

## CASE REPORT

# Eosinophils were Significantly Elevated in the Chronic Subdural Hematoma Fluids: Two Case Reports

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### SUMMARY

**Background:** Chronic subdural hematoma (CSDH) is a type of spontaneous or post-traumatic intracranial hemorrhage located between the dura mater and arachnoid membrane. It is a neurosurgical disease that often occurs in the elderly. Burr-hole drainage is the main treatment method, and smear microscopic examination of the drainage fluid is a common laboratory method.

**Methods:** A cranial magnetic resonance imaging (MRI) was performed, then blood and drainage fluid from patients with CSDH was collected and sent to the laboratory for routine laboratory tests.

**Results:** Both patients' cranial MRI indicated CSDH, while no significant abnormalities were found in blood-related tests. Microscopic examination of postoperative drainage fluid revealed a significantly increased proportion of eosinophils.

**Conclusions:** It is found that the mechanism of eosinophil infiltration in CSDH and its significance for patients are still unclear by combining the cases and relevant literatures. Further research is needed to study the distribution and changes of eosinophils and related chemokines in the peripheral blood and postoperative drainage fluid from CSDH patients, which is of great significance for the treatment and recurrence prediction of CSDH patients.

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#### KEYWORDS

eosinophils, chronic subdural hematoma, drainage fluid

#### INTRODUCTION

CSDH is one of the diseases that frequently occur in the central nervous system, and is more common in the elderly. The hematoma is located between the dura mater and arachnoid membrane with the formation of a capsule structure, accounting for approximately 10% of intracranial hemorrhage [1]. Literatures indicate that CSDH is associated with traumatic brain injury, while some patients have no obvious history of trauma. It may also be related to factors such as subdural effusion, application of anticoagulants, coagulation dysfunction, and long-term heavy alcohol consumption [2,3]. The pathogenesis of CSDH is that the displacement of brain parenchyma after trauma causes the bridging veins between the arachnoid membrane and the dura mater to tear, and the accumulation of blood and exuded cerebro-

spinal fluid forms a liquid hematoma with a capsule [4]. Due to the slow expansion of the hematoma, the symptoms are initially mild or asymptomatic. Patients usually present with non-specific symptoms such as headache, unsteady gait or cognitive impairment, and may also have focal neurological deficits such as hemiplegia or aphasia [5]. CSDH is mainly diagnosed based on medical history and MRI examination, and the treatment method is generally burr-hole drainage [6,7]. Routine and microbiological tests on the drainage fluid of CSDH patients can accurately identify various types of cells, crystals, bacteria, fungi, and other formed elements providing a basis for the treatment and prognosis evaluation of the disease. This article describes two patients with CSDH whose drainage fluid showed a significantly increased proportion of eosinophils (> 50%) in microscopic examination. Then relevant literature was reviewed to explore the possible relationship between eosinophil infiltration and the disease, as well as its value in treatment and prognosis of CSDH.

### CASE PRESENTATION

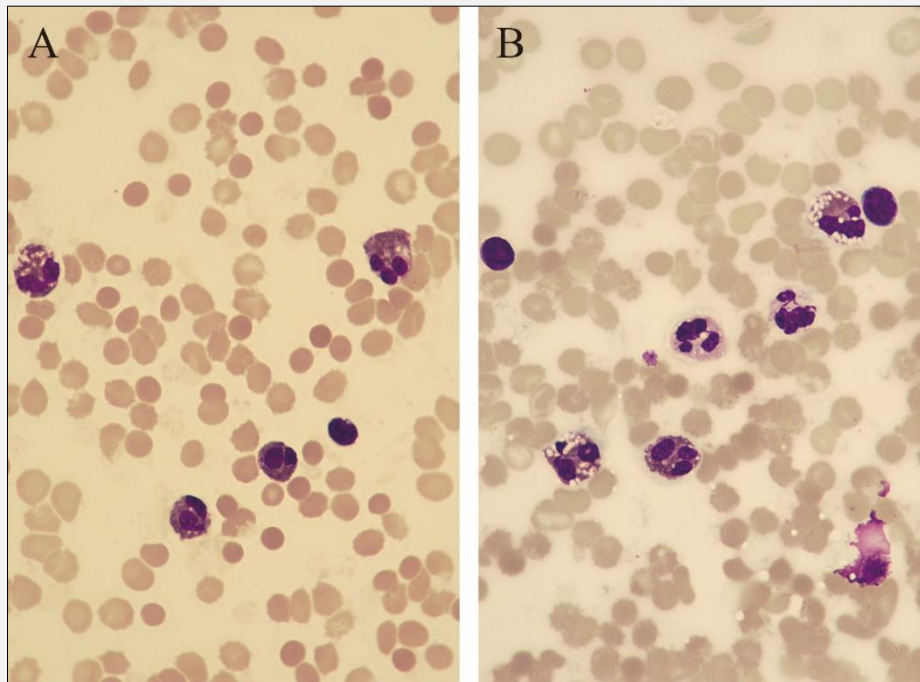
A 68-year-old male patient came to our hospital for treatment. Because he had an adverse right limb movement a week ago, accompanied by a headache, and the symptoms gradually worsened. He had a history of head trauma a month ago and was treated conservatively. Physical examination: Body temperature is 36.9°C; Blood pressure is 149/93 mmHg; Pulse rate is 70 beats/minute; Respiratory rate is 19 times/minute. Clear consciousness, bilateral pupils about 0.3 cm, light reflex exists, soft neck, normal left limb muscle strength, right limb muscle strength level 4, pathological reflex not induced. Cranial MRI examination showed: "bilateral CSDH, more on the right side". Laboratory tests showed a white blood cell count of  $7.82 \times 10^9/L$ , with a neutrophil percentage of 71.8%, lymphocyte percentage of 18.3%, and eosinophil percentage of 1.6%. The hemoglobin level is at 159.0 g/L, platelet count is  $300 \times 10^9/L$ , and coagulation function is normal. On the same day, the subdural hematoma was removed under general anesthesia. The drainage fluid was dark red and turbid. Nucleated cells were counted and classified: count of nucleated cell is 2,800 cells/L, with a neutrophil percentage of 15.0%, lymphocyte percentage of 30%, monocyte percentage of 3.0%, and eosinophil percentage of 52.0% (Figure 1A). Drainage fluid culture was negative. Three days after the operation, the computed tomography (CT) head scan showed that the effusion in the subdural hematoma was significantly reduced, and the drainage tube was removed. One week later, the intracranial condition was stable, the incision healed well, the vital signs were stable, and the patient was discharged from the hospital.

It happens that there was a similar case, a 73-year-old male, who developed unsteady walking without any obvious cause two days ago. Since the symptoms did not

improve significantly, he came to our hospital for treatment. He denied any history of trauma and had no dizziness or headache. Physical examination showed no abnormalities. Cranial MRI examination showed: "bilateral CSDH, obvious on the left side". Blood routine examination and coagulation function are normal. However, eosinophils account for 65% of nucleated cells in the drainage fluid (Figure 1B).

### DISCUSSION

The two patients presented above had normal circulating eosinophils in peripheral blood, and no parasite eggs were found in the feces, but the eosinophils in the drainage fluid from subdural hematoma were significantly increased. We know that the number and proportion of eosinophils increased in serosal effusion, which is mostly seen in trauma, pneumothorax, hemothorax, fungal infection, infarction, asbestos exposure or possible parasitic infection, and occasionally in tumor or tuberculous effusion, but these two patients did not have these conditions. We wonder where do the large number of eosinophils come from? With doubts, we consulted the literature and data. According to electron microscopic observation, the inner membrane of CSDH is collagen fibers without blood vessels; the outer membrane is rich in sinusoid capillaries. Besides red blood cells and platelets, the outer membrane is also infiltrated by a large number of eosinophils, which degranulate during cell division and release plasminogen. The plasminogen is activated by activator secreted by vascular endothelial cells [8], which might contribute to the fluidity of CSDH and the blood leakage from the vessels in the capsules. Regarding the mechanism of extensive eosinophil infiltration in the outer membrane of CSDH, a study found that eosinophil infiltration was observed in the subdural vascularized and hyalinized granulation tissue in 60% (30/50) of the cases. The degree of infiltration was related to the duration of the hematoma. In addition, mast cells were found in 7 out of 16 membranes stained with toluidine blue. It is possible that the eosinophils appear at this unusual site due to chemotactic stimulus caused by the mast cells as well as lymphocytes and hemosiderin pigment [9]. Osuka et al. found that eotaxin-3, the eosinophil-specific chemoattractant, was highly expressed in CSDH fluid. This could induce eosinophils to enter the outer membrane, resulting in the expression of TGF- $\beta$  and activation of the Smad signaling pathway. The TGF- $\beta$ /Smad pathway may be involved in the growth of CSDH [10], but they did not study the proportion of eosinophils in CSDH fluid. Kawaguchi et al. found that the levels of eotaxin-3, IL-5, eosinophil-derived neurotoxin (EDN), and eosinophil ratio in CSDH drainage fluid were significantly increased, and eotaxin-3 was correlated with IL-5, EDN, and eosinophil ratio. Eotaxin-3 is a chemotactic agent of eosinophils. IL-5 induces eosinophil degranulation and participates in its differentiation and maturation [11].



**Figure 1. Microscopic examination of eosinophils in drainage fluid of CSDH (Ridge stain, x 1,000).**

**A. Microscopic examination of eosinophils in drainage fluid from patient (Case 1).**

**B. Microscopic examination of eosinophils in drainage fluid from patient (Case 2).**

Although CSDH can be cured by simple surgery (such as drilling and flushing), the postoperative recurrence rate is still high. Inflammation, fibrinolysis, and angiogenesis have been reported to be associated with the occurrence and recurrence of CSDH. Eosinophils participate in inflammatory responses and play a key role in angiogenesis and fibrinolysis. A study on CSDH pathological specimens showed that dense eosinophil infiltration in the outer membrane was significantly associated with a reduced risk of CSDH recurrence. Eosinophils may reduce the risk of CSDH recurrence by promoting membrane formation, repair, and fibrosis [12,13]. However, some studies have shown that elevated preoperative peripheral blood eosinophils are an independent risk factor for CSDH recurrence [14]. At present, the mechanism of eosinophil infiltration in CSDH and its significance for patients are still unclear. Therefore, further research on the distribution and changes of eosinophils and related chemokines in the peripheral blood and drainage fluid of CSDH patients is needed, which is of great significance for studying new treatment methods and predicting the trend of recurrence.

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#### **Declaration of Interest:**

All authors have no competing interests to declare.

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