A woman with headache and ptosis

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Case

A 61-year-old woman presented to the ER with worsening right-sided headaches. She had noticed a painful blister behind her right 3rd molar about a week ago. Chills and rigors associated with myalgias and arthralgias followed. Two days later she developed right-sided headaches, which got worse over the next few days. Vital signs were normal on presentation. Physical examination did not reveal any signs of meningism, respiratory, abdominal or urogenital infection.

Her past medical history was significant for a lumbar laminectomy, depression, gastroesophageal reflux disease, hysterectomy and bladder suspension. Her medications included rabeprazole and paroxetine. She did not smoke or drink and denied recreational drug use.

Peripheral blood white cell count was 24.2 × 10⁹/l (4.0–10.0) with neutrophil predominance of 22.2. Hemoglobin was 135 g/l (120.0–160.0), platelets 301 × 10⁹/l (150.0–400.0), alkaline phosphatase 161U/l (40–135), alanine aminotransferase 34U/l (4–55), aspartate aminotransferase 16U/l (5–55) and albumin 31. ESR was 83 mm/h. Urea, creatinine and electrolytes were in the normal range. Intravenous acyclovir and morphine was commenced. Computerized scan (CT) of the head was reported normal. A lumbar puncture revealed red cell count of 9 × 10⁶ (0–1), white cell count of 16 × 10⁶ (0–5) with 74% neutrophils, proteins of 0.57 g/l (0.15–0.60) and glucose of 4.0 mmol/l (2.7–4.2).

Blood cultures grew gram-positive cocci in chains, subsequently identified as alpha-hemolytic Streptococcus. HSV PCR in the CSF came back negative. Acyclovir was discontinued. Ceftriaxone and Vancomycin were commenced. Headaches worsened over the next 2 days and spread to the occipital and left retro-orbital areas and she became photophobic. Five days after her presentation, ptosis of the left eyelid and restricted upward gaze of the eye was noticed. Rest of the neurological examination remained normal. Transesophageal echocardiogram did not show any vegetation and vancomycin was discontinued.

The differential diagnosis at this stage was cerebral abscess, cerebral venous thrombosis, Tolosa-Hunt syndrome (THS) and temporal arteritis. Although initial CT scan did not show any evidence of cerebral abscess, it is still a diagnostic consideration in the presence of evolving neurological signs and positive blood cultures.

THS is a rare disorder characterized by periorbital or hemicranial pain accompanied by diplopia. The diagnostic criteria for THS includes one or more episodes of unilateral orbital pain persisting for weeks if untreated, paresis of one or more of the third, fourth and/or sixth cranial nerves, demonstration of granulomatous material in the cavernous sinus, superior orbital fissure or orbit by MRI, resolution of pain within 72 h after commencement of corticosteroids and exclusion of other causes by appropriate investigations. Although THS was a strong possibility, other causes needed to be excluded.

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A diagnosis of temporal arteritis must be considered in a patient with high sedimentation rate, severe headache and ophthalmoplegia. Temporal arteritis is associated with visual symptoms in up to 50% of patients. Loss of vision due to optic nerve ischemia is the most common visual disturbance; diplopia and ophthalmoplegia may occur in 12–15% of cases. Temporal artery biopsy is warranted but high dose corticosteroids should not be withheld whilst awaiting biopsy results. Intravenous methyl prednisone at a dose of 1 gm daily was commenced. Her headache resolved and the eye signs abated completely over the next 24 h. A prompt resolution of symptoms after intravenous corticosteroids support a diagnosis of temporal arteritis but is non-specific and does not explain the positive blood cultures. Subsequently temporal artery biopsy results came back negative. Corticosteroids were discontinued.

A repeat CT scan of the head and neck showed a linear intraluminal filling defect in a segment of right internal jugular vein near the level of the right mandibular angle and another smaller filling defect above this level. Left internal jugular vein was incompletely opacified. Both the inferior and superior aspects of left internal jugular vein were only partially opacified. Magnetic resonance venography (MRV) of the head and neck showed complete thrombosis of the left internal jugular vein from jugular fossa to the level of chin. Two non-obstructing linear intraluminal defects were noted in the right internal jugular vein. Poor enhancement in the area of cavernous sinus and enlarged left superior ophthalmic vein was noticed, findings consistent with thrombosis. There was no evidence of acute venous infarction.

Discussion

In the light of new MR findings, Lemierre syndrome (LS) was thought to be the most likely diagnosis. However, disseminated malignancy and underlying thrombophilia must be excluded in widespread unprovoked venous thrombosis. CT scan of the chest, abdomen and pelvis did not reveal any evidence of malignancy. CT scan of the chest however, showed small pulmonary arterial filling defects and a small focal opacity in the medial right middle lobe. Tests for protein C, protein S and antithrombin III deficiency, activated protein C resistance, prothrombin gene mutations, homocysteine levels and antiphospholipid antibodies were ordered and came back normal. Intravenous heparin was commenced and ceftriaxone continued. A repeat MRV of neck and head 3 weeks later showed complete resolution of thrombosis in both internal jugular veins and cavernous sinus. Heparin was discontinued but ceftriaxone continued for another week.

LS is characterized by suppurative thrombophlebitis of the internal jugular veins and metastatic infection associated with acute oropharyngeal infection. Although considered rare, recent reports have suggested that its incidence has increased over the last 10 years. After the first reported cases in 1936, no cases were reported in the 1950s and 1960s. The number of published cases has increased in recent years with six articles appearing between 1980 and 1990, 50 more from 1991 to 2000 and 121 articles from 2001 to 2008. Most cases of LS occur in previously healthy adolescents and young adults and the most common site of primary infection is oropharynx, although otitis media, mastoiditis and sinusitis have also been reported. Sore throat, fevers, rigors and chills are the usual initial presenting symptoms. Tonsillar lesions and cervical lymphadenopathy may be detected. A septic thrombus forms in the jugular vein after 1–2 weeks of initial infection. The organism multiplies within the thrombus and septic emboli are thrown into distant sites. Additional signs and symptoms will depend on the site of the septic emboli.

Septic emboli may spread from the internal jugular vein to lungs, spleen, liver, joints, bones, endocardium, brain, meninges and soft tissues. Pulmonary involvement has been described in.
The joints are the second most common site of septic involvement. Extension of thrombus to cavernous sinus has been described. Pharyngitis symptoms may have cleared by the time the patients present with LS; hence a high degree of suspicion and a thorough history are important for the diagnosis.

Fusobacterium necrophorum is the most common infectious agent (82%); polymicrobial infections and infections due to Bacteroides spp, Peptostreptococcus spp, Staphylococcus aureus including community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), Streptococcus spp, Eikenella corrodens and Enterococcus spp have also been described. Diagnosis of LS is based on a compatible clinical picture, isolation of the causative organism from blood cultures, radiologic evidence of venous thrombosis; and chest X-ray or CT findings of infiltrates, effusions, cavitation’s or abscesses. Leukocytosis, mild thrombocytopenia and elevated sedimentation rate, C-reactive protein and liver enzymes are commonly found.

Treatment of LS includes high-dose intravenous antibiotics directed against the most common pathogens for 4–6 weeks. The antibiotic choice must include coverage against anaerobes as well as gram-positive and gram-negative aerobes. Vancomycin may be added if infection with CA-MRSA is suspected. Abscesses may require surgical drainage. The role of anticoagulant therapy in the management of LS is controversial. Involvement of cavernous sinus is generally regarded as an indication for anticoagulation. Severe sepsis and ongoing evidence of septic emboli despite optimal antibiotic treatment may necessitate surgical ligation or excision of the internal jugular vein. The mortality of LS was up to 90% before the advent of antibiotics; it is still unacceptably high up to 7–8% despite the use of modern antibiotics.

Conflict of interest: None declared.

References