Anti-Angiogenic Factor Soluble fms-Like Tyrosine Kinase-1 (sFlt-1) Identifies Patients at Risk for Severe Cerebral Vasospasm the First Day After Aneurysmal Subarachnoid Hemorrhage

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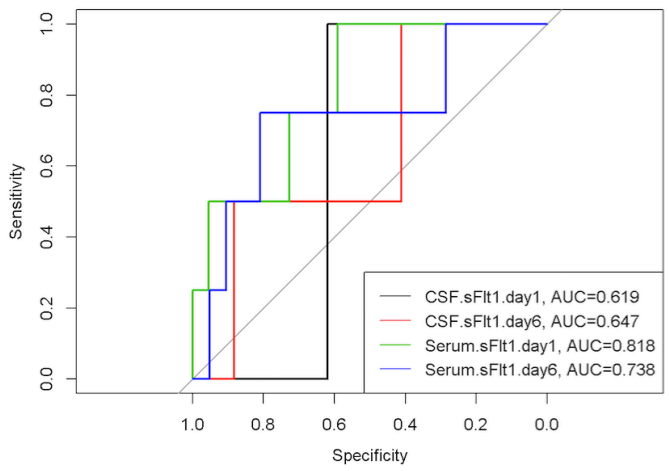
Introduction

The molecular mechanisms underlying cerebral vasospasm and delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage (aSAH) are incompletely understood. We hypothesized that circulating anti-angiogenic factors, such as soluble Fms-like tyrosine kinase-1 (sFlt-1) and soluble transforming growth factor ß (TGFß) co-receptor, soluble endoglin (sEng), are important markers of their pathophysiology.

Methods

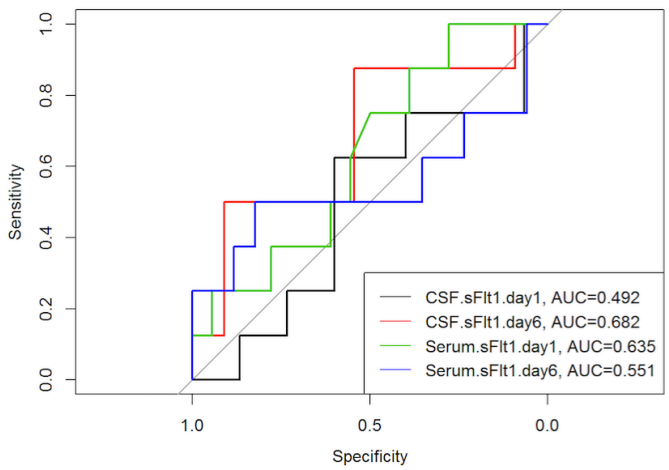
We performed a prospective study in aSAH patients and measured cerebrospinal fluid (CSF) and serum levels of sFlt-1 and sEng on post-bleed day 1 and 6 and correlated levels with incidence and severity of cerebral vasospasm and DCI.

Figure 1. Panel A.



Receiver operating characteristics for sFlt-1 and severe angiographic vasospasm.

Figure 1. Panel B.



Receiver operating characteristics for sFlt-1 and delayed cerebral ischemia.

Results

Twenty-seven patients with aSAH were enrolled in the study. Severe angiographic vasospasm was present in 14.8% of patients and DCI occurred in 33.3%. Serum sFlt1 levels were elevated on post-bleed day 6 in patients who developed vasospasm. However, on post-bleed 1, there were no differences in subjects who developed vasospasm. Interestingly, elevated serum sFlt-1 on post-bleed day 1 was found to predict the development of severe angiographic vasospasm with an area under the curve (AUC) of 0.818 with an optimal cut off value of 95 pg/ml. Alternations in sFlt1 were not associated with DCI. Serum and CSF sEng levels did not correlate with vasospasm or DCI (Figure 1, Panels A and B).

Conclusions

Serum levels of sFlt-1 are elevated in patients with aSAH who are at risk for severe vasospasm. Further studies with larger sample sizes are needed to evaluate whether sFlt-1 levels may predict onset of severe vasospasm and DCI.