CHRONIC PACHYMENINGITIS ASSOCIATED TO HYPEREOSINOPHILIA

CASE REPORT

J. CORREALE * — S. AMERISO * — F. MELI ** — R. REY * O. GARCEA * — D. MONTEVERDE *

SUMMARY — A male 22 years old patient who consulted due to headache and increasing visual loss is being presented. Alterations in the exam were represented by right amaurosis and left temporal hemianopsis. Pathological and tomographical studies revealed chronic pachymeningitis with eosinophilic infiltration. An elevated eosinophilia and an increasing in anti-A and anti-B isoagglutinins were associated to the clinical course. They returned to normal values after treatment with tiabendazol. Even though there is not a certain conclusion as regards the etiology, the probable parasitary nature of the process is outlined.

Paquimeningitis crónica asociada a hipereosinofilia: relato de caso.

RESÚMEN — Un paciente de 22 años de sexo masculino, que consulto por cefaleas y disminución de la agudeza visual es presentado. Los hallazgos patológicos del exámen físico estuvieron representados por amaurosis derecha y hemianopsia temporal izquierda. Los estudios tomográficos y anatomopatológicos permiticron concluir en una paquimeningitis crónica con infiltrado eosinofílico. Una importante eosinofília y un incremento en las isoaglutininas anti-A y anti-B se vieron asociadas al cuadro. Las mismas se normalizaron luego del tratamiento con tiabendazol. Si bien no se puede concluir con certeza en el diagnóstico etiológico, se plan⁺ca la probable naturaleza parasitaria del proceso.

Pachymeningitis case records have been classically attributed to syphilis, tuberculosis and alcoholism ²⁶. Nowadays cases of pachymeningitis reported are few and, in most of them the cause is uncertain, even though a pathological study is attained. The use of computed tomography (CT) scans showed lesions which were frequently clinically unsuspected. The presence of associated eosinophilia stablishes the possibility of trying to explain partially the cause of some of these lesions, whether as a direct consequence of the eosinophilic infiltration, by the neurotoxin produced by eosinophils, or representing part of the systemic repercussion of a case due to another etiology.

We refer to the case of a patient with headache and progressive visual loss. The CT showed a hyperdense laminar lesion which was markedly enhanced after the injection of contrast substance and engaged the left parasellar region and the free edge of the tentorium cerebeli. It was associated to a marked eosinophilia. The surgical biopsy demonstrated chronic inespecific pachymeningitis similar to others referred to by different authors 9,17.

^{*} Division of Neurology, J. M. Ramos Mejía Hospital, Buenos Aires; ** Neurological Research Center Dr. Raúl Carrea, Buenos Aires.

CASE REPORT

AO, a male 22 years old patient was admitted because he presented bilateral frontoorbital headache and progressive visual loss. The symptoms had begun in an insidious way 60 days before his admittance and had evolved slowly till two days before, at that time his symptoms worsened. He was being treated with corticosteroids without any improvement. The patient was born in Bolivia and he was a farmer. He had been in contact with dogs and cats and he had had repeated episodes of intestinal parasitosis in the past. He presented an amaurosis of the right eye and left temporal hemianopsis with macular involvement. Photomotor and consensual reflexes were slow in both eyes. Papillar atrophy, retinal edema and vessels sheating were observed in funduscopy with signs of periphlebitis in both eyes. No alterations appeared in the first lab study. Syphilis serology and tuberculin intradermal reaction were negative. Cerebrospinal fluid (CSF) study did not reveal any alteration in the cytochemical exam, nor in search for bacteria, mycobacteria or fungi. Immunological study showed: anti-nuclear factor (---), latex test for rheumatoid arthritis (---), L.E.cells (--), C3 fraction of complement 102 mg/%. Chest radiograph and hepatoesplenic scanning were normal. CT scan showed an expansive laminar lesion of the left side of the parasellar region, extending to the neighbourhood of the sphenoidal fissure and the optic foramen. In its medial part the lesion was intimately in touch with dorsum sellae, which was eroded. The involvement of the free edge of the homolateral tentorium cerebeli was noted. The lesion presented a discrete mass effect and a marked enhancement after the injection of contrast medium (Figs. 1 and 2). Digital subtraction angiography by femoral catheterization showed no alterations. After 20 days at the Hospital, the steroids were stopped. Thirty days later a right submaxilary painless adenopathy appeared. It was biopsed and the pathological report described a chronic inflammatory reaction of granulumatous type, with necrosis focuses and abundant eosinophils and histiocytes. PAS and Ziehl-Nielsen dyeing were negative. Hematological controls evidenced an elevation in the



Fig. 1 — Case AO: CT scans (axial views, contrast medium enhanced). Left cerebellar tentorium shows marked contrast medium enhancement (arrows) and peculiar thickening.



Fig. 2 — Case AO: CT scan. Coronal view precontrast. Hyperdense mass lesion involves left cavernous system (arrow).

eosinophils count reaching 84% of the WBC (Table 1). Stools were negative for ova and parasites. Hydatic serology (double diffusion and CIE) was negative. An aspiration puncture of the bone marrow did not evidence any alteration. A new CSF was normal. Second immunological study revealed: latex test for rheumatoid arthritis (--), C3 152 mg/%, antimitochondrial antibody (+) 1/160, anti-A agglutinins 1/1024 and anti-B 1/4096. Lymphocyte populations with monoclonal antibodies study revealed: T3 61%, T4 37%, TS 28%. Serologic titrations for toxocara (ELISA and hemagglutination) were negative.

The patient was operated on. A thickening of the duramater, with adherences to the temporal lobe was observed, so a debridement of it was performed and a meningeal and encephalic parenchyma biopsy was made. The pathological study revealed: pachymeningitis with marked fibrosis, neoformation vessels, inflammatory infiltrates with abundant eosinophils; cerebral parenchyma presented significant edema, microglial and astrocytic migration and

| Days since admittance | Relative value of eosinophils | Absolute value of eosinophils |
|--------------------------|----------------------------------|----------------------------------|
| First day | 0 | 0 |
| 50 | 9% | 2520 |
| 71 | 25% | 3000 |
| 78 | 37% | 4662 |
| 88 | 78% | 11700 |
| 96 | 80% | 12000 |
| 149 | 84% | 25200 |
| 166 | 47% | 5120 |
| 187 | 9% | 620 |
| 206 | 0 | 0 |
| 330 | 1% | 89 |

Table 1 — Case AO: eosinophilia figures evolution.

eosinophilic infiltration: specific lesions of parasitic agents were not observed (Fig. 3). Empirical treatment with tiabendazol was begun in the 154th day of hospitalization, 3 g per day during 5 days, completing 3 series. Hematological control after the first series of treatment showed a decrease in the number of eosinophils and they returned to normal values after the last series. Antimitechondrial antibodies were negativized and decrease in the titration of anti-A and anti-B agglutinins at 1/64 for both was observed. The CT showed no changes with the exception of those due to surgical procedure. Visual abnormalities remained without changes after following up for one year. Eosinophil counts performed 4 months and a year after treatment were normal.



Fig. 3 — Case AO: biopsy material (hematoxylin-eosin). Above: pachymeningitis, inflammatory infiltration with abundant eosinophils (\times 400). Below: the same view with greater magnification (\times 1000).

COMMENTS

Gowers⁹ as well as Wilson²⁶ consider two types of pachymeningitis: the so called external, attributed to processes that have the skull bones as their source (like osteomyelitis and traumatisms with secondary infection), granulomas in the same All of them generate limited hyperplasic reaction. location or middle ear infections. These pachymeningites, with headache and sometimes slight temperature, can afterwards injure venous sinuses, causing phlebitis thrombosis or septicemia, and must be differentiated from extradural abscesses. The second group refers to what these authors call internal pachymeningitis, which can be seen in cases of traumatisms, syphilis, tuberculosis and alcoholism, for instance. However modern neuropathological studies consider that in most cases one cannot ascertain such etiologies; so, most of them culminate having no determined cause 9. Feringa and Weatherbee 9 related a case of hypertrophic granulomatous cranial pachymeningitis with progressive visual loss in a patient undergoing chronic dialysis. After necropsy etiology could not be established and it was designed as allergical unspecific granulomatosis. Quite opposite to what has previously been commented, isolated involvement of the arachnoid in the posterior fossa happens to be relatively frequent in association with middle ear infections, encephalic traumatisms, sinusitis, plaguicide intoxications and stroke, thus forming 1% of neurosurgical interventions according to some statistics 20.

In a similar way as the cases reported by Kobayashi and coll.¹⁷, our patient presented tomographic lesions expressed by hyperdense laminar left parasellar image with extension to the sphenoidal fissure, the optic foramen and the rectus oculi superior muscle. This lesion eroded the dorsum sellae and extended in a marked way along the free edge of the tentorium cerebelli, enhancing after the injection of contrast medium. Just like in other cases referred to in the literature 9.17, in our patient it was impossible to determine a definite cause justifying chronic pachymeningitis even though meningeal and adenopathy biopsy was performed. The presence of eosinophils in peripheral blood is sometimes associated with dysfunction of different organs. The underlying causes are various and they include parasitoses, allergical aftections, neoplasias and vasculitis⁸.

Patients in which the cause for eosinophilia is unknown and present a count of cosinophils greater than 1500/mm³ at least during 6 months and have developed lesions in some organs can be said to bear hypereosinophilic syndrome 4. Different organs may be affected by the presence of these elements; among them: lungs, liver skin, eyes, muscles, lymph nodes, heart and nervous system 4.8.11,13.23. Eosinophils and their products (basic or cationic proteins) are openly neurotoxic. Moore and coll. ¹⁹ described the development of neurological involvement in 65% of studied patients bearers of hypereosinophilic syndrome, with repercussion through three physiopathological mechanisms: encephalopathy, sensitive polyneuropathy, thromboembolic phenomena on the central nervous system. On occasions more than one mechanism can be seen. Similar complications have been seen in patients having eosinophilia with a known cause ²³.

Some of these cases present a definite eosinophilic meningeal infiltration which justifies neurological symptomatology. This way of involvement has been described in relation to some infectious diseases such as helminthiasis and more rarely *Coccidioidis* immitis ¹⁸, meningitis by lymphomas ^{14,16} and in one case of disseminated glioblastoma ⁶. On the contray sometimes hypereosinophilic syndrome may be accompanied by neurological symptoms and eosinophilic pleocytosis in the CSF with pathological studies not revealing meningeal or parenchymatous infiltration ²⁵. Even though the patient presented normal amount of eosinophils initially, we may point out to the possibility that such an eventuality might be evident during weeks or months despite the existence of symptoms ²³. On the other hand, the patient was receiving prednisone, a drug frequently used in the treatment of this group of affections ^{8,19,23}, showing a marked and progressive increase in the number of eosinophils once this medication was stopped.

The decrease obtained in the count of eosinophils, as well as the dropping of the titles of anti-A and anti-B agglutinins, after tiabendazol administration, suggest the possibility of a parasitic etiology. Several parasites are mentioned as being able to produce meningoencephalitis or eosinophilic meningoradiculomyelitis, and among them: Angiostrongylus cantonensis, Taenia solium, Gnathostoma spinigerum, Bailisascaris procyanis, Paragonimus westermani, Fasciola hepatica and Toxocara canis 3,10,12,15,18. Nevertheless, most of these agents show an important eosinophilic pleocytosis accompanying the increase of eosinophils in peripheral blood with the exception of toxocariasis, which may not present such a characteristic in CSF ¹⁰. Most nematodes develop cases of visceral larva migrans with systemic involvement. Diagnosis is sometimes difficult due to low possibilities of visualizying larvae in the lesions. On the other hand, methods for antibodies detection may, in many cases, give cross-reactions with other parasites having surface antigens with similar structures. Histopathologically, they resemble granulomas or chronic inflammatory phenomena in which the lacking of visualization of the larvae turns them completely unspecific.

Toxocariasis represents most common cause for visceral larva migrans (VLM) with encephalic involvement 10. Affectation of the nervous system is represented by the formation of granulomas containing eosinophils which express themselves clinically by means of focal deficits, seizures or behavioural disturbances. Ocular involvement is frequent, with progressive visual loss, strabismus and ocular pain. Funduscopy can show isolated granulomas or exudative endophtalmitis. Ocular disease may be the only manifestation and sometimes it must be differentiated from retinoblastoma. This parasitosis, just like others previously mentioned, happen to show counts of white cells from 30000 to 100000/mm³ with 50 to 90% of eosinophils. An increase in the titles of anti-A and anti-B agglutinins can be found, since the parasite presents a surface antigen similar to human hemagglutinins 3,12,21,22. Presence of larvae is rarely detected in the feces and biopsies or necropsy tissues. Immunodiagnostic tests with ELISA permit 78% sensitivity and 99% specificity 21. The illness is generally autolimited, in spite of eosinophils being able to persist. It is possible that some of the lesions might be produced by immune phenomena, notwithstanding that this mechanism would not represent the most frequent genesis of the lesions observed in the nervous system 21.

Normalization of eosinophils absolute and relative counts, as well as the decrement of anti-A and anti-B agglutinins levels after the empirical treatment with a wide spectrum antiparasitary drug (Fig. 4) guides the diagnostical possibility of this case of chronic pachymeningitis towards a parasitic process, perhaps secondary to an infection with *Toxocara canis*. The fact that the larva was not identified in the feces nor in biopsies does not discard the diagnosis since, as it was previously stated, this



Fig. 4 — Laboratory findings evolution: ———, eosinophils; — — —, anti-A and anti-B isoagglutinins; — · · - -, antimitochondrial antibodies; ////, treatment with tiabendazol.

eventuality is extremely rare. Negativity of specific serology for toxocara might be due to an error margin, represented by a number of false negatives which the study methodology presents. The presence of antimitochondrial antibodies could be homologated to the findings performed by different authors in relation to cases of multiparenchymatous granulomas, associated to Sjögren disease, sarcoidosis or primary biliary cirrhosis, in which such findings suggest a group of entities not yet correctly defined but with the autoimmune phenomena playing an important role 5.7. Antimitochondrial antibodies negativation after antiparasitary treatment sets forth the possibility that some of the patients with elevated titles of them without an evident pathology migth correspond to asymptomatic parasitosis bearers 2. The pathological finding of a noncaseous granulomatous process with meningeal involvement and lymphadenopathies, even if it makes us consider sarcoidosis diagnosis, this seems to be slightly probable due to the abscence of associated thoracic involmement, lack of response to steroids and the possibility of attributing the histopathological findings to multiple etiologies 24 Presence of eosinophilic infiltrates makes us finally consider this case as a lesion caused by direct cellular infiltration or through neurotoxins as it was already mentioned.

By what has been stated, we believe that this case represents chronic pachymeningitis of a probable parasitary etiology. Nevertheless this cannot be certainly stated in analogous way as it happened with other authors 9.17, and it must be added to other descriptions in which tomographic findings similar to those observed in this patient guide the diagnosis to tentorial pachymeningitis 17.

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