A CASE OF MULTIPLE CEREBRAL SINUSES THROMBOSIS SHORTLY FOLLOWED BY SUBARACHNOID HEMORRHAGE IN A YOUNG PATIENT WITH MYELOFIBROSIS

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Introduction

Primary myelofibrosis (PMF) is a chronic myeloproliferative neoplasm associated with bone marrow fibrosis, extramedullary hematopoiesis, anemia, hepatosplenomegaly [(1,2)]. It's underlying cause appears to be the neoplastic transformation of early hematopoietic stem cells and alteration of the bone marrow cytochemical environment leading to eventual wide spread consequences. The most common complications of PMF are portal hypertension, gastrointestinal bleeding, acute myeloid leukemia transformation, venous and arterial thrombosis potentially affecting any vascular territory though splenic infarction is the most frequent[(2)]. Hemorrhagic complications are common, especially involving the digestive tract, but multiple sites of bleeding are possible and among them life threatening hemorrhages usually involve the gastro-intestinal and cerebral vasculature[(3)]. In the following we present a case of a patient with cerebral venous thrombosis and subsequent subarachnoid hemorrhage following a diagnosis of primary myelofibrosis by about one year

Case presentation

A 40 year old female was brought to our service after a first time seizure preceded by a 5 day period of progressively worsening headache and diplopia. Her medical history consisted of a previous diagnosis of primary myelofibrosis complicated by hepatosplenomegaly, esophageal varices and hypertensive gastropathy, for which she was receiving treatment at that time with Momelotinib (a trial JAK2 inhibitor drug),she had also recently recovered from an adverse reaction to Ciprofloxacin (manifested as Stevens-Johnson syndrome).

Clinical examination revealed palpable hepatosplenomegaly, slight neck stiffness, abduction palsy and hypertropia of the left eye, on the second day of admission she developed a slight motor deficit of the right limbs which remitted after another 2 days.

Head MRI revealed multiple sites of cerebral venous thrombosis at the level of the superior sagittal sinus, left transverse sinus and cavernous sinus. As well as venous congestion of the pial veins on the cerebral convexities of both hemispheres. Also, there were signs of subarachnoid hemorrhage on the same imaging study.

Spinal tap was performed and recent subarachnoid hemorrhage was confirmed by macroscopically bloody CSF.

Of note was the fact that the patient had no overt lab test modifications suggesting a hemorrhagic diathesis (platelets=202*10^3/mm^3, INR=1.17, Quick time=13.5s, aPTT=22.3), leukocytosis a known bleeding risk factor in prefibrotic MF[(3)] was also absent.

The patient was started on anticonvulsant therapy (Levetiracetam), Nimodipine and pain relievers. Despite evidence of cerebral vein thrombosis, anticoagulation was postponed by 12 days and was initiated after a CT scan confirmed the absence of recent intracranial bleeding.

She was discharged with instructions to keep taking Levetiracetam for another 3 months and to continue anticoagulation therapy for at least 3 months or until her hematologist decided that the bleeding risk was no longer acceptable. A follow-up MRI was performed 6 months later and it showed partial restoration of blood flow through cerebral venous sinuses without signs of rebleeding.

Discussion

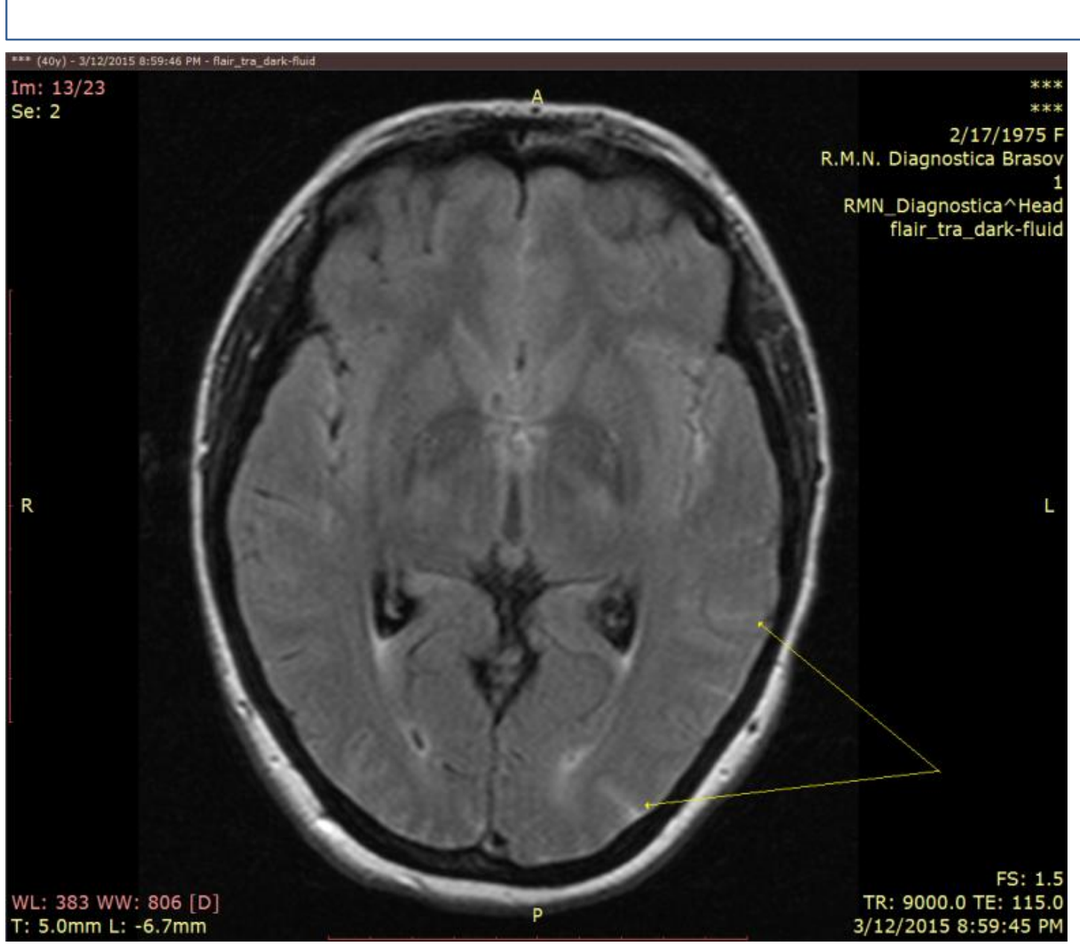
The order in which symptoms occurred indicates that the patient first developed cerebral venous thrombosis with progressively worsening headache and the left abducens palsy is best explained by involvement of the sixth nerve at the cavernous sinus which appeared to be occluded by thrombosis. Most likely the subarachnoid hemorrhage was a subsequent event and the cause of her seizure.

Regarding the etiology of SAH (once aneurismal and traumatic causes are excluded) there remain two possibilities which are not mutually exclusive but for which treatment options are diametrically opposed, namely:

- Cortical vein congestion secondary to sinus thrombosis followed by rupture and secondary bleeding in the subarachnoid space, cases of SAH secondary to cerebral venous thrombosis (CVT) are not frequent occurrences but some have been reported[(4,5)].
- A hemorrhagic diathesis associated with PMF such as a functional platelet abnormality[(3,6)], or vascular proliferation[(7)] .

In the eventuality that CVT was the triggering event of SAH then prompt anticoagulation would be the best therapeutic approach, however if SAH resulted as consequence of a hemorrhagic diathesis secondary to PMF, then anticoagulation would only add to the problem.

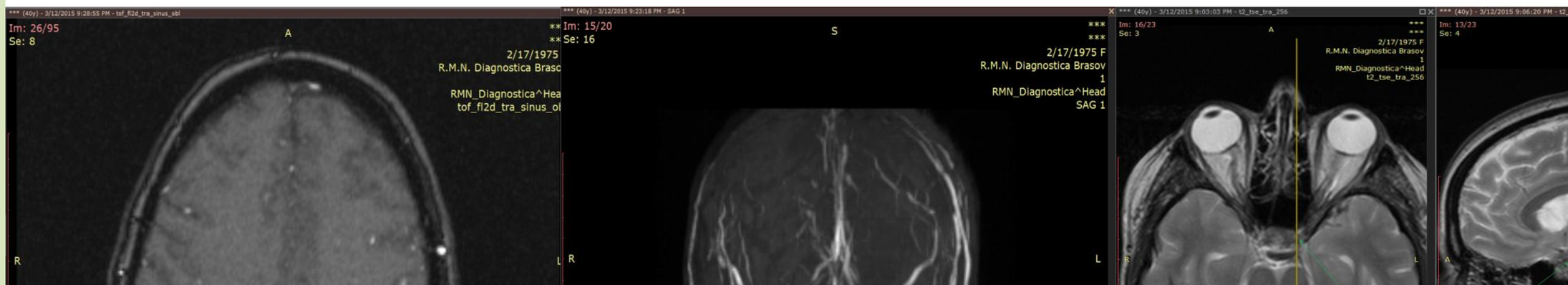
Also the patient had hepatosplenomegaly and portal hypertension with esophageal varices and hypertensive gastropathy, adding to the hemorrhagic risk of anticoagulation. Given that, the etiology of SAH was unknown and an estimation of her bleeding risk was difficult to provide, an empiric therapeutic course was chosen (anticoagulation with heparin as its effect is short lasting), fortunately for the patient she recovered completely and suffered no other hemorrhage during anticoagulation suggesting in retrospect that most likely SAH was a consequence of CVT in this particular case.



SAH in FLAIR has subtle signs: note the hyperintensity of the subarachnoid spaces between the parietal sulci and within the Sylvian fissure on the left side (pointed at by the yellow arrows)

The superior sagital sinus has impeded flow similar to "empty Δ sign"

Venous reconstruction shows absence of flow in left transverse sinus. Pointed at by the green arrows is hypointense region situated at the level of the cavernous sinus which is most likely a thrombus.



Congestion of pial veins seen on T2*

Accumulations of blood in the subarachnoid spaces within the Sylvian sulci, as well as in the IV-th ventricle

Conclusions

Coexistence of CVT and SAH within the context of a disease that is prone both thrombotic and hemorrhagic complications, such as myelofibrosis raises a therapeutic dilemma for which currently (to our knowledge at least) there is no standard treatment approach.

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