Factor XI deficiency and delayed hemorrhages after resection of choroid plexus papilloma: illustrative case

Cristina Mancarella, MD,1 Alessandra Marini, MD,1 Rocco Severino, MD,1 Paolo Missori, MD,2 Cristina Santoro, MD,3 and Sergio Paolini, MD1,2

1Department of Neurosurgery, IRCCS Neuromed, Pozzilli (IS), Italy; 2Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy; and 3Hematology, Hemophilia and Thrombosis Center, University Hospital Policlinico Umberto I, Rome, Italy

BACKGROUND  Factor XI deficiency, also known as hemophilia C, is a rare inherited bleeding disorder that may leave routine coagulation parameters within normal range. Depending on the mutation subtype, prolonged activated partial thromboplastin time may occasionally be found. The disease has an autosomal transmission, with an estimated prevalence in the general population of approximately 1 in 1 million. Heterozygosis accounts for partial deficits, but the tendency to bleed is unrelated to the measured activity of factor XI. Diagnosis usually follows unexpected hemorrhages occurring spontaneously or after trauma or surgical procedures.

OBSERVATIONS  Few cases have been reported in the neurosurgical literature, all occurring spontaneously or after head trauma. Owing to its subtle features, the true incidence of the disease is probably underestimated. The authors report a case of a patient with previously undiagnosed factor XI deficiency who underwent uncomplicated resection of a fourth-ventricle papilloma and experienced delayed, severe hemorrhagic complications.

LESSONS  The known association between choroid plexus tumors and intracranial bleeding raised differential diagnosis issues. This report may serve to help to investigate delayed hemorrhages after cranial surgery.

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KEYWORDS  choroid plexus; delayed hemorrhage; hemophilia C

Factor XI (FXI) deficiency, also known as Rosenthal syndrome or hemophilia C, is a rare, inherited bleeding disorder with a prevalence in the general population of approximately 1 in 1 million.1 Higher frequency has been found in some populations, such as Ashkenazi Jews and Iraqi Jews, who have a heterozygosis rate of 9%.2 The prevalence in the Italian population has been estimated to be approximately 1 in 1,000.3

More than 190 mutations have been described involving the FXI gene, located on the long arm of chromosome 4.4 FXI activity is usually below 15 IU/dl in homozygous forms and between 15 and 40 IU/dl in heterozygous forms. The occurrence of bleeding is unpredictable, however, and normally unrelated to the FXI clotting activity.5 Although prolonged activated partial thromboplastin time (APTT) may occasionally be found, most patients have normal coagulation parameters on routine laboratory tests. The suspicion is usually raised by unexpected bleeding occurring spontaneously or after trauma or surgical procedures.1 Few cases have been reported in the neurosurgical literature, all related to spontaneous hemorrhages and only sporadically to trauma.6–14 An association between FXI deficiency and intracranial hemorrhages after craniotomy procedures has not been documented so far. We report a case of undiagnosed FXI deficiency that manifested with delayed, severe hemorrhages after uncomplicated resection of a fourth-ventricle tumor.

Illustrative Case

A 63-year-old woman with a 10-day history of headache, gait disturbance, and dysmetria had a magnetic resonance imaging (MRI) diagnosis of a fourth-ventricle tumor causing obstructive hydrocephalus (Fig. 1). She had no personal or family history of bleeding. Routine preoperative test results, including coagulation parameters, were within normal range. The patient underwent surgery through a telovelar approach. A neoplasm mildly adherent to the floor of the fourth

ABBREVIATIONS  APTT = activated partial thromboplastin time; CT = computed tomography; F = factor; MRI = magnetic resonance imaging.

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ventricle was removed, and hemostasis was easily achieved. The first postoperative course was uneventful, and both computed tomography (CT) and MRI, performed at 24 and 48 hours, respectively, showed complete tumor resection without bleeding signs (Fig. 2A and B). Three days after surgery, the patient developed mild gait disturbance. CT showed a small blood clot within the fourth ventricle, with ventricular enlargement (Fig. 3A). Surgical removal of the clot and external ventricular drainage were performed with no complications and no neurological sequelae. The patient's postoperative CT scan was normal (Fig. 3B). Three days after the second operation, the patient showed drowsiness and confusion. CT showed a recurrent, large hemorrhage within the fourth ventricle (Fig. 4A). The patient underwent emergency surgery, and a thick clot mixed with swollen branches of the choroid plexus was removed. Her postoperative CT scan was satisfactory (Fig. 4B). The patient remained comatose, though responsive. Meanwhile, pathological examination yielded a diagnosis of choroid plexus papilloma. A literature search showed a clear association between choroid plexus tumors and intracranial hemorrhage, which was considered a possible explanation for such an unusual course. At the same time, hematological counseling was
operative hemostasis was easily achieved and stable, as con-

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FXI deficiency is a subtle bleeding disorder whose prevalence is probably underestimated. This report illustrates a possible pattern of presentation in neurosurgical practice. Normal intraoperative bleeding and uncomplicated hemostasis do not exclude the diagnosis. Recurring postoperative hemorrhages, even several days after surgery, should raise the suspicion and call for extended coagulation screening.

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Conception and design: Severino, Paolini. Acquisition of data: Mancarella, Marini. Analysis and interpretation of data: Marini. Drafting the article: Mancarella. Critically revising the article: Missori, Santoro, Mancarella, Paolini. Reviewed submitted version of manuscript: Santoro, Paolini. Study supervision: Santoro.

**Correspondence**
Cristina Mancarella: IRCCS Neuromed, Pozzilli (IS), Italy. cristina.mancarella@gmail.com.