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January 2021 Critical Care Case of the Month: Ataque Isquémico Transitorio in Spanish

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History of Present Illness:

The patient is a previously healthy 61-year-old Spanish-speaking woman who was unable to speak after awakening. Per Emergency Medical Service she was found to be aphasic upon their arrival. While in the Emergency Room the patient was able to speak, alert and oriented x4, with all her symptoms spontaneously resolved. The patient denied fever, chills, blurred vision, headache or any history of migraines, TIA, or stroke.

The patient had a similar event about two weeks earlier which also spontaneously resolved. During that time, the patient had a non-contrast CT head and an MRI of the brain, both of which were unremarkable. Her home medications include aspirin 81 mg and atorvastatin 40 mg daily.

Past Medical History, Family History and Social History

The patient denies tobacco use or use of illicit drugs. She reports that she will occasionally drink alcohol. There is no family history of strokes.

Physical Examination

- Vitals: BP 123/80 mm Hg, T-max of 36.5° C, heart rate 72 bpm, SpO2 97%.
- HEENT: scleral icterus.
- Lungs: clear
- Heart: regular rhythm
- Abdomen: soft without organomegaly, masses or tenderness
- Skin: jaundiced
- Neurological examination:
 - Alert and oriented x4 with no focal neurological deficit observed
 - Cranial nerves II to XII were intact
 - Normal motor function
 - Normal speech
 - No facial asymmetry or facial droop
 - Normal mood and affect

Which of the following *laboratory tests* should be ordered?

1. None. She should be sent home.
2. Serum calcium/phosphorus

3. Liver function studies
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

Based on the initial history and physical examination, a variety of laboratory and radiologic studies are indicated. Because the physical examination shows scleral icterus and jaundice, liver function testing (lactic dehydrogenase [LDH], alanine transaminase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], and bilirubin) is indicated (Table 1).

Table 1. Liver function testing

Laboratory test	Value	Normal Range
Total bilirubin	5.8 mg/dL	0.1-1.2 mg/dL
Direct bilirubin	0.56 mg/dL	<0.3 mg/dL
LDH	405 U/L	140-280 U/L
Alanine transaminase (ALT)	7 U/L	7-55 U/L
Aspartate transaminase (AST)	24 U/L	8-48 U/L
Alkaline phosphatase (ALP)	85 U/L	40-129 U/L

[Click here to display Table 1 in an enlarged window.](#)

There is no apparent indication for serum calcium or phosphorus at this time.

Based on the above, what ***additional laboratory testing*** should be obtained?

1. Complete blood count
2. Reticulocyte count
3. Serum haptoglobin
4. 1 and 3
5. All of the above

Correct!
5. All of the above

The total bilirubin is increased while the direct bilirubin is minimally elevated. Therefore, the indirect (unconjugated) must be elevated. In the absence of bruising or

bleeding into a body organ the most common cause would be hemolytic anemia (1). The elevated serum LDH is consistent with LDH released from red blood cells in a hemolytic anemia. Additional laboratory testing of a complete blood count, reticulocyte count and serum haptoglobin would confirm the diagnosis. The diagnostic work-up done while the patient was in the emergency department was showed a hemoglobin of 8.1 g/dL (normal 12.0 to 15.5 g/dL), a hematocrit of 24.1 (normal 35.5 to 44.9), a mean corpuscular volume (MCV) of 96.7, and a platelet count of $24 \times 10^3/\text{mcL}$ (normal 150,000-300,000 cells/mcL). The reticulocyte was increased at 9.4% and the serum haptoglobin was decreased at <30/mg/dL consistent with haptoglobin binding to hemoglobin released during hemolysis. Prothrombin time (PT), partial thromboplastin time (PTT), creatinine and blood urea nitrogen (BUN) were all normal.

The patient was admitted with an initial diagnosis of hemolytic anemia and transient aphasia of unclear etiology.

What ***imaging studies*** should be ordered?

1. Brain MRI
2. Chest X-ray
3. Head CT angiography
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3 or 5. All of the above

A chest x-ray has been shown to be of benefit only when indicated (2). In this case, it could be argued that a search for possible lung lesion which might account for the neurological findings through a metastasis is possible.

An initial CT of the head was ordered (Figure 1).

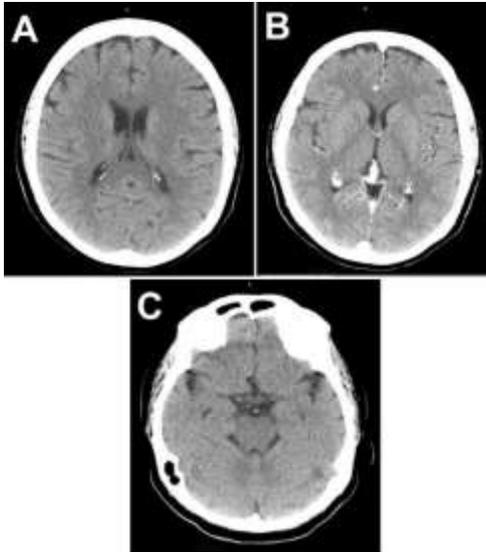


Figure 1. Initial CT of head. [Click here to display Figure 1 in an enlarged window.](#)

It was followed by a head CT angiogram (Figure 2).

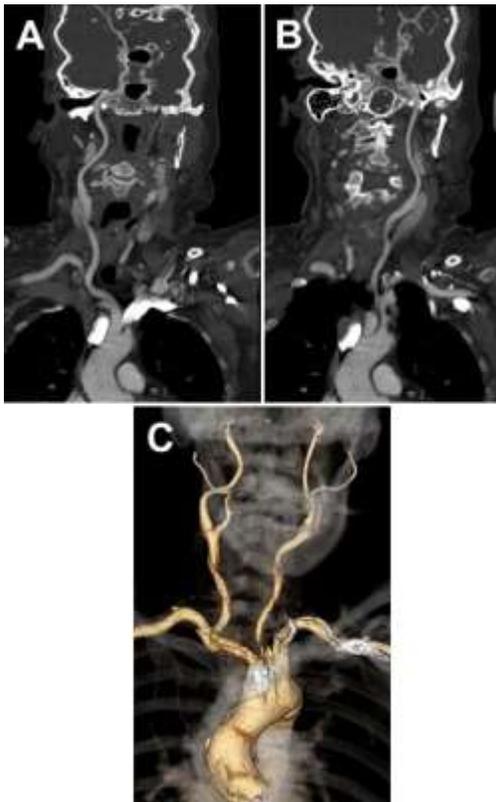


Figure 2. CT angiogram of head. [Click here to display Figure 2 in an enlarged window.](#)

What do the head CT and CT angiogram show?

1. The head CT angiogram is normal
2. The head CT angiogram shows a lesion in the lower portion of the carotid artery
3. The head CT is normal
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

Both the head CT scan and the CT angiogram were interpreted as normal. The narrowing of the left common carotid artery seen in the composite view (Figure 2C) is an artifact and not confirmed in the other view of the left common (Figure 2B).

Which of the following are considerations in the differential diagnosis?

1. Disseminated intravascular coagulation (DIC)
2. Immune thrombocytopenia (ITP)
3. Thrombotic thrombocytopenic purpura (TTP)
4. 1 and 3
5. All of the above

Correct!
5. All of the above

All are considerations. Their characteristics are summarized in Table 2 (3).

Table 2. Comparison between ITP, TTP and DIC (3).

Parameter	ITP	TTP	DIC
Pathogenesis	Autoantibodies	Endothelial defect	Thrombus mass
Clinical Condition	Not sick	Sick	Sick
Red cells	Normal	Schistocytes	Schistocytes
PT (INR)	Normal	Normal/ Slightly increased	Increased
PTT	Normal	Normal/ Slightly increased	Increased
Fibrinogen	Normal	Slightly increased	Decreased
Fibrin monomers	Normal	Slightly increased	Increased
Fibrin degradation	Normal	Slightly increased	Increased
D-dimers	Normal	Slightly increased	Increased
Thrombi	Absent	Present	Present

[Click here to display Table 2 in an enlarged window.](#)

The differential diagnosis included TIA/stroke and possible TTP initially, but TTP was less likely as the patient had normal

renal function with no evidence of purpura or petechiae. Additional laboratory and radiological studies were indicated to further narrow the differential diagnosis.

Which laboratory test would *confirm a diagnosis of TTP?*

1. ADAMTS-13
2. Anti-thrombin 3
3. Bone marrow aspiration
4. 1 and 3
5. All of the above

Correct!
1. ADAMTS-13

A test for ADAMTS-13 was ordered with a very low level confirming TTP (4-7). ADAMTS13 is an enzyme primarily synthesized in the liver. Its main function is to cleave von Willebrand factor anchored on the endothelial surface. While the test was pending, the patient was started on corticosteroids with no significant clinical response appreciated. The diagnosis of TTP was confirmed when a very low ADAMTS-13 level was reported.

For TTP patients clinically unresponsive to corticosteroids, what *alternative therapies can be used?*

1. Plasma exchange
2. Rituximab
3. Vincristine
4. 1 and 3
5. All of the above

Correct!
5. All of the above

Wu et al (8) reported that ADAMTS13 response to early plasma exchange therapy in patients with acquired TTP has prognostic value. In their study of 19 patients, recovery of ADAMTS13 activity to more than 10% within 7 days was significantly associated with a timely clinical response. In contrast,

patients whose ADAMTS13 level failed to exceed 10% by 7 days tended to experience TTP exacerbation, treatment refractoriness, or death.

Our patient had a dramatic clinical response to plasma exchange and Rituximab (5). She was deemed stable for discharge with Rituximab, outpatient plasmapheresis and follow up.

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