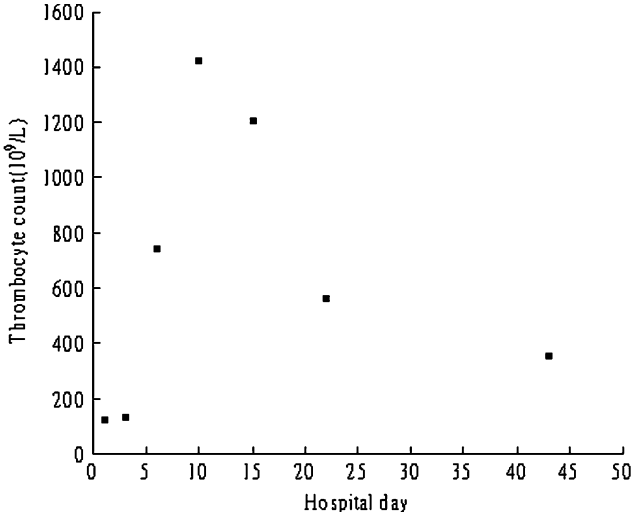

Fig. 1 Thrombocytosis developed during the treatment course of amoxicillin/clavulanate in a patient with pneumonia

Extreme thrombocytosis, defined as a platelet count greater than or equal to $1{,}000 \times 10^9$/l [6, 7], is rarely seen in general practice. There are limited data on the etiology of this abnormality [7, 8]. Buss et al. [8] stated a large-scaled study including a total of 280 patients with extreme thrombocytosis, 231 (82%) had reactive thrombocytosis, 38 (14%) had a myeloproliferative disorder, and 11 (4%) had cases of uncertain etiology. Reactive thrombocytosis was more common than myeloproliferative disorder. Symptoms of bleeding and/or vaso-occlusive phenomena were noted in association with extreme thrombocytosis in 21 (56%) of the myeloproliferative disorder patients but in only 10 (4%) of the reactive thrombocytosis patients.

Among antibacterial antibiotics, thrombocytosis was an uncommon adverse effect in the β lactam antibiotics—penicillin and cephalosporin derivatives. Combination of β lactam antibiotics and β lactamase inhibitors were also reported to be associated with thrombocytosis [2–4]. However, extreme thrombocytosis has been rarely reported. In a study of antifungal therapy [9], a patient was noted as having extremely high thrombocytosis, up to $1{,}056 \times 10^9$/l, on the forth day after treatment and lasted 4 days after therapy.

Amoxicillin/Clavulanate is an intravenous and oral antibacterial combination consisting of seminsynthetic antibiotic amoxicillin and the β lactamase inhibitors-clavulanate. The drugs are used to as a common empiric antibiotic for lower respiratory tract infections, especially the infection caused by β lactamase producing strains of *H. influenzae* and *M. catarrhalis*. In this report, because of the clinical course, we highly suspect the administration of amoxicillin/clavulanate was the cause of the extreme thrombocytosis, despite the fact that partial contribution of community acquired pneumonia cannot be ruled out completely.

The most complications of extreme thrombocytosis were hematological bleeding and vaso-occlusive disease [6, 7]. Wiwanitkit [7] stated that 7.9% of the cases with secondary thrombocytosis experienced bleeding and vaso-occlusive complications. Fortunately, no complications occurred as the previous report in our patient.

In conclusion, amoxicillin/clavulanate is a common empiric antibiotic for community acquired pneumonia. However, extreme hrombocytosis might occur during the treatment course. Although no complications occurred in our patient, we should pay attention to possible adverse effects in such cases.

References

1. Frye JL, Thompson DF. Drug-induced thrombocytosis. J Clin Pharm Ther 1993;18:45–48.
2. Finsterer J, Kotzailias N. Thrombocytosis under ciprofloxacin and tazobactam/piperacillin. Platelets 2003;14:329–331.
3. Moody SB, Pawlicki KS. Thrombocytosis and hyperkalemia associated with the use of ticarcillin/clavulanic acid. Drug Intell Clin Pharm 1987;21:292–293.
4. Kristjansson K, Cox F, Taylor L. Ticarcillin/clavulanic acid combination. Treatment of bacterial infections in hospitalized children. Clin Pediatr (Phila) 1989;28:521–524.
5. Elliott MA, Tefferi A. Thrombosis and haemorrhage in polycythaemia vera and essential thrombocythaemia. Br J Haematol 2005;128:275–290.
6. Buss DH, Stuart JJ, Lipscomb GE. The incidence of thrombotic and hemorrhagic disorders in association with extreme thrombocytosis: an analysis of 129 cases. Am J Hematol 1985;20:365–372.
7. Wiwanitkit V. Extreme thrombocytosis: what are the etiologies? Clin Appl Thromb Hemost 2006;12:85–87.
8. Buss DH, Cashell AW, O'Connor ML, Richards F, Case LD. Occurrence, etiology, and clinical significance of extreme thrombocytosis: a study of 280 cases. Am J Med 1994;96:247–253.
9. Saathoff AD, Elkins SL, Chapman SW, McAllister SF, Cleary JD. Thrombocytosis during antifungal therapy of candidemia. Ann Pharmacother 2005;39:1238–1243.