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MUHC-MNH

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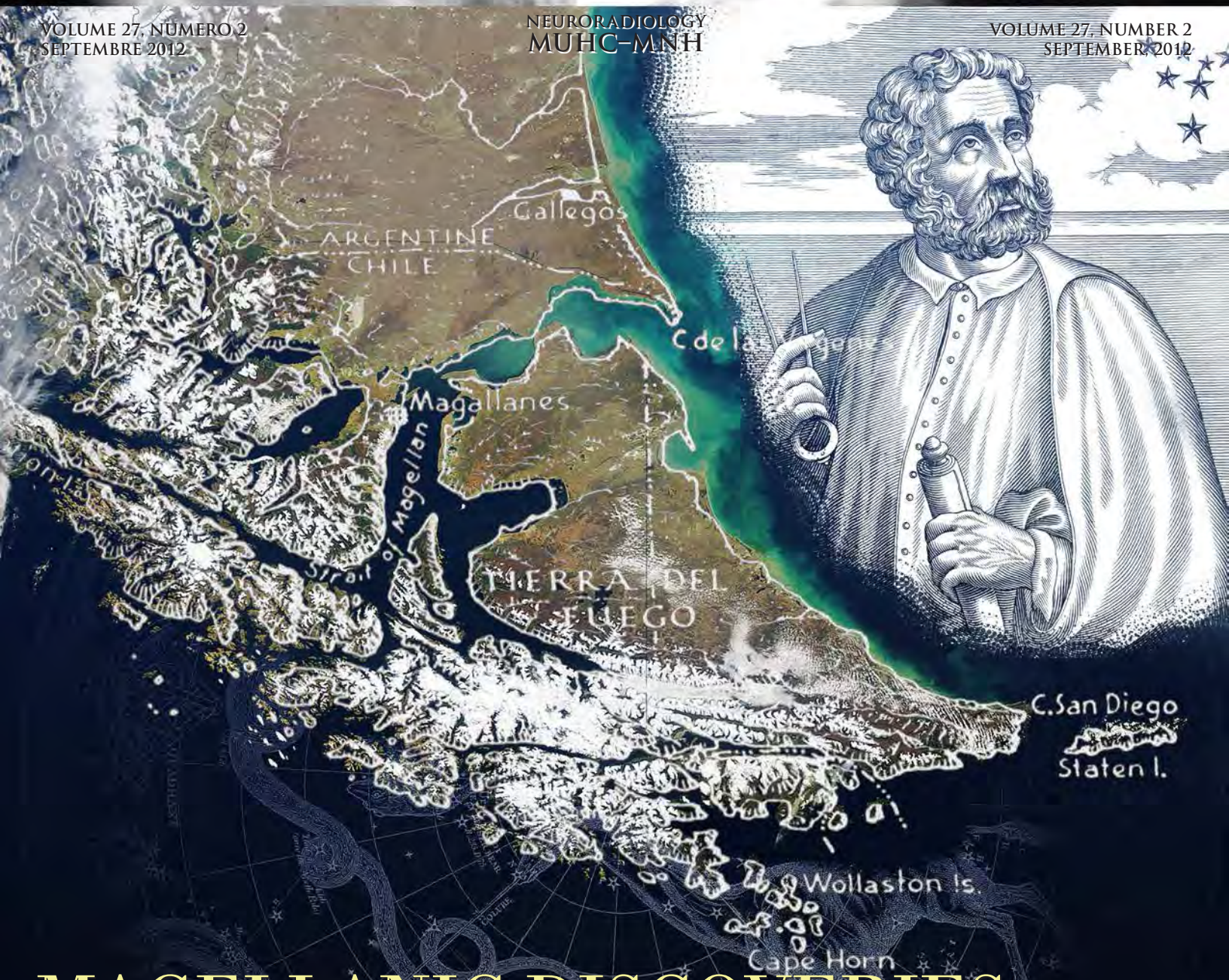
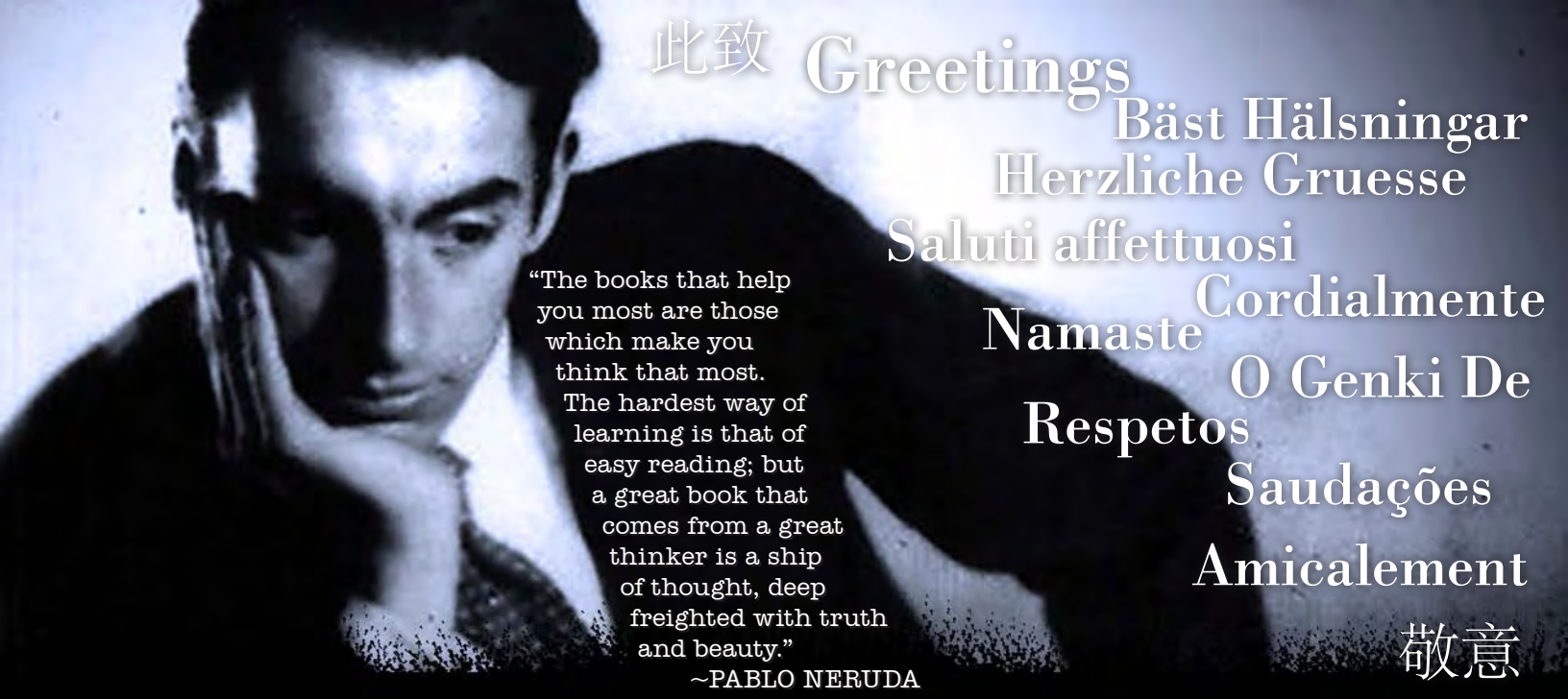
NEUROIMAGE

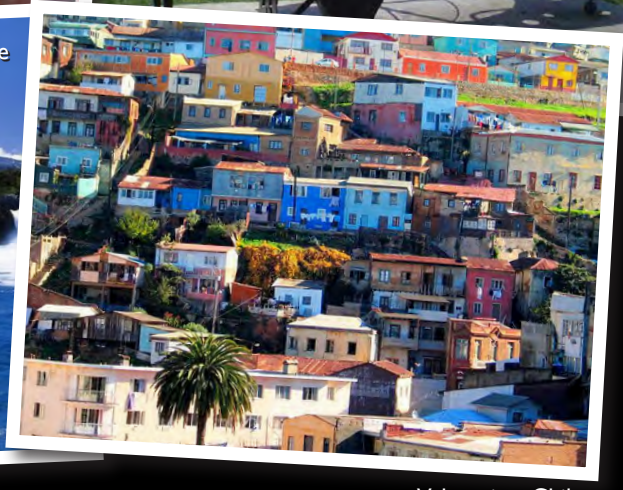


MAGELLANIC DISCOVERIES

IN THIS ISSUE ...



Earlier this year, we took a cruise down around South America, on ths MS Veendam ship. It was the east-west cruise, from Buenos Aires to Valparaiso, and then to Santiago.


Valparaiso, Chile

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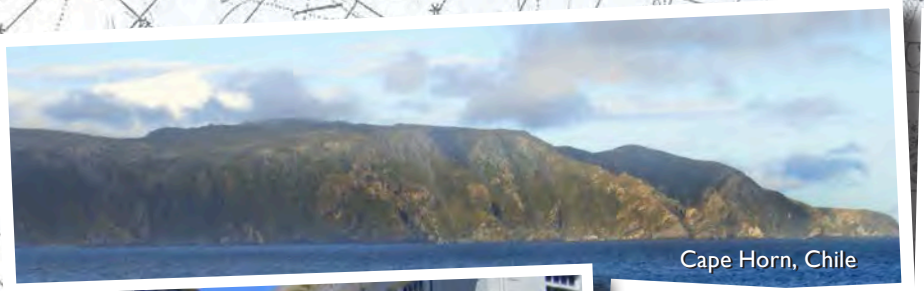
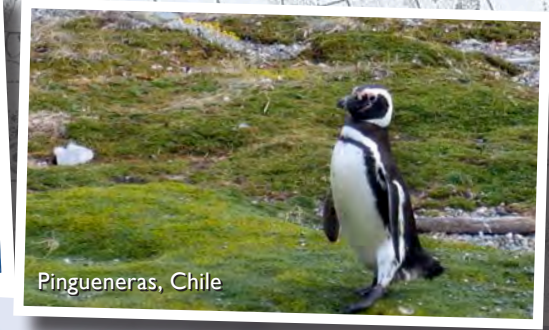


Cape Horn, Chile



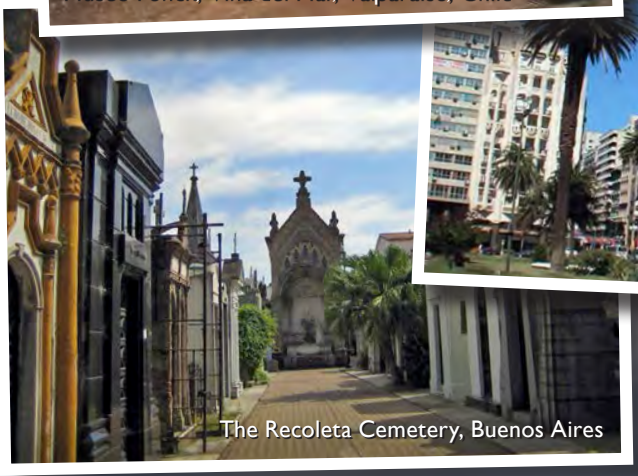
Pingueneras, Chile

Museo Fonck, Viña del Mar, Valparaíso, Chile

Amalia Glacier, Chile

Palacio Salvo, Montevideo, Uruguay

Ascensores in Valparaiso



The Recoleta Cemetery, Buenos Aires

The cover page designed by Jean-Paul Acco, was inpired by this cruise, mainly because the voyage took us near the Strait of Magellan, which he thought can be used as a theme for great discoveries. I have taken many photographs, and a few are included in this issue. Souvenirs of Buenos Aires, Montevideo, Cape Horn, Ushuaia, Punta Arenas, Puerto Mount and Frutillar, Valparaïso and Santiago.

I have loved Valparaïso and its memories, its ascensores. I have been playing Oswaldo ``Citano`` Rodriguez song often since. Santiago has our best souvenir, the city and its surrounding mountains, and every word about the city and its history from our excellent guide, Renée de Venzac.

Ushuaia, Argentina

¡GRACIAS

Centre universitaire de santé McGill
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Les meilleurs soins pour la vie
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Montreal, February 13th, 2012

Ruby Tuesday
Casa Matriz
Carmencita 25, Local 1
Las Condes - Santiago

Dear Sir,

On January 21, we stopped at your restaurant at Santiago airport, located near Gate 12, just before boarding the plane for Buenos Aires. My wife bought a coffee and forgot her wallet on the counter. Once in the plane, she realized that, and ran quickly back. Your gentleman at the counter had put the wallet aside and gave it back to her.
I was very appreciative of that gesture and on the way back we stopped at the stand to give the gentleman a small token of our gratitude. The local manager took it and gave me your address so I would let you know about this very honest gesture of your employee, and likewise of all your employees.

I hope you make it known to the said employee and all your staff at that place.

Sincerely yours,

Denis Melançon M.D.
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Comet Lovejoy over Santiago, Chile

Hereditary Spastic Paraparesis (HSP) with white matter involvement

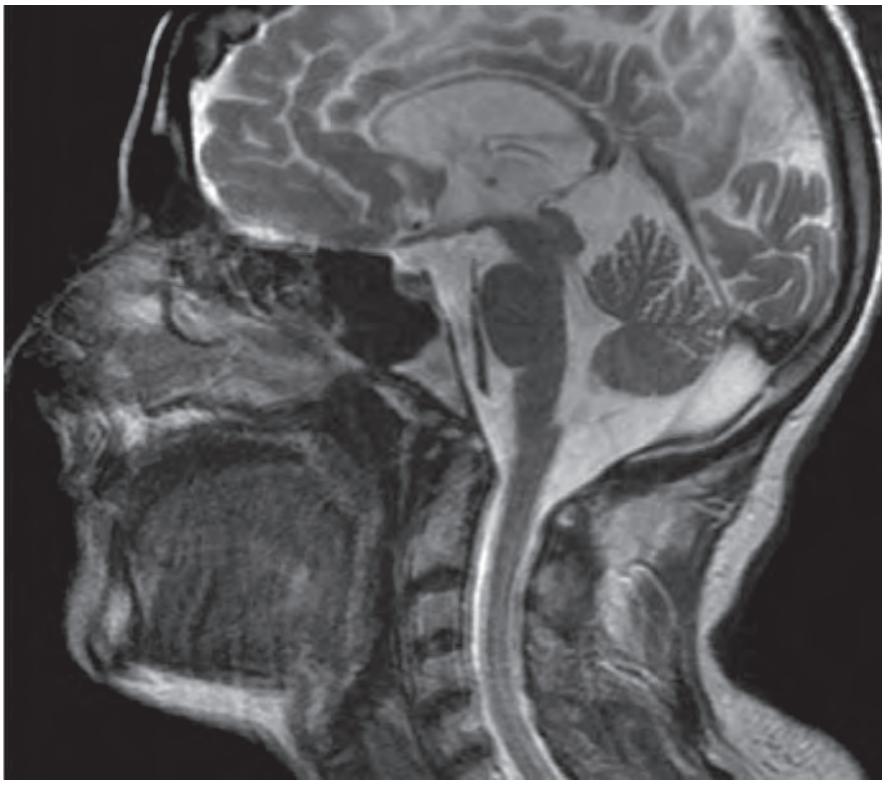
Roberta La Piana

White matter alterations, seen as hyperintense signal in T2-weighted images, have been reported in some forms of hereditary spastic paraplegia. They are usually non-specific, often punctiform and located in the periventricular white matter or in the centrum semiovale.1 Thinning of the corpus callosum is another finding sometimes associated to hereditary spastic paraplegias.2,3

Beside non-specific findings, some neuroradiological signs can be helpful in orienting the diagnosis among the different forms of hereditary spastic paraplegia, as our case documents.

A 35 year-old female patient presented at our Institute with spastic paraparesis and signs of cognitive decline. The brain MRI performed showed a diffuse cerebral atrophy, mainly involving the white matter and the anterior portion of the corpus callosum (Figure 1). An abnormal T2-hyperintense signal was so noted bilaterally in the anterior periventricular white matter (Figure 2A). At the six-year follow up MRI (Figure 2B), a slight progression in the degree of cerebral atrophy was noted. The thinning of the corpus callosum and the signal alteration in the anterior periventricular white matter were unchanged since previous; interestingly, both these findings evoked a specific involvement of the anterior forceps.

A recent work by Riverol et al (2009) analysed a series of patients with spastic paraparesis due to mutations in the Spatacsin Gene (SPG11); they reported white matter alterations similar to those documented in our patient. The signal abnormality described by Riverol et al involved the fibers that from the genu of the corpus callosum extend into the frontal white matter, namely the anterior forceps. Since the appearance of these abnormalities in the axial sequences resembles the profile of the "ears of the linx", the authors proposed to use this new imaging sign to orient the neuroradiological diagnosis and eventually to guide the genetic tests.



In our patient the evidence of the thinning of the anterior part of the corpus callosum (Figure 1) and the "ears of the lynx" sign (Figure 3) helped us to formulate the correct diagnostic hypothesis. Given that 60% of patients with hereditary spastic paraparesis and thin corpus callosum have mutations in the Spatacsin Gene (SPG11),2 the prompt identification of the "ears of the lynx" sign can be crucial in accelerating the diagnostic process of these patients.

***Figure 1** Sagittal T1-weighted MR image showing the thinning of the corpus callosum, especially involving the anterior portion.*

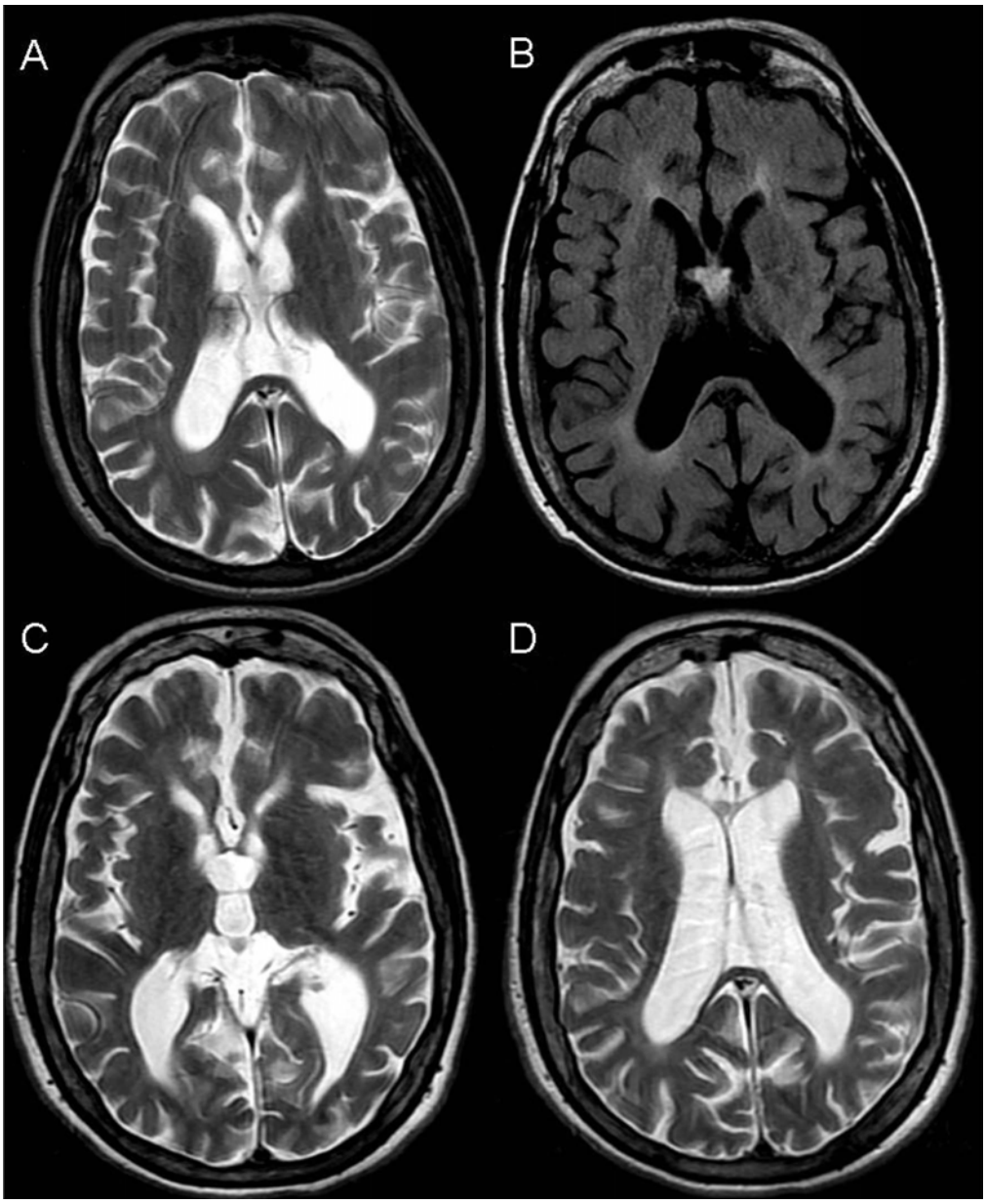
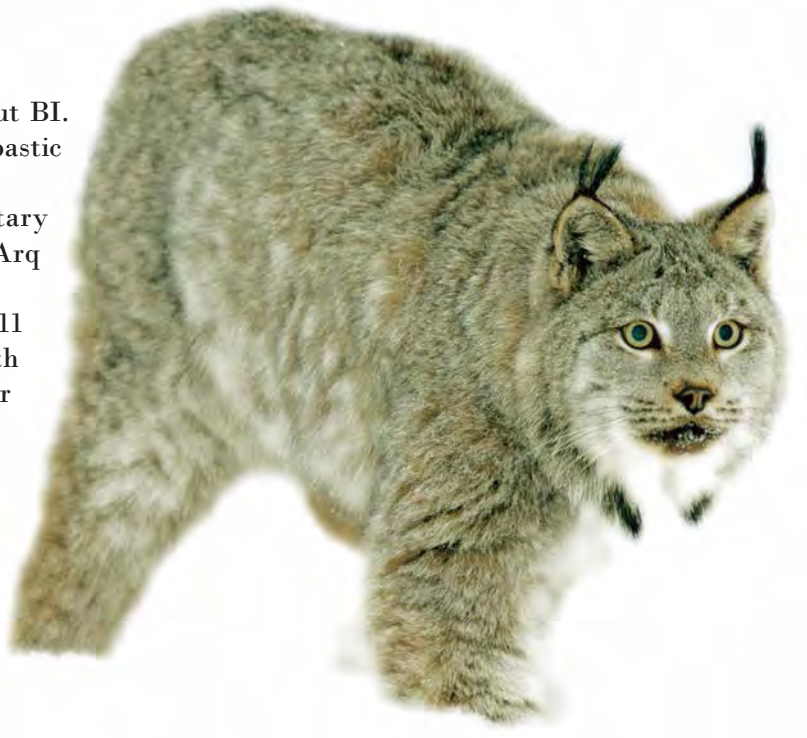


Figure 2 *Upper row, axial T2-weighted (A) and FLAIR (B) MR images showing the diffuse cerebral atrophy, the involvement of the anterior part of the corpus callosum and the hyperintense signal in the anterior periventricular white matter. Lower row, T2-weighted MR images performed at six year follow up after the first exam showing a mild progression of the cerebral atrophy.*

Figure 3 *Ears of the linx. The profile of the ears and in particular the hair tufts can be evoked by the T2 signal abnormalities associated to hereditary spastic paraplegia caused by mutations in the SPG11 gene.*



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2. Teive HA, Iwamoto FM, Della Coletta MV, et al. Herditary spastic paraplegia associated with thin corpus callosum. Arq Neuropsiquiatr 2001;59:790-92
3. Stevanin G, Azzedine H, Denora P, et al. Mutations in SPG11 are frequent in autosomal recessive spastic paraplegia with thin corpus callosum, cognitive decline and lower motor neuron degeneration. Brain 2008;131:772-784
4. Riverol M, Samaranch L, Pascual B, et al. Forceps minor region signal abnormality "Ears of the Lynx": an early MRI finding in spastic paraparesis with thin corpus callosum and mutations in the Spatacsin Gene (*SPG11*) on chromosome 15.

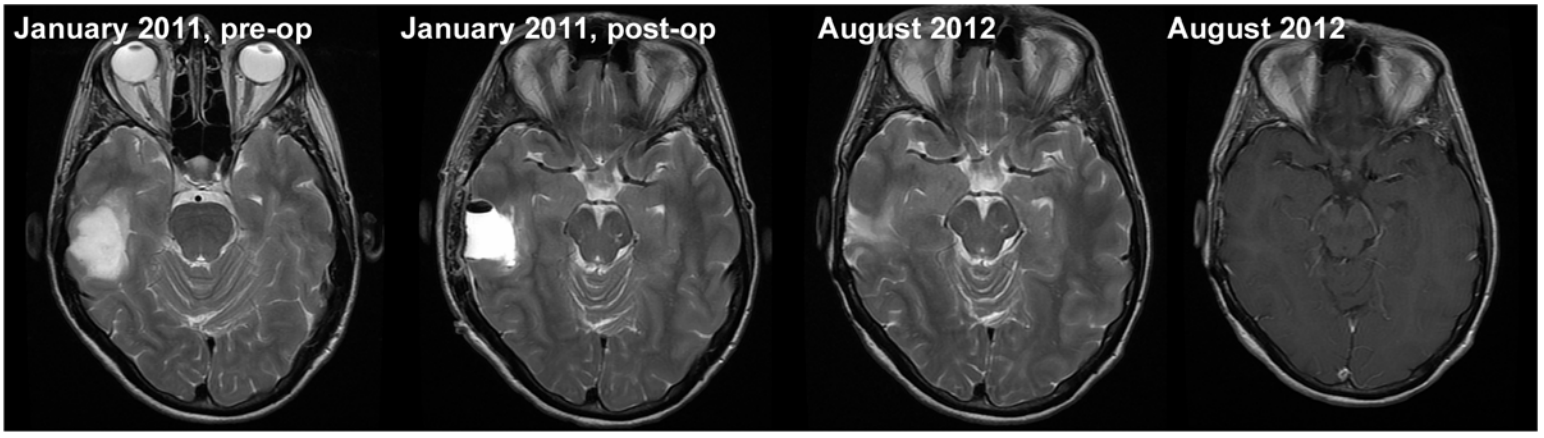
The Emerging Significance of Isocitrate Dehydrogenase

Kevin Petrecca

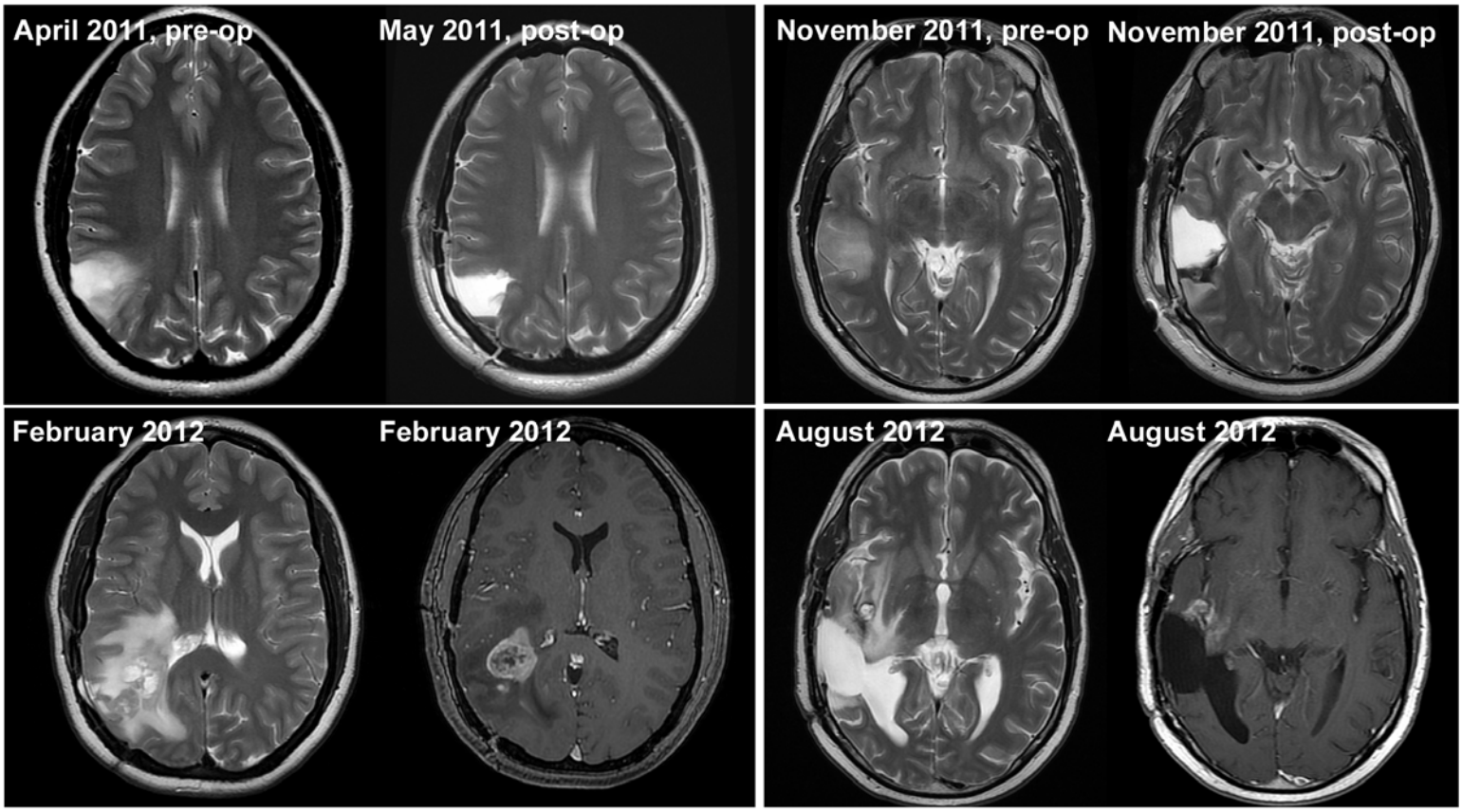
Isocitrate dehydrogenase genes *IDH1* and *IDH2* are mutated in >70% of grade 2 and 3 gliomas and secondary glioblastomas (grade 4), with R132 (*IDH1*) and R172 (*IDH2*) accounting for the large majority of mutations (Yan et al., 2009). These mutations are of prognostic significance as they are associated with drastically different survival. Grade 3 astrocytoma patients with *IDH* mutation have a median overall survival of 65 months. In contrast, those without mutation have a median overall survival of only 20 months. Similarly, glioblastoma patients with *IDH1* or *IDH2* mutation had a median overall survival of 31 months, whereas those with wild-type *IDH1* or *IDH2* have a 15-month median overall survival. In addition to prognostic significance they also serve as biomarkers that can be used to distinguish grade 1 gliomas from grade 2 and 3 gliomas, and primary glioblastomas from secondary glioblastomas.

Mutation of IDH leads to elevated levels of 2-hydroxyglutarate (2-HG). In wild-type *IDH1*, R132 interacts with C-3 carboxylate of isocitrate inhibiting α-ketoglutarate (α-KG) binding to wild-type IDH1. Mutation of R132 to other amino acids significantly reduces the isocitrate binding while making α-KG binding more favourable, leading to enzymatic reduction of α-KG to produce 2-HG. Converting α-KG to 2-HG is a shared feature between mutant IDH1 and IDH2 and this accumulation of the oncometabolite 2-HG is thought to play a role in gliomagenesis (Guo et al., 2011).

How does IDH mutation lead to oncogenesis? Emerging evidence suggests that the mutant IDH promotes the CpG island methylator phenothype. This methylation remodels the genome leading to altered gene transcription and tumor development (Turcan et al., 2012). Similarly, IDH mutation has also been shown to affect the methylation status of certain histones, leading to the inhibition of normal cell differentiation thus promoting gliomas formation (Lu et al., 2012).



Illustrative case demonstrating stability of a grade 2 mutant IDH astrocytoma.



Illustrative cases demonstrating rapid recurrence and transformation of two grade 2 wild-type IDH1 astrocytomas to a grade 4 gliomas.

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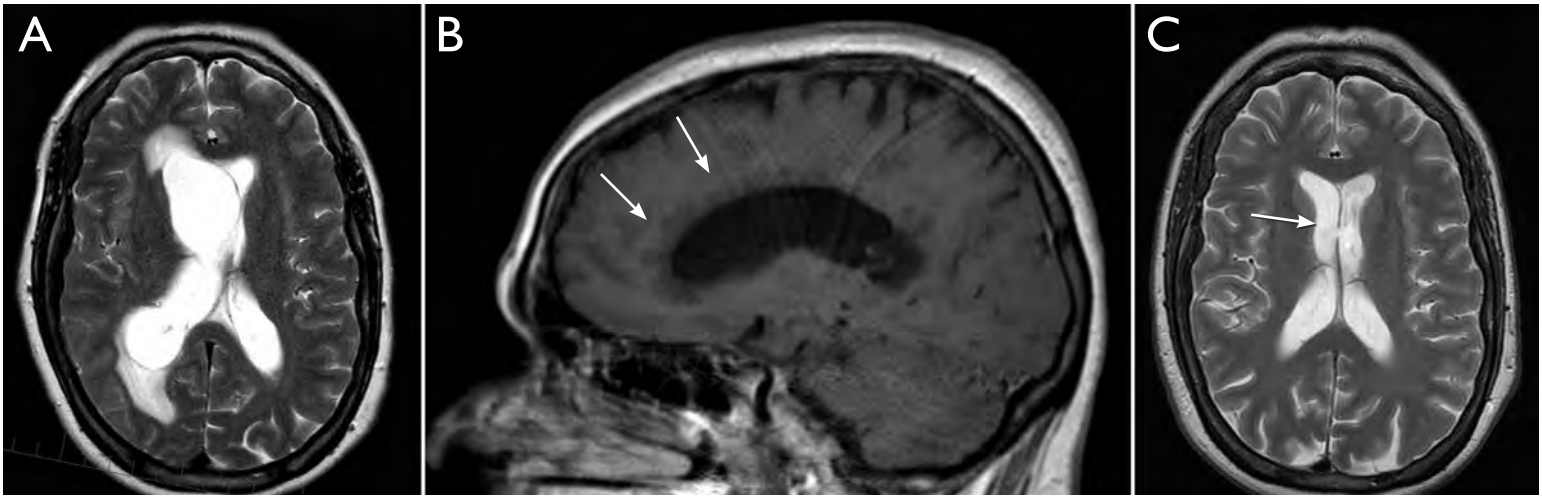
Transependymal Flow
... follow-up observations

Denis Melançon

Last Neuro Image has shown examples of transependymal CSF flow through radiations of the corpus callosum, and also along the temporal and occipital horns. (pages 9-10-11)

One of those examples was Figure. 3, (see below) where right unilateral transependymal flow was present at the frontal and occipital horns. Figure 3c showed resolution of the unilateral ventricular dilatation and transependymal flow following fenestration of the septum pellucidum. Non specific inflammatory changes were reported from the biopsy at the time of surgery in the region of Munro.



Patient was well for many months afterward, without a shunt.

Figures 1-a,b show flow phenomena induced in the left lateral ventricle from passage of CSF through the fenestration, maintaining normal and equal ventricular size.

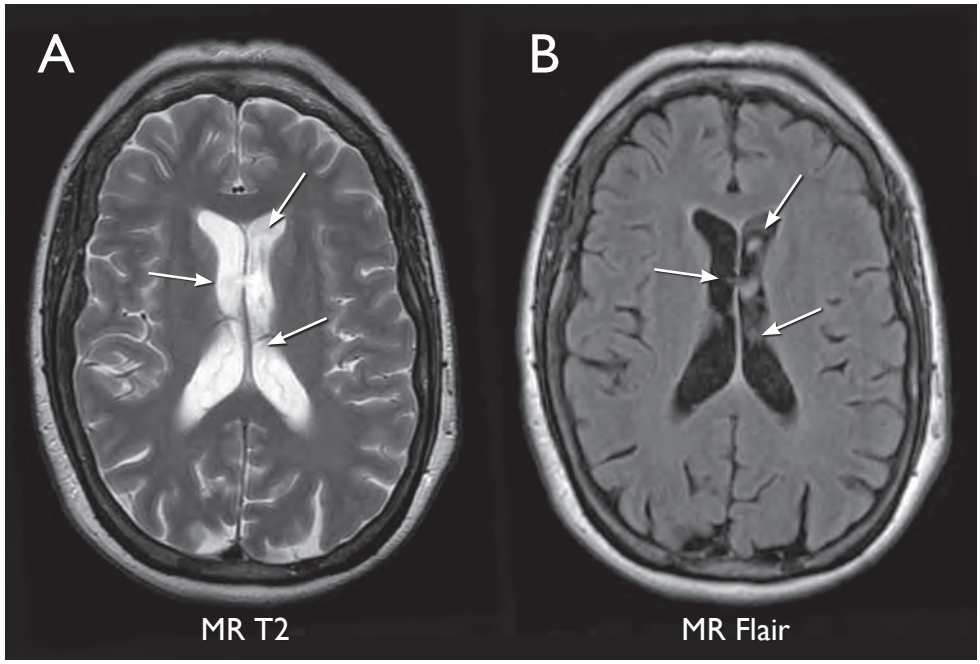


Figure 1

Eventually however, she presented gradual enlargement of both lateral ventricles, equally, with now transependymal CSF flow around both lateral ventricles, which required a ventricular drain *Figure 2-a,b,c.* Note the absence of of flow arifacts in either lateral ventricle compared to Figure 1.

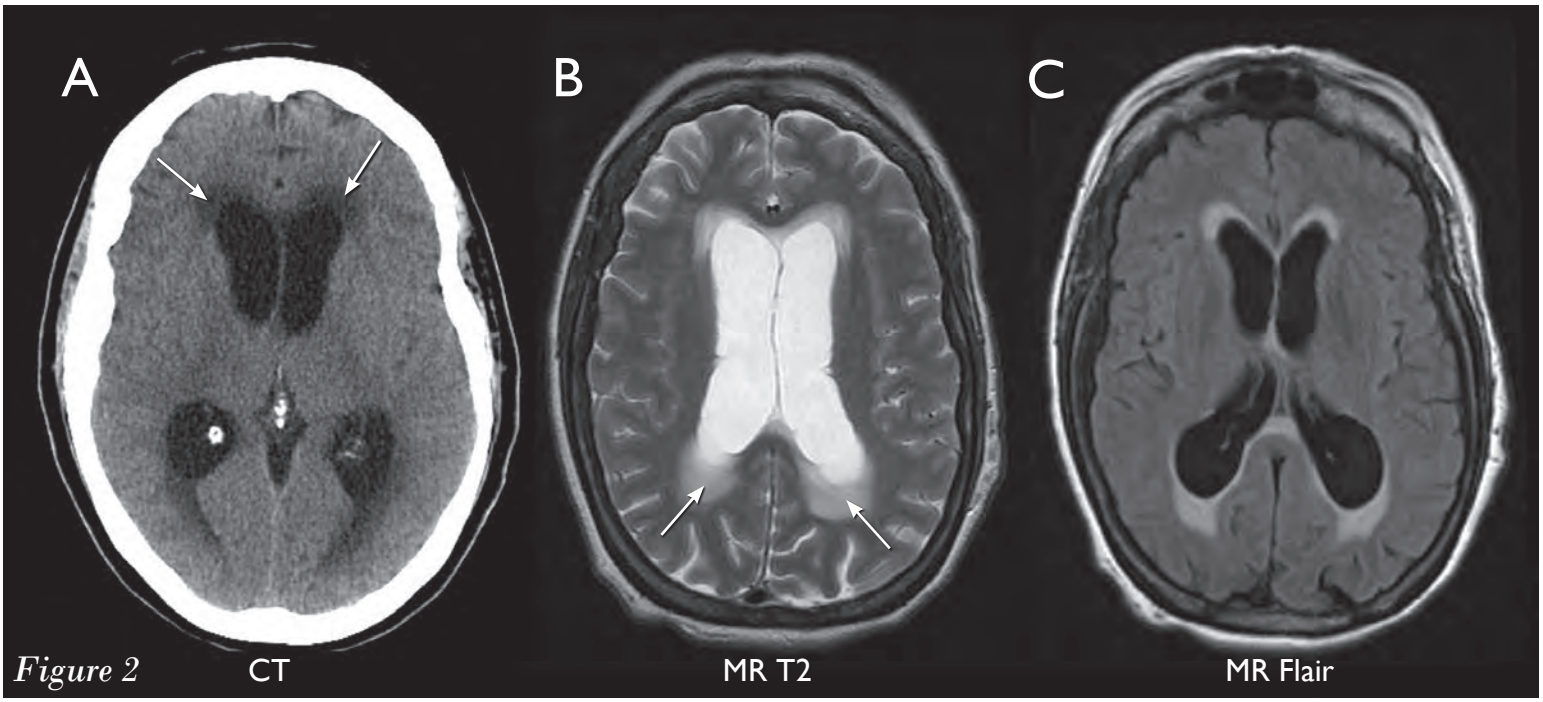


Figure 2

In the process of investigation, a large tumour of the left kidney was discovered, *Figure 3*. Because of the risk of a VP shunt malfunction, a right ventricular-subarachnoid space shunt was inserted. *Figure 4*

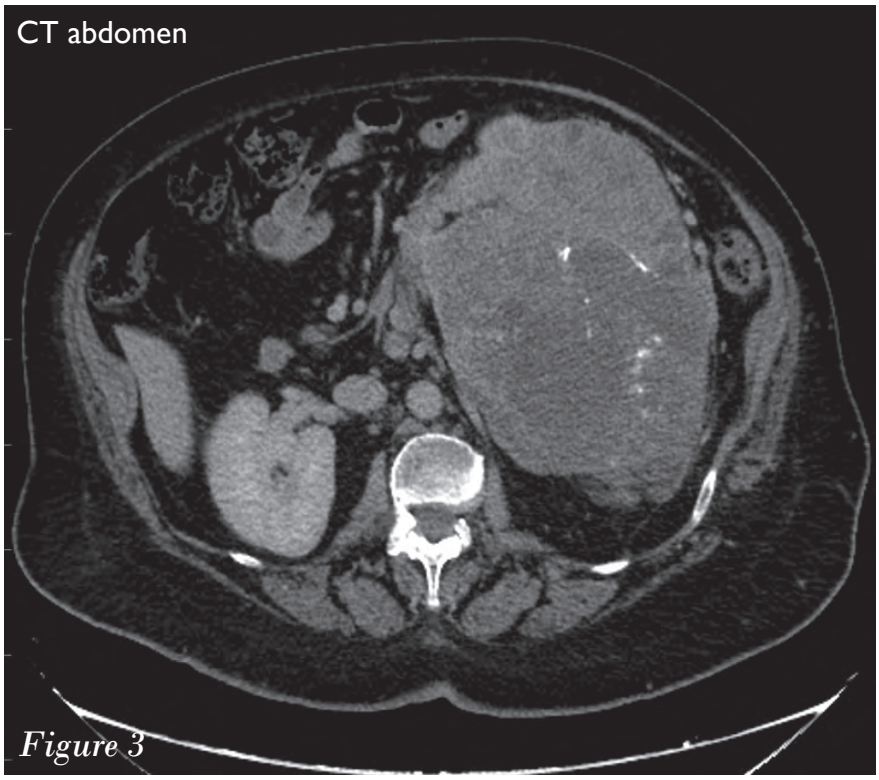


Figure 3

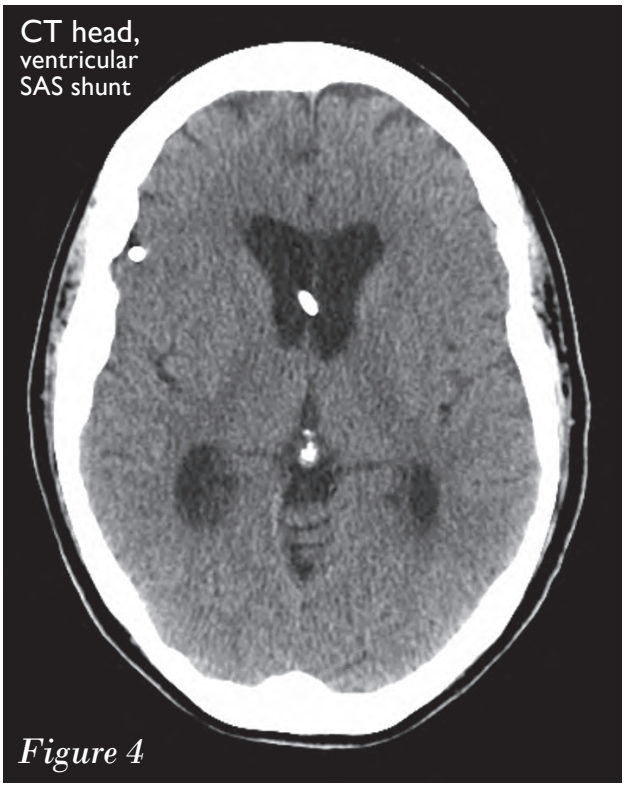


Figure 4

This very unique manifestation of obstruction at both foramina of Munro sequentially without tumour is hard to explain; could it be reaction of the pillars of the fornix, a limited form of limbic encephalitis?

Use of patient's images courtesy of Dr David Sinclair.