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Treatment For Thrombocytopenia Complicated with Intracranial Venous Sinus Thrombosis and Bleeding with Eltrombopag: A Case Report

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1. Abstract

A case of primary immune thrombocytopenia (ITP) was reported, in which a patient developed intracranial venous sinus thrombosis accompanied by subarachnoid hemorrhage during oral administration of 25 mg/d of Eltrombopag. The patient discontinued the use of Eltrombopag and received symptomatic treatment with active anticoagulation, resulting in significant improvement. It is suggested that Eltrombopag increases the risk of intracranial venous sinus thrombosis. During the drug treatment of ITP patients, close observation of platelet and coagulation function is necessary.

2. Introduction

Intracranial venous sinus thrombosis (CVST) is a rare condition, occurring in less than 1% of strokes, and is the leading cause of stroke in young adults. Intracranial venous sinus thrombosis accompanied by subarachnoid hemorrhage is even rarer, primarily triggered by genetic and acquired pre-thrombotic conditions, as well as infections [1]. Eltrombopag is a thrombopoietin receptor agonist (TPO-RA), capable of rapidly elevating platelet counts to treat thrombocytopenia [2], but it also elevates the risk of thrombosis, encompassing both venous and arterial thrombosis [3]. This study details a case of a middle-aged ITP patient treated at our hospital who developed intracranial venous sinus thrombosis with subarachnoid hemorrhage during treatment with Eltrombopag, and reviews relevant literature to enhance understanding of this condition and the medication.

3. Case Data

A 52-year-old female patient was admitted to our hospital on December 10, 2023 due to “headache with nausea and vomiting for 1+days”. Past history: he has a history of hypertension for 10 years, and has been treated with felodipine for a long time, and his blood pressure is basically normal; The original ITP was diagnosed 8 years ago. One year ago, the patient began to take oral Eltrombopag 25mg QD, and the platelet count basically maintained in the normal range. He denied smoking, diabetes, infection, oral hormone history, and other history of thrombosis. Admission blood routine: white blood cell count 19.14×109/L, hemoglobin 152g/L, red blood cell count 5.26×1012/L, platelet count 190×109/L. Head CT (2023-12-10): subarachnoid hemorrhage (Figure 1). CTA of the head and neck showed the formation of emboli in the right transverse sinus (Figure 2). Stop taking Eltrombopag, give enoxaparin sodium 6000iu q12h subcutaneous injection of anticoagulation, and give fluid infusion and analgesic symptomatic treatment. On December 11, the patient’s condition worsened and he was lethargic. The muscle strength of the right limb was grade 1 and that of the left limb was grade 3. CT examination (2023-12-11): hemorrhagic cerebral infarction (Figure 3). MRI showed multiple cerebral infarction with hemorrhage (Figure 4). Continue the anticoagulation with enoxaparin sodium until 12-25. The patient’s condition improved and discharged. Rivaroxaban 15mg bid was taken orally after discharge. During the period, the platelet was

detected. On January 1, the platelet decreased to the minimum of 14, the anticoagulation was stopped, and the platelet was infused, and avatripropa 20mg QD was given orally. There was no thrombotic event during the follow-up (2024-5-30). During the period, the blood routine monitoring showed that the platelet count basically maintained in the normal range, and the follow-up patients recovered to the normal muscle strength of the left limb, and the muscle strength of the right limb was grade 4. They took care of themselves in daily life.

23121001250 攀枝花学院附属医院·攀枝花中西医结合医院检验报告单

共1页/第1页

姓名(Name)：祝全军 性别(Sex)：女 年龄(Age)：52岁 编号(No)：常858

科别(Dept)：急诊内科 床号(Bed No)： 标本(Sample)：EDTA抗凝全血 样本状态：

病员号(CaseNo)：2022005091 36 送检医师(doc)：才滨骏 诊断(Diag.)：头痛

申请项目(ApplyItem)：★门急诊血型,★静脉血常规超敏C 备注：

序号	项目名称	结果	提示	单位	检验方法	生物参考区间
1	*红细胞计数(RBC)	19.14	H	*10^9/L	流式细胞计数法	4.0-10.0
2	*红细胞计数(RBC)	5.26	H	*10^12/L	流压聚焦阻抗法	3.5-5.0
3	*血红蛋白量(HGB)	152	H	g/L	SLS血红蛋白法	110-150
4	*血小板计数(PLT)	190		*10^9/L	流压聚焦阻抗法	100-300
5	中性粒细胞百分比(NEU%)	93.4	H	%	流式细胞计数法	39.8-76.5
6	淋巴细胞百分比(LYMPH%)	3.70	L	%	流式细胞计数法	23.1-49.9
7	单核细胞百分比(MONO%)	2.60	L	%	流式细胞计数法	4.3-10.0
8	嗜酸性粒细胞百分比(EOS%)	0.10	L	%	流式细胞计数法	0.6-5.4
9	嗜碱性粒细胞百分比(BASO%)	0.20	L	%	流式细胞计数法	0.3-1.4
10	中性粒细胞绝对数(NEU#)	17.89	H	*10^9/L	流式细胞计数法	1.80-8.89
11	淋巴细胞绝对数(LYMPH#)	0.71	L	*10^9/L	流式细胞计数法	1.26-3.35
12	单核细胞绝对数(MONO#)	0.49		*10^9/L	流式细胞计数法	0.25-0.95
13	嗜酸性粒细胞绝对数(EO#)	0.01		*10^9/L	流式细胞计数法	0.01-0.59
14	嗜碱性粒细胞绝对数(BASO#)	0.04		*10^9/L	流式细胞计数法	0.01-0.07
15	*红细胞比积(HCT)	0.443			红细胞计数脉冲法	0.35-0.50
16	*平均红细胞体积(MCV)	84.2		fL	计算法	82.0-95.0
17	*平均红细胞血红蛋白量(MCH)	28.9		pg	计算法	27.0-31.0
18	*平均红细胞血红蛋白浓度(MCHC)	343		g/L	计算法	320-360
19	红细胞分布宽度(CV)(RDW)	13.0		%		12.2-14.8
20	红细胞分布宽度(SD)(RDW)	39.8	L	fL		41.2-53.6
21	血小板压积(PCT)	0.250		%		0.19-0.39
22	平均血小板体积(MPV)	13.30	H	fL		9.2-12
23	血小板分布宽度(PDW)	21.8	H	fL		9.8-15.2
24	大型血小板比率(P-LCR)	49.6	H	%		19.7-42.4
25	未成熟细胞百分比(IG%)	0.9	H	%	流式细胞计数法	0-0.6
26	未成熟细胞绝对值(IG#)	0.18	H	*10^9/L	流式细胞计数法	0-0.06
27	ABO血型(ABO)	"O"型			盐水介质法	
28	RH(D)血型(RH(D))	阳性(+)			盐水介质法	
29	超敏C反应蛋白(HSCRP)	8.30	H	mg/L	免疫散射比浊法	0-5

备注：*项目表示川渝互认项目

申请时间：2023/12/10 16:54:37 采样时间：2023/12/10 18:29 检验者：郁芳 审核者：杨洪东

接收时间：2023/12/10 18:35 报告时间：2023/12/10 18:42

备注:此报告仅反映送检样本检测结果.

Figure 1

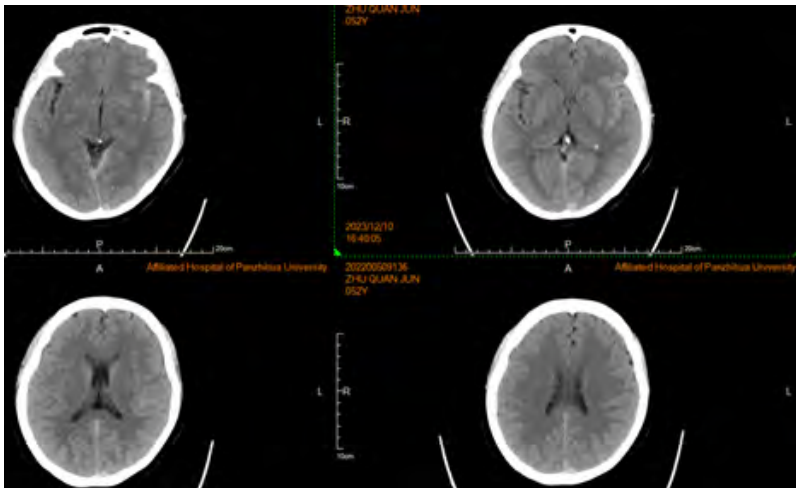

Figure 2

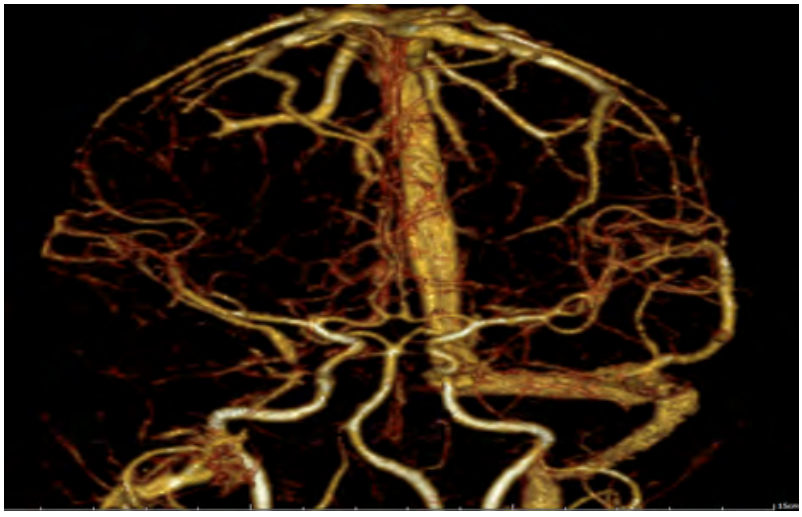

Figure 3

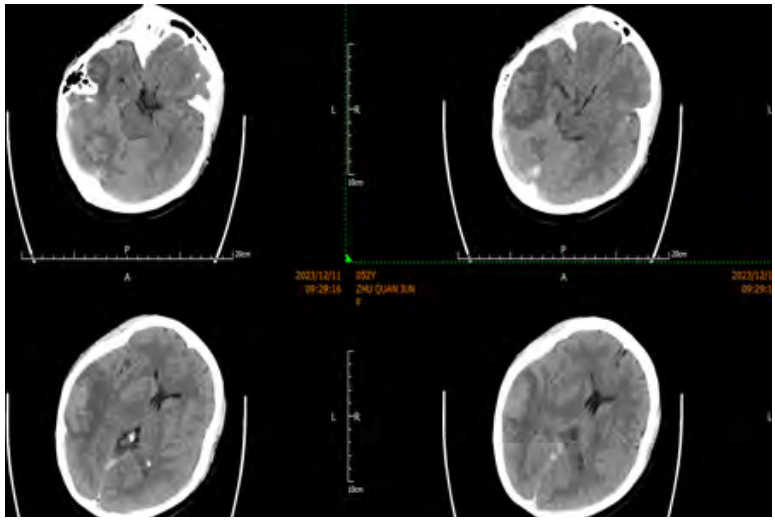

Figure 4

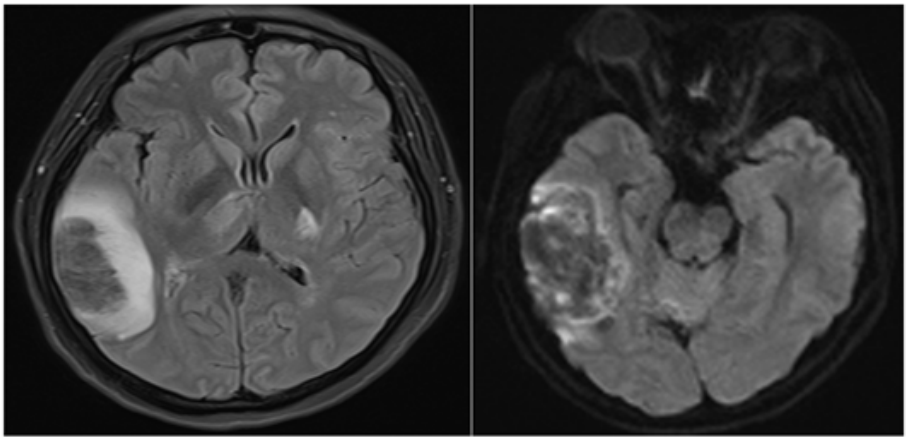

Figure 5

4. Discussion

Intracranial venous sinus thrombosis has a low incidence rate. Clinical manifestations include headaches, focal neurological symptoms, seizures, and coma. Diagnosis primarily relies on imaging tests. Anticoagulation is the primary treatment for CVST. For critically ill patients, a combination of local thrombolysis, mechanical thrombectomy, and anticoagulation therapy is often employed [4]. As an oral thrombopoietin receptor agonist, Eltrombopag induces megakaryocyte proliferation and differentiation, and stimulates platelet production. There have been multiple reports of thromboembolic complications, including arterial thrombosis, pulmonary embolism, and deep venous thrombosis, with most events occurring within the first year of drug treatment[5]. Experimental studies in phase II, III, or long-term use of Eltrombopag have shown that Eltrombopag does not affect platelet function, yet thrombosis has been reported[6-7]. Research indicates racial differences in the pharmacological properties of Eltrombopag; compared to the Caucasian population, CYP1A2 and UGT1A3 enzyme activities are lower in Chinese and Caucasian individuals, while CYP2C8 and UGT1A1 enzyme activities are lower in Asian compared to non-Asian populations[8-10]. Consequently, the clearance rate of Eltrombopag is relatively lower in Asian individuals. Further exploration is needed to determine whether this lower clearance rate is associated with a higher incidence of thrombosis; further clinical research on dosing for Asian patients is also warranted. In this study, the ITP patient was a middle-aged woman with a history of hypertension only, but no risk factors such as smoking, thrombosis, atrial fibrillation, or diabetes. She experienced an intracranial venous sinus thrombosis event following treatment with Eltrombopag, indicating that the use of Eltrombopag may contribute to the development of such thrombosis. After in-hospital anticoagulation therapy and ongoing oral rivaroxaban treatment, the patient made a good recovery. Following discharge, she continued to take alfatripopa orally to maintain her platelet count. To date, no further thrombotic events have occurred, and we will continue to monitor her closely.

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