ACUTE ZOSTER ENCEPHALOMYELITIS IN A CASE OF PANCREATIC HEAD NEOPLASM WITH FULMINANT PROGRESSION: CASE PRESENTATION

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ABSTRACT

Encephalitis is a rare complication of cervical - cranial zoster infection. Myelitis is a similar, severe complication of thoracic zoster. They occur in patients with immune deficiencies, in 5-21 days after the rash and progress in the same time frame.

We are presenting the case of a 54 year old male with rapid evolution of an ascending encephalomyelitis with onset at 17 days after a left cervical-thoraco-brachial zoster episode.

Neurologic examination: lower limb paresthesia, ascending to the trunk, unstable gait, which becomes impossible with closed eyes, absent deep tendon reflexes, bilateral Babinski sign. After 48 hours, left cerebellar syndrome appears, in one week the patient had asymmetrical tetraparesis and in 11 days he becomes paraplegic, left side more affected than the right one. After 16 days, the clinical state stabilizes, he begins moving his right lower limb.

Lumbar puncture on admission: CSF albumin 1220 mg% (after 3 days it becomes normal); 81 cells/mm^3, 100% mononuclear cells, 50 cells after 3 days and after a week 23 cells/mm^3.

Cervical and thoracic spine MRI performed on the 3rd day from admission was normal but after repeating it in 10 days it showed T2, STIR and FLAIR hyper intense intraspinal, infra- and supratentorial lesions, well contoured, with homogenous gadolinium enhancement: demielinating lesions.

He received Aciclovir, Solumedrol, Insulin and symptomatic treatment.

After 2 weeks from leaving the hospital with symptomatic treatment and kinetic therapy, he returns in a septic state, with deep bed sores, positive blood cultures (Fusobacterium nucleatum, Staphylococcus Epidermidis) and urine cultures (Klebsiella). The outcome was death in 4 days.

Differential diagnosis – polyradiculoneuritis, paraneoplastic syndrome, cerebral and vertebral metastases.

Pathology exams: low grade acinary adenocarcinoma of the pancreatic head, invasive, with a solid pattern.

The particularity of the case: the severity of the acute ascending encephalomyelitis, the fulminant evolution of the pancreatic cancer, the disruption of the blood-brain barrier by an inflammatory and tumoral mechanism, showed on spine and brain contrast MRI.

Key words: herpes zoster encephalomyelitis, paraneoplastic syndrome, adenocarcinoma of the pancreatic head

INTRODUCTION

Encephalitis is a rare complication of cervical - cranial zoster infection. Myelitis is a similar, severe complication of thoracic zoster. They occur in patients with immune deficiencies, in 5-21 days after the rash and progress in the same time frame.

The purpose of this paper is presenting a very severe case of an acute ascending encephalomyelitis following a paraneoplastic zoster infection episode in a patient with a pancreatic head neoplasm with atypical presentation and undiagnosed during life. The fulminant progression of the pancreatic cancer is noted, as well as the disruption of the blood brain barrier by an inflammatory and tumoral mechanism, shown by contrast MRI of the brain and spine.

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CASE PRESENTATION

54 year old male, free lancer, from the urban area, is admitted as an emergency in the Neurology Ward of Constanta County Emergency Hospital for lower limb paresthesia and gait difficulty that occurred 5 days previous to admission.

He is a smoker, drinks alcohol occasionally, uses oral antidiabetic medication and had a typical zoster rash in the left anterior upper trunk, neck and left arm, no longer present on admission, for which he didn't follow any treatment.

Neurologic examination on admission: the patient was conscious, oriented, afebrile, no neck stiffness, lower limb paresthesia, ascending towards the trunk, unstable gait, impossible with eyes closed, vibratory anesthesia, absent DTR, positive bilateral Babinsky sign.

The residual lesions after the zoster rash can be observed (Figure 1).

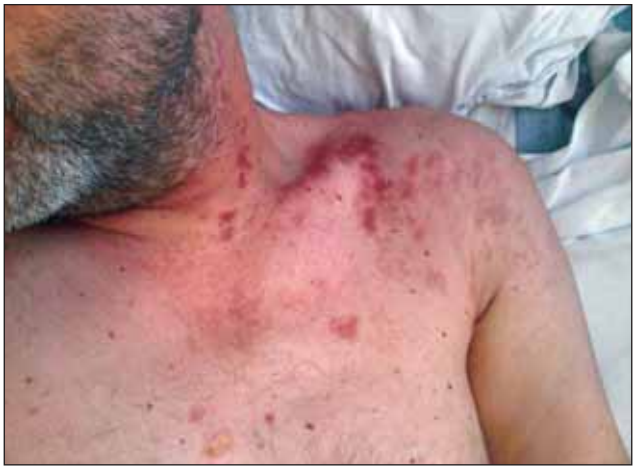

FIGURE 1. *Residual left cervical-thoracic and brachial zoster rash*

The initial diagnosis was polyradiculoneuritis.

The lumbar puncture performed on admission (02.10.2012) showed albumino cytological dissociation, with albumihorachia of 1220 mg/l (normal < 350 mg/l), CSF chloride of 117.5 mmol/l, glucose of 150 mg/dl and 81 cells/mm^3, 100% mononuclear cells, negative cultures.

RPR and HIV tests were negative.

Thoracic Rx and abdominal echography were normal.

The patient received steroid treatment initially (Methilprednisolone 1g/day, 5 days), gastric protection, neurotrophic medication, peripheral vasodilating drugs.

During the first week of admission, tetraparesis occurs, left > righ, and also left upper limb ataxia.

The lumbar puncture is repeated on 05.10.2012 and on the CSF analysis: albumins of 300 mg/l, glucose level of 167 mg/dl, 50 cells/mm^3, with 98% mononuclear cells. The third lumbar puncture, on 09.10.2012, showed albumin levels of 170 mg/l, glucose level of 176 mg/dl and 23 cells, 95.7% mononuclear cells.

The constantly high values of blood glucose levels were treated with rapid action insulin, 8Ux3/day before the main meals.

The contrast brain, cervical and thoracic MRI performed in the 3rd day were normal.

The typical rash, asymmetric tetraparesis, bilateral Babinsky sign and left upper limb ataxia, together with the progression of the albumino cytological dissociation with pleiocytosis with a tendency to normalize in approximately 2 weeks, oriented us towards a diagnosis of zoster encephalomyelitis.

We started treatment with Acyclovir 2 g daily in 5 oral doses.

Neurological examination on the second week of admission: normal eye movement, no nystagmus, no neck stiffness, no sensory deficits of the face, brachial biparesis, left > right, absent DTR, left limbs ataxia, worsened by eye closure, asymmetric paraplegia (right lower limb 1/5 – lightly moves the lower right limb distally, left lower limb 0/5), sphincter control impairment, painful hypoesthesia of the inferior trunk, abdomen and lower limbs bilaterally, positive bilateral Babinski sign, muscular atrophy of the lower limbs, worse distally, left more than right.

After 2 weeks, the progression of the disease stopped.

MRI imaging of cervical and thoracic spine was repeated, which showed (Figure 2a-2e): left posterior – lateral C5-C6 disc protrusion that compresses the left C6 nerve root; left posterior - lateral C6-C7 disc protrusion that compresses the left C7 nerve root; hypersignal intramedular lesions on T2 and STIR: C1-C2, C5-C6, C6-C7, T1, T2-T3, T4 well contoured, homogenous, with a sagital diameter of 14 mm, some of whom swell the spine, with homogenous gadolinium fill: demielinating lesions.

Brain contrast MRI (Figure 3a, 3b): pericerebral liquid spaces normally dimensioned; T2, FLAIR sections and diffusion sequence show hypersignal lesions in the medulla oblongata, pons, midbrain and right cerebellum and also right temporal-parietal lobe. The lesions are well contoured, with a maximal diameter of 10/8 mm, homogenous gadolinium fill.

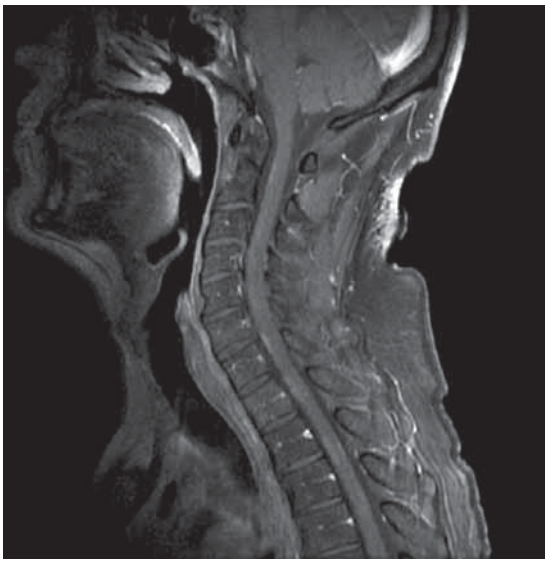

FIGURE 2A. *Cervical and thoracic spine MRI: sagittal sections T1 + contrast.*

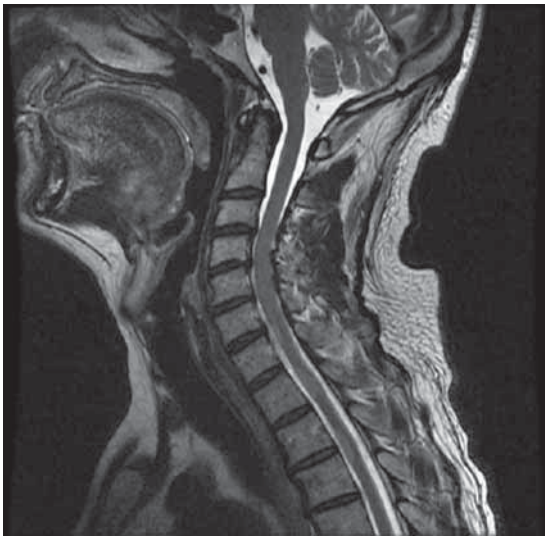

FIGURE 2B. *Cervical and thoracic spine MRI: sagittal sections T2*

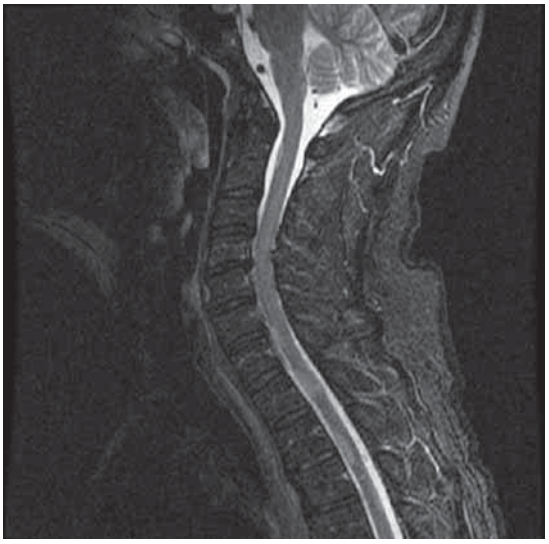

FIGURE 2C. *Cervical and thoracic spine MRI: sagittal STIR sections*

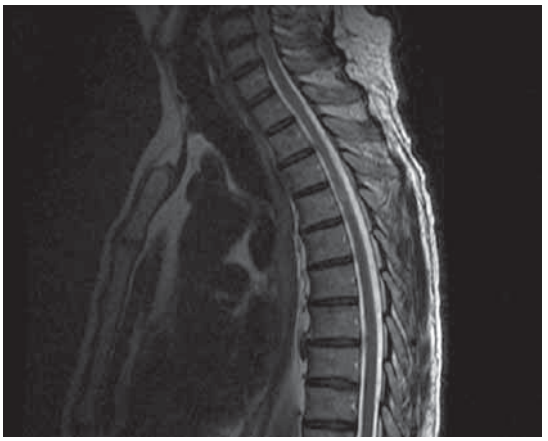

FIGURE 2D. *Thoracic spine MRI: sagittal T2 sections*

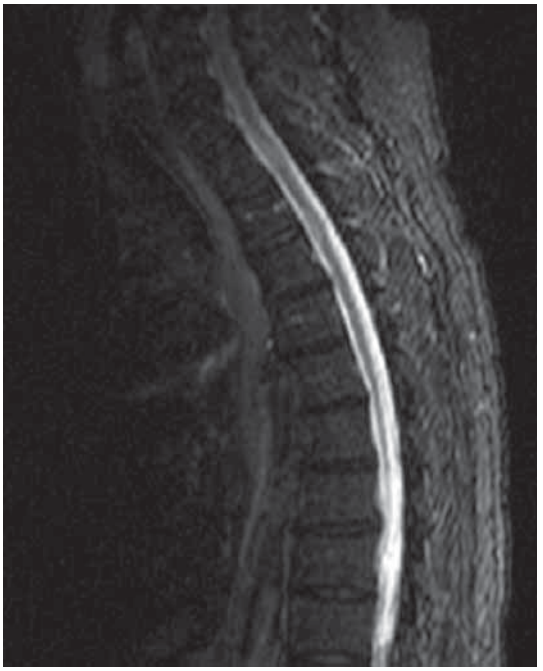

FIGURE 2E. *Thoracic spine MRI: STIR sagittal sections*

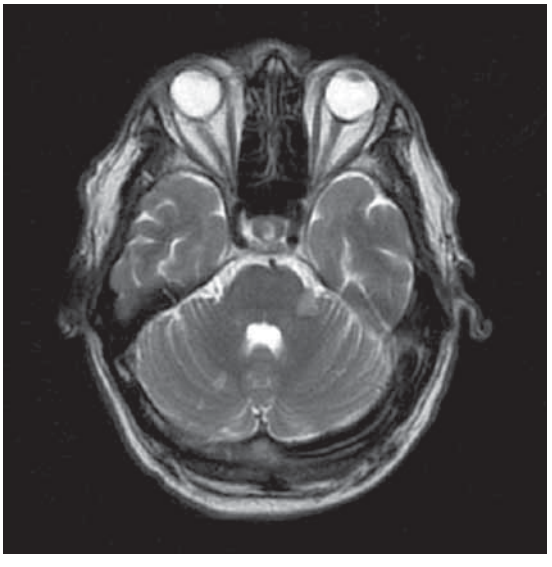

FIGURE 3A. *Brain MRI, axial T2 sequence*

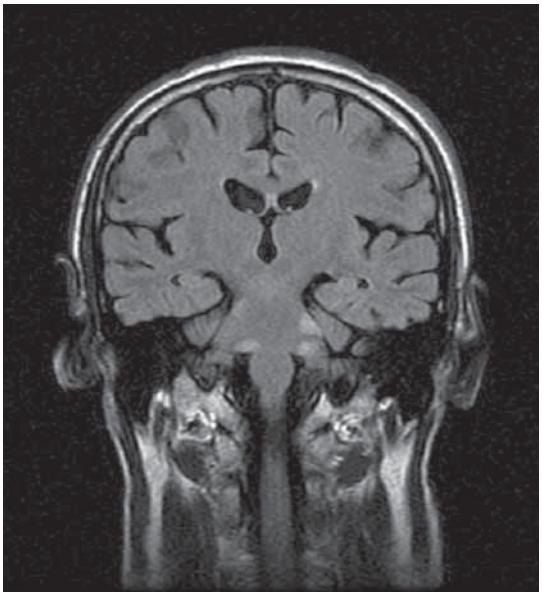

FIGURE 3B. *Brain MRI, FLAIR coronal sequence.*

After 3 weeks of treatment, the motor deficit of the lower limbs was slightly improved, at which point the patient is sent to a motor rehabilitation facility.

The patient returns to the Neurology ward after 14 days of symptomatic treatment and kinetic therapy, in a severe septic state, with bronchopneumonia, deep bed sores, both of the sacrum and calcaneus regions, with blood cultures positive for Fusobacterium nucleatum and Staphylococcus epidermidis. Urine cultures were positive for Klebsiella.

Death occurred in 4 days from readmission.

Differential diagnosis of the encephalitis:

Paraneoplastic encephalomyelitis, which was excluded by the normalization of the biochemistry values of the CSF and by the clinical improvement following steroid and antiviral therapy. In our case, the paraneoplastic manifestation was only the cutaneous one.

Metastatic brain and spine lesions, which were excluded by the contrast brain and spine MRI imaging

The pathology diagnosis (Figure 4,5) was: septic state, bronchopneumonia, malingnant pancreas head tumor.

In Pathology literature, the acinar cell carcinoma is described as an uncommon neoplasia, <1% of pancreatic neoplasia. It occurs at the mean age of 60, rarely in children. The macroscopic characteristics of this kind of carcinoma: it is tipically a large, more than 10cm, well-delineated, nodular, fleshy mass with fibrous bands and frequent necrosis. Focal degenerative cystic changes may occur. Micro-

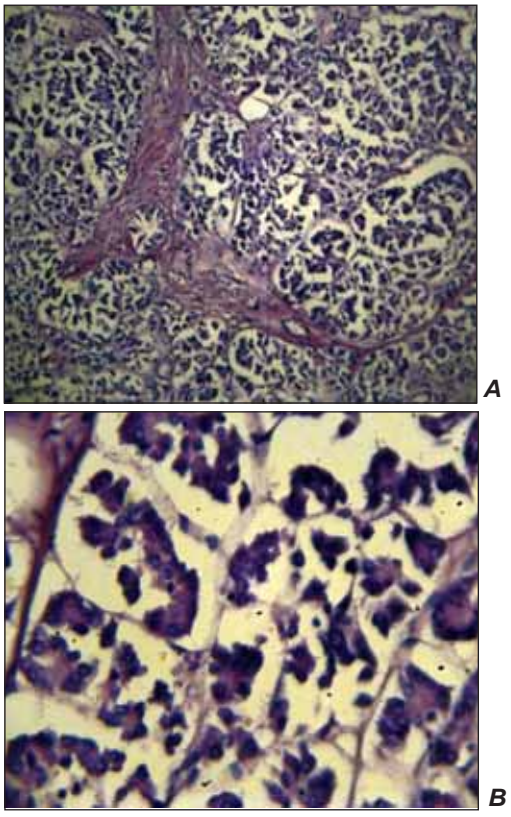

FIGURE 4 A,B. *Pancreas microscopic aspect: low grade acinary adenocarcinoma*

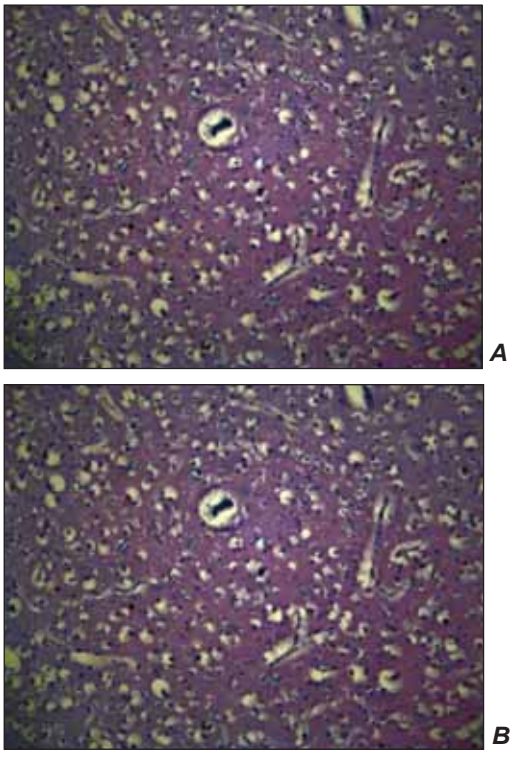

FIGURE 5 A,B. *Microscopic aspect of the nerve tissue – on the observed microscopic sections from the brain hemispheres: neuronal body retraction is observed, with diffuse cytoplasmic basophylia, with nuclear hypercromasy and picnosis, in the absence of an inflammatory reaction, suggestive for neurodegenerative disorders. Central cromatolysis and apoptosis are also present.*

scopic features: sheet like, stroma-poor growth pattern, overall basophilia, round nuclei with prominent nucleoli. It may contain cytoplasmic granules (sometimes acidophilic), rosette-like acinar formations. Variable amounts of endocrine elements are quite common. (1)

The particularity of the case is the encephalomyelitis occurring after a paraneoplastic cervical thoracic and brachial zoster infection on the grounds of a malignancy of the pancreas with atypical presentation and undiagnosed until the autopsy.

DISCUSSIONS

The first diagnosis – Polyadiculoneuritis was suspected due to the clinical course and the result of the fist CSF exam (2,3). The clinical progression was represented by the lower limb paresthesia and gait difficulty, with an ascension to the upper limbs. These signs were preceded by the cutaneous zoster episode 17 days earlier (4). The polyradiculoneuritis suspicion was excluded by the progression of the albumin – cytology dissociation in the CSF, showed by the 3 lumbar punctures and CSF exams performed on admission, after 3 days and after 7 days, and by the clinical evolution with asymmetrical tetraparesis, left brachial ataxia, bilateral Babinski sign (which was positive from admission).

The absence of the encephalitic syndrome with fever, altered state, followed by frontal and temporal lobe disturbances, focal signs, epileptic seizures and alteration of consciousness, suggested the suspicion of a **paneoplastic eparncephalomyelitis**.

Guichard et all in 1956 and then Bariety et all define the "paraneoplastic cutaneous, neurologic, endocrine, hematologic, gastrointestinal, renal, bone, etc. manifestations" as those clinical signs which are determined by the presence of a malignancy, these manifestation evolving in parallel to the malignancy, disappearing once it is excised and reappearing if the malignancy reappears or if there is a metastasis (5).

It is to be noted that the various clinical manifestations of paraneoplastic syndrome can overpower those of the primary tumor. Their onset can be before, during or after the primary malignancy that led to them is diagnosed. All the malignant tumors, including brain tumors, can be accompanied by these syndromes. Specific histologic changes are absent (5).

The amelioration of the CSF changes and the clinical signs made the diagnose of paraneoplastic encephalomyelitis improbable, the cutaneous rash remaining the only paraneoplastic change (6,7)

The typical rash, asymmetric tetraparesis, bilateral Babinsky sign and left upper limb ataxia, together with the progression of the albumin cytological dissociation with pleiocytosis with a tendency to normalize in approximately 2 weeks, oriented us towards a diagnosis of **zoster encephalomyelitis.**

The clinical aspect of herpetic encephalitis, with fever, altered state, followed by frontal and temporal lobe disturbances, focal signs, epileptic seizures and alteration of consciousness were not present in our patient (8).

Immune suppression is the main risk factor for a herpetic encephalitis: AIDS, transplantation, malignancy and advanced age. (9). Diabetes has been implicated as a predisposing factor in the development of herpes zoster associated neurological disease.

The onset of the central nervous system symptoms usually occurs days to weeks after the herpes zoster eruption.

Classically, in the CSF there can be: lymphocytic pleocytosis with high normal-to-elevated protein levels and normal glucose levels. Cell counts and protein levels do not seem to correlate with disease severity (9).

The first lumbar puncture (02.10.2012) showed elevated CSF albumin level of 1220 mg/l (normal < 350mg/l), CSF chloride of 117.5 mmol/l, glucose of 150 mg/dl and 81 cells/mm^3, 100% mononuclear cells, negative cultures. The lumbar puncture is repeated on 05.10.2012 and on the CSF analysis: albumins of 300 mg/l, glucose level of 167 mg/dl, 50 cells/mm^3, with 98% mononuclear cells. The third lumbar puncture, on 09.10.2012, showed albumin levels of 170 mg/l, glucose level of 176 mg/dl and 23 cells, 95.7% mononuclear cells.

The clinical aspect of herpetic myelitis was better shown by the tetraparesis with final paraplegia, absent DTR, level sensory deficits, sphincter impairment and muscular atrophy of the lower limbs.

The severity of ascending zoster encephalomyelitis can be observed.

Another rare finding is the contrast MRI imaging aspect shown on the cerebral and spine sections. The classic imaging aspect of herpetic encephalitis at onset (10,11): cortical and subcortical temporal pole, insular cortex, hypocampic and parahypocampic giri T2 hypersignal. Often, the lesions extend to the frontal orbital lobe or in the contralateral temporal lobe, with the same predilect topography for the limbic system. The lenticular nucleus is spared. The limbic topography is very suggestive for her-

petic encephalitis. The patognomonic images are present at 1-2 weeks from onset, as petechial hemorrhages predominantly in the giri (characteristic noncontrast T1 hyperintensity due to the methemoglobin) and necrosis. Herpetic encephalitis is a necrotic hemorrhagic type of encephalitis.

Starting day 8, the disruption of the blood brain barrier occurs, with moderate marginal enhancement, nodular or giral, homogenous. There is no mass effect in any of the stages. After 4-6 weeks, there can be vast areas of necrosis with parenchimal defects and cortical atrophy. This is a sequelar stage, if the patient survives (10).

Our images were completely different from this typical pattern. Also, herpetic encephalitis can usually be shown in the first 24 hours. In our case, the MRI performed in the 3rd day was normal. This nodular homogenous aspect was present in our second MRI images performed in the 10 th day.

Brain contrast MRI (Figure 3a, 3b): pericerebral liquid spaces normally dimensioned; T2, FLAIR sections and diffusion sequence show hypersignal lesions in the medulla oblongata, pons, midbrain and right cerebellum and also right temporal-parietal lobe. The lesions are well contoured, with a maximal diameter of 10/8mm, homogenous gadolinium fill.

MRI imaging of cervical and thoracic spine was showed (Figure 2a-2e): hyperintense spinal lesions on T2 and STIR: C1-C2, C5-C6, C6-C7, T1, T2-T3, T4 well contoured, homogenous, with a sagittal diameter of 14 mm, some of whom swell the spine, with homogenous gadolinium fill: demielinating lesions.

Herpetic myelitis is rare and is seen in the spinal territory corresponding to the rash affected dermatome (12,13).

The disruption of the blood brain barrier was produced by an inflammatory and tumoral mechanism, shown on MRI imaging.

The specific diagnosis of the herpetic encephalitis is well sustained by detection of the DNA using PCR of the CSF, test that we couldn't perform. Polymerase chain reaction in combination with detection of intratecal specific imunoglobulin G antibody, represents the most accurate method of diagnosis of neurological infections including HZE. Treatment with acyclovir should be instituted empirically in suspected cases (14,15).

None of the initial signs of a pancreatic cancer were present, such as: abdominal pain, weight loss, jaundice, digestive intolerance, palpable gall bladder, migratory thrombophlebitis, GI bleed, splenomegaly (16).

Herpes zoster infections occurs in 25% of the cases of malignant tumors.

The differential diagnosis with metastatic brain and spine lesions was also made, but they were excluded by the contrast brain and spine MRI imaging.

CONCLUSION

The gravity of the acute ascending encephalomyelitis, the fulminant progression of the pancreatic malignancy and the patient's death by a septic state, all contribute to a trap case compared to the available diagnostic and therapeutic means.

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