underlying malignancies and AQP4-IgG may be an indicator of a paraneoplastic immune response. Further investigations should be performed to firmly establish the clinical utility of AQP4-IgG.

Sangsu Han,* Rahul A. Sharma,† Harman Sekhon,† David Munoz,‡ Danah H. Albreiki†
*McMaster University, Hamilton, Ont.; †The Ottawa Hospital, Ottawa, Ont.; ‡St. Michael's Hospital, Toronto, Ont.

Originally received Jun. 23, 2019. Final revision Dec. 30, 2019. Accepted Jan. 3, 2020.

Correspondence to:
Danah H. Albreiki; dalbreiki@toh.ca.

References

1 Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015;85:177–89.
2 Jarius S, Wandinger KP, Borowski K, Stoecker W, Wildemann B. Antibodies to CV2/CRMP5 in neuromyelitis optica-like disease: case report and review of the literature. Clin Neurol Neurosurg 2012;114:331–5.
3 Sepulveda M, Sola-Valls N, Escudero D, et al. Clinical profile of patients with paraneoplastic neuromyelitis optica spectrum disorder and aquaporin-4 antibodies. Mult Scler 2018;24:1753–9.
4 Cai G, He D, Chu L, Dai Q, Xu Z, Zhang Y. Paraneoplastic neuromyelitis optica spectrum disorders: three new cases and a review of the literature. Int J Neurosci 2016;126:660–8.
5 Deuel LM, Bunch ME. A case of paraneoplastic neuromyelitis optica associated with small cell lung carcinoma. J Neuroimmunol 2018;316:130–2.

Footnotes and Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Can J Ophthalmol 2020;55:e129–e132
0008-4182/17/$-see front matter
https://doi.org/10.1016/j.jcjo.2020.01.005

Thrombotic thrombocytopenic purpura in chronic myelogenous leukemia

Thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by the pentad of microangiopathic hemolytic anemia, thrombocytopenia with purpura, acute kidney injury, neurologic abnormality with fluctuating mental status, and fever.[1,2] It has an incidence ranging from 3.7 to 11 cases per million and risk factors that include female gender, Afro-Caribbean ancestry, and obesity.[2] The prevailing pathophysiologic theory for TTP asserts that patients have a deficiency or defect in A disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13 (ADAMTS13), a protease that cleaves large multimers of von Willebrand factor.[3] When these multimers are not cleaved, they build up disproportionately to normal von Willebrand factor in the blood stream and trigger platelet-rich microthrombi formation and subsequent mechanical hemolysis.[3,4] This process is usually caused by a genetic mutation in the *ADAMTS13* gene or by an autoimmune process; however, it may also be triggered by infection,[3] pregnancy,[3,4] or medications.[5] Although pieces of the classic pentad are the most common presentation for TTP, ophthalmologic manifestations also rarely occur. We present a case of TTP secondary to dasatinib therapy with the ocular manifestation of papilledema.

A 33-year-old African American male presented with a chief complaint of throbbing, bilateral headache for several days in both his forehead and occipital region with associated intermittent arm numbness and blurry vision. His medical history was significant for chronic myelogenous leukemia (CML) in molecular remission, hypertension, stage II chronic kidney disease, and syphilis, for which he received penicillin treatment 14 years ago. His family history was significant for hypertension and type II diabetes. His surgical, ocular, and social history was unremarkable. The patient's current medications included valsartan/hydrochlorothiazide and dasatinib 50 mg daily, a chemotherapeutic agent for his CML. Physical examination showed ecchymoses over his lateral chest and right lower extremity. Ocular examination showed a best-corrected visual acuity measured at 20/25 OD (right eye) and 20/20 OS (left eye). Pupils were 4 mm in the dark and 3 mm in the light in both eyes (OU). Extraocular motility was full without any deficit. External and slit-lamp examinations were normal. On fundus examination, he had bilateral Frisen grade 1 papilledema, along with peripapillary angioid streaks. Humphrey visual field testing was normal, and optical coherence tomography global thickness of the retinal nerve fibre layer was 138 OD and 129 OS (Fig. 1), consistent with disc edema OU. Laboratory studies revealed a hemoglobin level of 8.7 g/dL, platelet count of 22 000/μL, elevated lactic acid dehydrogenase, elevated reticulocyte count, and schistocytes on blood smear. Due to bicytopenia, waxing and waning neurologic complaints, and current use of dasatinib, there was high suspicion for TTP confirmed by positive ADAMTS13 activity assay. He was started on high-dose prednisone therapy and plasmapheresis treatment. Owing to the presence of papilledema, magnetic resonance imaging (MRI) of the brain and orbit was performed, revealing a partially empty sella (Fig. 2). Magnetic resonance venography (MRV) demonstrated moderate focal stenosis of the distal right transverse sinus (Fig. 3) without evidence of thrombosis confirmed by computed tomography venogram (CTV).

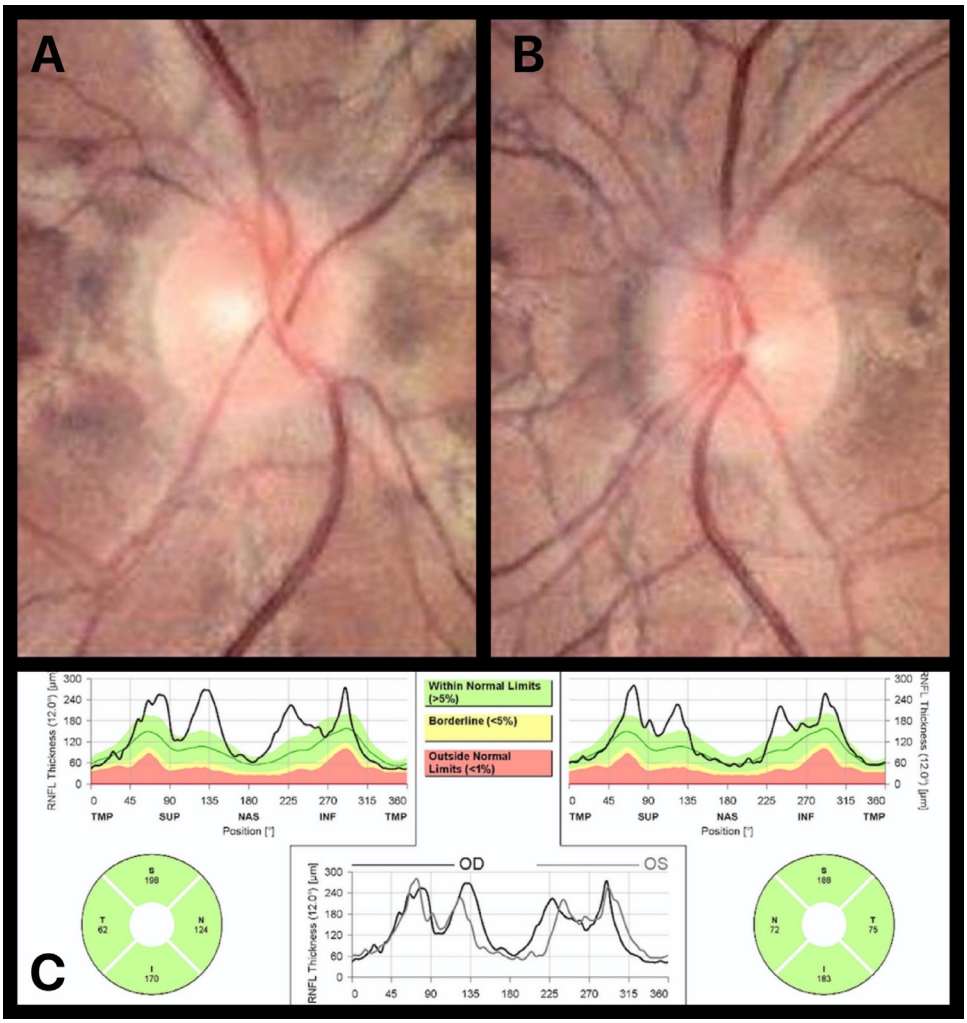

Fig. 1—Fundus photographs of the right (A) and left (B) fundi demonstrating Frisen grade 1 papilledema and angioid streaks. Optical coherence tomography of the retinal nerve fibre layer consistent with optic disc edema (C).

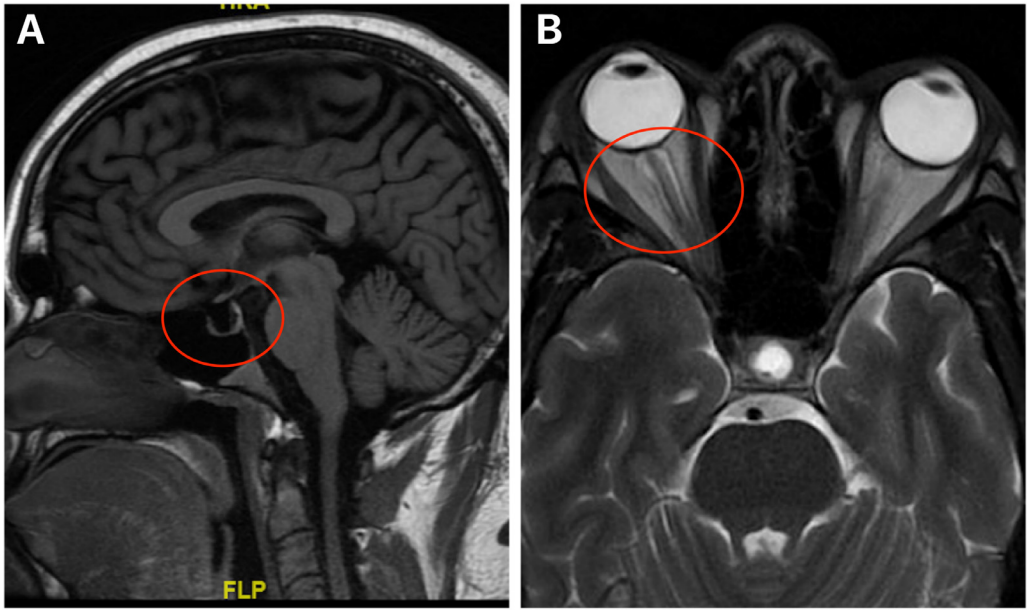

Fig. 2—Sagittal T1 (A) and axial T2 (B) magnetic resonance images of the brain and orbit demonstrating empty sella and fluid in the optic nerve sheath, respectively.

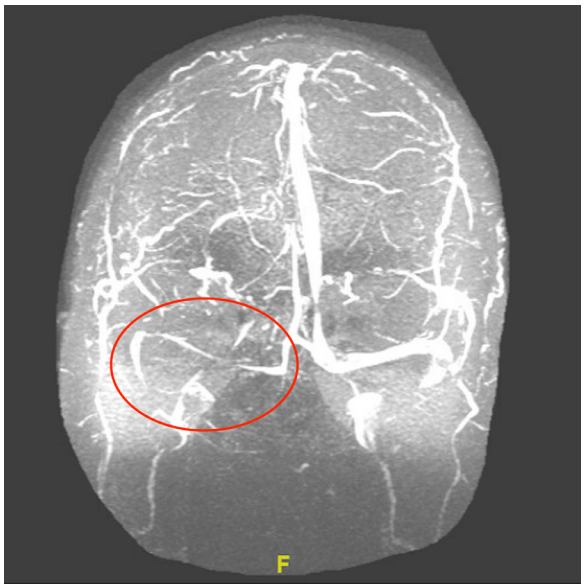

Fig. 3—Magnetic resonance venography demonstrating stenosis of the right transverse sinus.

Lumbar puncture revealed an elevated opening pressure of 50 cm of H_2O and otherwise normal cerebrospinal fluid. Repeat rapid plasma reagin testing was negative. A diagnosis of increased intracranial pressure (ICP) secondary to TTP and co-existing anemia was made. The asymmetry demonstrated by the MRV could be explained by a physiologic left transverse sinus dominance or a component of transverse sinus stenosis contributing to the increased ICP. This could be further elucidated if the asymmetry were to remain constant on repeat MRV. His hemoglobin and platelet counts normalized with the prednisone and plasmapheresis therapy, and the patient was started on Diamox 1000 mg daily to treat his elevated ICP. This dose was deemed appropriate despite his decreased kidney function, as his creatinine clearance was estimated to be greater than 50 mL/min, at which point dose modification may be considered. At 1 month of follow-up, his creatinine remained within normal limits at 1.26 mmol/L.

Dasatinib is a tyrosine kinase inhibitor that acts on BCR-ABL kinase and is used in the treatment of CML.[5] TTP is a rare disease characterized by the classic pentad of microangiopathic hemolytic anemia, thrombocytopenia with purpura, acute kidney injury, neurologic abnormality with fluctuating mental status, and fever.[1,2] Ocular manifestations of this disease are under-recognized and have been reported to occur in 14–20% of cases.[6] We reviewed the literature for the various ophthalmologic manifestations of TTP and found the following reported: both serous[4] and traction[7] retinal detachments, papilledema from malignant hypertension,[8–10] retinal hemorrhages,[11] retinal vascular occlusion including central retinal artery occlusion or central retinal vein occlusion,[12] choroid vasculopathy,[1] retinal pigment epithelium tear (thought to be owing to increased perfusion pressure secondary to hypertension as well as damage to the choroidal vasculature),[11] optic disk neovascularization,[7] vitreous hemorrhage,[7] homonymous hemianopia (possibly owing to petechial hemorrhages related to areas of microangiopathy),[1,10] and various cranial nerve palsies (possibly owing to thrombotic ischemia).[1] Our patient presented with the ocular finding of papilledema; however, he did not have concomitant malignant hypertension as seen in previous cases.[8–10] After our review, we found no other cases of TTP presenting with papilledema in a patient without malignant hypertension. Additionally, though it has been reported in the literature, microangiopathic hemolytic anemia (MAHA) secondary to tyrosine kinase inhibitor use is very rare. Three cases have been reported after imatinib use,[13,14] and to our knowledge, only 2 cases of dasatinib-induced MAHA have been reported in the literature.[5,15] We believe that our patient had a side effect of the treatment of the underlying disease, CML (i.e., CML treated with dasatinib leading to TTP, which in turn provoked intracranial hypertension from the underlying anemia and thrombocytopenia).

To support our hypothesis of increased ICP secondary to TTP and co-existing anemia, we examined alternate etiologies. First, the papilledema could have been secondary to malignant hypertension; however, physical examination showed a normal blood pressure. An MRV and subsequent CTV were then performed to investigate the possibility of venous sinus thrombus, which could have occurred secondary to thrombi from TTP or a hypercoagulable state owing to the patient's underlying malignancy. We also performed MRI of the brain and orbit to assess for any metastases that could have increased ICP directly (by mass effect) or indirectly (through blockade of arachnoid granulations and, thus, cerebrospinal fluid outflow). Additionally, though the patient had a prior negative rapid plasma reagin test, we repeated this test to investigate for neurosyphilis. The MRV and CTV did not show any evidence of thrombus formation, and the MRI did not reveal any metastases. The repeat rapid plasma reagin also returned negative.

It is our hope that this article increases awareness of the possibility of MAHA occurring in a patient on tyrosine kinase inhibitor therapy and possible ophthalmic and neuro-ophthalmic complications occurring either directly or indirectly from a side effect of the drug after ruling out direct disease progression or metastasis. We also emphasize that ophthalmologic findings in TTP may aid in early diagnosis and treatment.

Jared Raabe,* Ashwini Kini,† Andrew G. Lee†,‡,§,¶,‖

*University of Texas Medical Branch, Galveston, TX; †Houston Methodist Hospital, Houston, TX; ‡Weill Cornell Medicine, New York, NY; §University of Texas MD Anderson Cancer Center, Houston, TX; ¶Texas A and M College of Medicine, Bryan, TX; ‖The University of Iowa Hospitals and Clinics, Iowa City, IA

Originally received Sep. 27, 2019. Final revision Nov. 21, 2019. Accepted Jan. 12, 2020.

Correspondence to:
Andrew G. Lee, MD; aglee@houstonmethodist.org.

References

1 Percival SP. Ocular findings in thrombotic thrombocytopenic purpura (Moschcowitz's disease). Br J Ophthalmol 1970;54:73–8.

2 Said A, Haddad RY, Stein R, Lerma E. Thrombotic thrombocytopenic purpura. Disease-a-Month 2014;60:500–4.
3 Tsai HM. Pathophysiology of thrombotic thrombocytopenic purpura. Int J Hematol 2010;91:1–19.
4 Zhao C, Qu Y, Sui R, et al. Delayed visual recovery in pregnancy-associated thrombotic thrombocytopenic purpura with bilateral serous retinal detachment. Doc Ophthalmol 2013;126:163–9.
5 Demirsoy ET, Mehtap O, Atesoglu EB, et al. Dasatinib-induced immune mediated-thrombotic thrombocytopenic purpura. Transfus Apher Sci 2018;57:222–4.
6 Bobbio-Pallavicini E, Porta C, Brocchieri A, Saporiti A, Tacconi F. Ocular involvement in acute thrombotic thrombocytopenic purpura. Haematologica 1995;80:194–5.
7 Lewellen DR, Singerman LJ. Thrombotic thrombocytopenic purpura with optic disk neovascularization, vitreous hemorrhage, retinal detachment, and optic atrophy. Am J Ophthalmol 1980;89:840–4.
8 Bashir T, Alfishawy M, Babigumira M, Bashir T. Malignant hypertension and thrombotic thrombocytopenic purpura: false friends. Am J Case Rep 2015;16:374–6.
9 Dunea G, Muehrcke RC, Nakamoto S, Schwartz FD. Thrombotic thrombocytopenic purpura with acute anuric renal failure. Am J Med 1966;41:1000–6.
10 O'Brien JL, Sibley WA. Neurologic manifestations of thrombotic thrombocytopenic purpura. Neurology 1958;8:55–64.
11 Hartley KL, Benz MS. Retinal pigment epithelial tear associated with a serous retinal detachment in a patient with thrombotic thrombocytopenic purpura and hypertension. Retina 2004;24:806–8.
12 Schwartz SG, Hickey M, Puliafito CA. Bilateral CRAO and CRVO from thrombotic thrombocytopenic purpura: OCT findings and treatment with triamcinolone acetonide and bevacizumab. Ophthalmic Surg Lasers Imaging 2006;37:420–2.
13 Al Aly Z, Philoctête Ashley JM, Gellens ME, González EA. Thrombotic thrombocytopenic purpura in a patient treated with imatinib mesylate: true association or mere coincidence? Am J Kidney Dis 2005;45:762–8.
14 Ojeda-Uribe M, Merieau S, Guillon M, et al. Secondary thrombotic microangiopathy in two patients with Philadelphia-positive hematological malignancies treated with imatinib mesylate. J Oncol Pharm Pract 2016;22:361–70.
15 Martino S, Daguindau E, Ferrand C, et al. A successful renal transplantation for renal failure after dasatinib-induced thrombotic thrombocytopenic purpura in a patient with imatinib-resistant chronic myelogenous leukaemia on nilotinib. Leuk Res Rep 2013;2:29–31.

Footnotes and Disclosure

The authors report no conflict of interest and received no financial support or sponsorship.

Can J Ophthalmol 2020;55:e132–e135
0008-4182/17/$-see front matter
https://doi.org/10.1016/j.jcjo.2020.01.003

Tolosa-Hunt syndrome: case series on the timed use of diagnostic magnetic resonance imaging

Tolosa-Hunt syndrome refers to an idiopathic granulomatous inflammation of the cavernous sinus or superior orbital fissure that manifests as painful ophthalmoplegia.[1,2] Clinical features include periorbital pain in conjunction with ipsilateral ocular motor nerve palsies (third, fourth, and/or sixth cranial nerves), as well as possible involvement of the ophthalmic, maxillary, and mandibular divisions of the trigeminal nerve and the facial nerve.[3,4] Despite its tendency to resolve spontaneously, the syndrome is noted to relapse and remit, and it is known to be glucocorticoid responsive.[5] With an estimated annual incidence of one case per million, the syndrome is rare and occurs equally among men and women.[6]

According to the diagnostic criteria of the International Headache Society, patients present with the previously noted constellation of symptoms.[4] In 2004, the criteria were redefined to include magnetic resonance imaging (MRI) or biopsy to identify granulomatous inflammation of the superior orbital fissure or cavernous sinus, which can be particularly useful in ruling out other neoplastic, infiltrative, and infective etiologies. Contrast-enhanced MRI findings may include abnormal tissue in an enlarged cavernous sinus appearing isointense to gray matter and well enhanced with gadolinium.[7] However, in certain cases initial MRI can be normal, calling into question the timing of brain imaging and its necessity in diagnostic confirmation.[8] Here we present a case series involving 2 patients with Tolosa-Hunt syndrome who initially presented with normal MRI.

The 2 cases in this series initially presented with a referral between 2015 and 2016. Patients had previously undergone a contrast-enhanced MRI that revealed no abnormal pathology of the cavernous sinus or superior orbital fissure, but on repeat scans they had enhancing lesions within the region. A retrospective chart review was conducted to document relevant presentation, management, and outcome information.

A 47-year-old female with a known history of diabetes and obesity was referred for left abducens palsy associated with left-sided periorbital paresthesia and left-sided headaches of 3 months' duration. The patient had previously developed left pupil–sparing oculomotor nerve palsy (diplopia and left ptosis) associated with headache 1 year before the referral. She underwent MRI within 2 months, which revealed no noted abnormalities aside from microangiopathic disease (Fig. 1A). The oculomotor nerve palsy and the headache resolved over 3 months, and it was attributed