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Letters

Involvement of smell and taste in giant cell arteritis

Sir: The early diagnosis of giant cell arteritis (GCA) is essential in order to try and prevent the often irreversible neurological complications. In addition to ischaemia of the anterior visual system, extraocular palsies,[1] transient ischaemic attacks and cerebral infarcts most commonly of the brain stem, have all been reported.[2 3] In this paper two patients are described in whom the first manifestation of the disease was an abnormality of olfaction and gustation.

A 69 year old woman completely lost her sense of taste in September 1985. This spontaneously returned in May 1986, but for the subsequent two months she experienced a heightened sense of taste, in particular mildly sweet things tasted unpleasantly sweet. Her sense of taste recovered fully in July 1986. Concurrent with her loss of taste she became anorexic, lost weight and suffered night sweats. After May 1986 she experienced generalised headaches with some scalp soreness and occasional sharp shooting pains in her scalp, her jaw felt stiff but she did not experience true jaw claudication. There were no visual or joint symptoms. When admitted to hospital in September 1986 examination revealed tender but pulsatile temporal arteries, normal vision, intact taste but absent smell in the right nostril (the smell in the left being normal). Her erythrocyte sedimentation rate (ESR) was initially 104 mm/h, her haemoglobin 10·4 g/l and the temporal artery biopsy showed typical changes of GCA including multinucleate giant cells. Within hours of starting prednisolone (60 mg/day) her headaches disappeared and her appetite improved. Her ESR fell to 20 mm/h after ten days.

Three months prior to admission a 64 year old woman became aware of an unpleasant "smouldering" or "smoke-like" smell which caused her to request a visit from the local council environmental health officer. However, neither he nor her family could detect this smell. After being constantly present for two months, the smell became intermittent, lasting for four days at a time and then being absent for a similar period. Six weeks after the onset of this smell the patient developed headaches with a feeling that her hair "was being pulled". The pain which was initially right sided but then generalised, was associated with lethargy but no visual, joint or jaw symptoms. Five days before admission she developed diplopia on looking to the right with horizontal separation of the images. Initial examination revealed a complete right 6th cranial nerve palsy, right retinal damage due to previous detachment surgery but no recent visual abnormalities, general scalp tenderness but non-tender, pulsatile temporal arteries. Her initial ESR was 20 mm/h but rose to 56 mm/h one week after admission; her haemoglobin was normal. A temporal artery biopsy was reported as showing "intimal proliferation, disruption of the elastic lamina and mononuclear infiltration of the adventitia and media consistent with GCA". Treatment with prednisolone (60 mg/day) resulted in a dramatic improvement in the headache within 24 hours, and in the diplopia within one week, and the abnormal smells completely disappeared.

The exact sites of the neurological lesions in these two cases cannot be determined as neither came to necropsy. It seems likely however that ischaemia of the olfactory nerves and mucosa as well as possibly of the corda tympani nerves was involved. The vasa nervorum to both these nerves are supplied by branches of the external carotid artery and are hence liable to the arteritic process in GCA.[4] There was no evidence of tongue necrosis which could contribute to taste loss. The awareness of these unusual symptoms was particularly helpful in encouraging the author to pursue the diagnosis in the second case, where four ESR estimations prior to the temporal artery biopsy had only been between 20–26 mm/h. Abnormalities of smell and taste have not been previously reported in GCA. It remains to be determined whether olfactory involvement in GCA is an overlooked feature of the disease or just a rarity.

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Sarcoid meningitis, high adenosine deaminase levels in CSF and results of cranial irradiation

Sir: Sarcoid meningitis is often difficult to distinguish from tuberculosis meningitis. The adenosine deaminase (ADA) level in the cerebrospinal fluid (CSF) has been reported as a useful marker to support the latter.[1–4] Standard treatment for neurosarcoidosis is corticosteroids and only rarely has radiotherapy been tried in resistant cases. We present our results in a case of sarcoid meningitis with high ADA level in CSF in which radiotherapy was instituted because of the secondary effects of steroids therapy.

A 24 year old white man was well until aged 20 when he began to complain of transitory episodes of diplopia, dizziness and gait unsteadiness. He presented with peripheral facial palsy that resolved spontaneously. Four years later he was seen for the first time in another hospital because of the headache. Lumbar puncture was performed and CSF contained 40 white blood cells (WBC) (80% lymphocytes), protein 145 mg/dl and glucose 16 mg/dl. A radiograph of the chest showed bilateral hilar lymphadenopathy with diffuse interstitial reticulonodular pattern. Scalene lymph node biopsy demonstrated noncaseating epithelioid cell without acid fast bacilli, consistent with sarcoidosis. Steroid therapy (40 mg daily of prednisone) was instituted with clinical improvement, but he soon developed Cushing's syndrome. Following a spinal strain he developed intense backache without sciatica that prevented him from walking. He was then transferred to this hospital, 7 months after his first admission. On physical examination a Cushingoid habit was apparent. There was reduction of lumbar lordosis with limitation on motion of the lumbar spine. There were no signs of radicular affectation and the rest of the general examination was normal. On neurologic examination there were no signs of meningeal irritation. A bilateral sixth-nerve palsy was evident. Serum calcium level was normal as were the liver function tests,

haemogram and ESR, and radiographs of the hands. There was hypercalciuria (300 mg per 24 h) and serum angiotensin converting enzyme (ACE), and ADA were normal. Spine radiographs revealed diffuse osteoporosis with loss of height in several vertebral bodies. Pulmonary galium[67] citrate scanning showed uptake by bilateral hilar lymph nodes and parenchyma. A new lumbar puncture yielded 20 WBC (100% lymphocytes), protein 179 mg/dl and glucose 18 mg/dl with a simultaneous blood glycaemia of 78 mg/dl. Bacteriological studies were negative. ADA was 10·7 U/l (normal value 0–2 U/l; distinctive value for tuberculosis over 8 U/l) and ACE 5·6 U/l (normal up to 2 U/l). IgG level was 14·2 mg/dl and there were no oligoclonal bands. Precontrast CT head scan showed a mild enlargement of the ventricular system and obliteration of the basal cisterns. After contrast infusion, there was marked subarachnoid enhancement. Calcium and vitamin D supplements were administered with the development of hypercalcaemia; this therapy was stopped and calcitonin added, with slow improvement of his backache.

In order to treat the neurological manifestations and given the secondary effects of corticosteroids that prevented increasing the dose, alternative therapies were considered. Whole brain radiotherapy was instituted. He received 3000 rad over 3 weeks in 10 sessions, 300 rad each time and was discharged on prednisone 30 mg daily. One month later his neurological symptoms had improved and examination only revealed a discrete sixth-nerve paresis. CT showed a marked decrease of contrast enhancement in the basal subarachnoid space with a moderate increase in the ventricular size. Serum and urinary calcium levels were normal. CSF contained 4 cells/mm^3, 139 mg/dl protein and a glucose level of 38 mg/dl (simultaneous blood glucose 72 mg/dl). ADA was 4 U/l and ACE 3·6 U/l. A progressive decrease in prednisone dosage was intiated and he was discharged on a maintenance dose of 10 mg daily.

One month later he was readmitted because of a recent-onset picture of intense somnolence, bradypsychia and disorientation with polydipsia and polyuria. On physical examination there were signs of moderate dehydration and neurological exam failed to reveal any change except for confusional state with lethargy. Biochemical studies revealed a serum sodium level of 160 mmol/l with an increased osmolality of 336 msm/kg. Urinary sodium and osmolality were inappropriately low for serum values. After rehydration and vasopressin replacement, biochemical abnormalities were corrected but the neurological status remained unchanged. CT revealed a discrete increase in ventricular size with minimal basal meningeal enhancement and without evidence of parenchymatous lesions. CSF contained 12 WBC (100% lymphocytes), 171 mg/dl protein and 10 mg/dl glucose. ADA again increased to 23 U/l. Functional endocrine studies of the anterior pituitary demonstrated a normal function, except for the supression of the suprarrenal axis secondary to steroid therapy. A course of dexamethasone (4 mg every 6 h) was given, soon improving his condition and regaining a normal consciousness level. A year later, he remains currently stable on 15 mg daily prednisone and desmopressin therapy.

Sarcoid meningitis with low glucose, as in our case, often pose diagnostic problems with other usually infectious disorders, tuberculosis being one of the most important especially in countries where, as in Spain, it is highly prevalent. ADA has been found increased in several types of meningitis, the greatest values corresponding to tuberculosis[1-4] and some authors suggest that a high level in CSF supports a tuberculosis disorder.[4 5] ADA has been reported increased in serum of patients with sarcoidosis,[6 7] but we are not aware of any previous report of its value in CSF of sarcoid meningitis. As our case shows, ADA level may be raised in this situation, probably reflecting an intense inflammatory state with lymphocytic activation. In fact, we found it raised in other kinds of lymphocytic meningitis, as in cryptococcal, listerial and brucellar meningitis (unpublished data). Thus, we think that ADA level in CSF cannot be used alone to distinghish between sarcoidosis and tuberculosis in a case of lymphocytic meningitis with glucose consumption in which bacteriological results are not yet available.

Another important problem that neurosarcoidosis poses is treatment. Currently, the cornerstone of the therapy is corticosteroids and when these agents fail or secondary effects prevent increasing the dosage, as in our case, one must resort to alternative therapies which are few in number Radiotherapy was used to treat hilar adenopathy before steroids were available. It was also used locally in other locations.[8 9] There are only two previous reports about the use of radiotherapy in neurosarcoidosis. Grizzanti *et al*[10] described a patient with meningitis and intractable seizures which stopped after 1000 rad total dose. Bejar *et al*[11] described another patient with nodular brain lesions who failed to respond to steroids yet improved after 3000 rad total dose. In our case the response can be considered as partial. One month after irradiation, there was an improvement of clinical picture, radiological signs of arachnoiditis and CSF abnormalities, including the ADA level. However, one month later a clinical deterioration consistent with hypothalmic involvement by sarcoidosis occurred coinciding with a new worsening in CSF parameters including an increase in ADA level. CT did not reveal changes, except for an accentuated ventricular enlargement, perhaps due to inflammatory or scarring tissue in sarcoid meninges.

We conclude that ADA level may be increased in sarcoid meningitis, not helping to differentiate it from tuberculous meningitis. Radiotherapy may be an optional therapeutic alternative in patients with important steroid-related problems, helping to lessen the inflammatory process. However, this response may only be partial as in the case here presented. Therefore, now therapeutic strategies are to be tried in these problematic cases.

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Escherichia coli meningitis and disseminated strongyloidiasis

Sir: *Escherichia coli* is a rare cause of meningitis in adults, and has a high mortality rate.[1-5] It is particularly associated with cranial trauma and neurosurgical procedures,[4,6] but spontaneous cases have been reported in an older age group often with a background of diabetes or alcohol abuse.[4] We describe a patient in whom *E coli* meningitis occurred as a manifestation of disseminated strongyloidiasis.

The patient, a 65 year old Indian man, was transferred to the Neurological Unit for investigation of neck stiffness, pyrexia and drowsiness. Ten days previously he had presented to the referring hospital with a 4 week history of abdominal pain and diarrhoea. No cause for the abdominal symptoms was found despite extensive investigations including sigmoidoscopy and examination of stool for ova and parasites. Two months previously he had complained of severe left temporal headache and had an ESR of 120 mm/1h. Giant cell arteritis was diagnosed on temporal artery biopsy and the patient was commenced on prednisolone, 80 mg daily, to good effect. At the time of his current admission he was taking 30 mg daily. There was no other past history of relevance and he was not on any other medication. The patient had lived in England since 1976, returning briefly to India for a visit in 1983.

On examination the patient was cachectic and had a temperature of 38·5°C. He was unconscious but localised to painful stimuli. He had marked neck stiffness and positive Kernig's sign. Cranial nerve examination was normal and pupils reacted equally to light. Tendon reflexes were symmetrical throughout and both plantar responses were flexor. On general examination the pulse rate was 100/minute, he was tachypnoeic with a respiratory rate of 32/minute, and had fine crepitations throughout both lung fields; the abdomen was diffusely tender but there were no palpable masses. Investigations revealed an ESR of 52 and a haemoglobin of 11·3 g/dl with normal indices. The white cell count was $8{\cdot}9 \times 10^9$/l (90% neutrophils, 7% lymphocytes, 2% monocytes and 1% eosinophils). Blood biochemistry was normal and syphilis serology was negative. A chest radiograph which had been normal 7 days previously now showed patchy shadowing in both lung fields. The CSF contained profuse gram negative rods, a raised protein of 410 mg/100 ml, an elevated white cell count of 9,000/mm^3 (80% neutrophils) and a reduced sugar of 0·5 mmol/l. CSF culture resulted in a profuse growth of *Escherichia coli* (E coli) sensitive to chloramphenicol and cephtazidine. Blood and urine cultures were negative. CT showed mild diffuse cerebral atrophy. Sputum examination 24 hours after admission revealed larvae identified as *Strongyloides stercoralis*. These were subsequently found in the patient's faeces and urine.

On admission the patient was treated with chloramphenicol 1g four times daily and cephtazidine 2g three times daily. Twenty four hours later when the systemic strongyloides infestation was diagnosed he was started on thiabendazole 1g twice daily. He required oxygen and nasogastric feeding and showed little sign of improvement. Eight days later his level of consciousness deteriorated further and the following day he died. Permission for postmortem examination was refused.

This patient presented with *E coli* meningitis preceded by a 4 week history of abdominal pain. In retrospect, both these symptoms were attributable to disseminated strongyloides infection which had been activated by steroid therapy. However, this diagnosis was not considered until larvae were found in the sputum, by which time the patient was extremely debilitated and died despite appropriate therapy.

Gram negative meningitis is an unusual infection in adults.[1-5] Spontaneous cases present acutely and run an aggressive course.[4] *E coli* meningitis has a high mortality rate ranging from 50% to 90%[2-4] particularly in the presence of bacteraemia or coma.[4] An association between *E coli* meningitis and predisposing factors such as diabetes and alcohol abuse is well recognised but the association with strongyloidiasis is emphasised only in parasitology literature.[7-10]

Strongyloidiasis is one of the major human intestinal nematode infections and is usually caused by *Strongyloides stercoralis*[11] which is endemic in the tropics, subtropics and south eastern part of the United States. Humans are the main host and infection is usually acquired from soil contaminated by filariform larvae which penetrate intact skin, enter the blood stream and pass into the lungs. They then ascend to the mouth, are swallowed and reach the small intestine where some larvae burrow into the mucosa. After moulting twice they become female hermaphrodite worms. Eggs are produced by parthogenesis and transform into larvae which are either excreted or become infective, penetrating the mucous membrane of the bowel or perianal skin and re-entering the same cycle. This primary infection may be asymptomatic or may cause abdominal pain, diarrhoea and occasionally malabsorbtion.[11]

The capacity of strongyloides to replicate within the host is extremely rare among helminth infections and is the explanation for two of its most significant characteristics. Firstly, the ability for this infection to persist for many years after the carrier has left the endemic area and secondly, the phenomenon of dissemination (hyperinfection). In chronic strongyloidiasis a balance is reached between parasite and host whereby worms are restricted in number and confined principally to skin and gut but cannot be eradicated. However, if host defences break down the larvae multiply rapidly, penetrate the intestinal serosa and spread via the blood stream throughout the body. Immunosuppression is well recognised as a cause of disseminated strongyloidiasis.[12-14] In a review of 103 patients by Igra Siegman,[8] 89 were immunocompromised, 67 by therapy and 22 by disease, particularly lymphatic malignancy. Any organ may be attacked by the invading larvae particularly, as in our case, the lung, causing pulmonary cavitation, consolidation or diffuse infiltration. The presence of blood eosinophilia, often a clue to parasitosis, is frequently absent in disseminated disease[15-17] and a low eosinophil count is regarded as an ominous prognostic sign.[14,17,18] Invasion of the meninges and brain, sometimes with cerebral abscess formation also occurs.[14,19-21] Strongyloides larvae have been isolated from the CSF of two patients with hyperinfection[22,23] and in both of these cases gram negative bacilli were also detected in the CSF. Secondary bacterial infection, par-