Neuro-Behçet's syndrome; two unusual presentations of a rare disease.

Behçet's syndrome (forthwith BS) is a multisystem disorder that has been classified under the sero-negative spondarthritides. Its clinical expression is dominated by an oculo-muco-cutaneous syndrome of recurrent oro-genital ulceration and iritis. In up to a quarter of the cases of BS there is simultaneous neurological disease that mostly comprises one or more components of a meningo-encephalo-myelitis [1]. Two further patients with neuro-BS are reported here.

CASE REPORTS:

Case 1

A 30 year old seamstress developed recurrent oral ulcers followed by genital two years prior to her admission to hospital. With the onset of oral ulceration she experienced a malaise so severe that she was forced to abandon her job. The aphthous ulcers were extremely painful and she lost one stone in weight. Three months before her admission she developed occipito-frontal headaches. They were increasing in severity and were exacerbated by coughing and sneezing. She did not give a history of either nausea or vomiting. One week prior to her admission she developed diplopia. There was no relevant past medical or family history lthough she had been on oral contraceptives over the preceding 3 years.

On examination she had bilateral papilloedema with normal visual acuity. There was a right sided 6th nerve palsy and bilateral first degree phasic horizontal nystagmus. The rest of the neurological examination was normal. She had tongue tip ulcers and pustules over the face and neck.

Her ESR was 97 mm/hr, haemoglobin 11.8 g/dl, white cell count 11.6 $x10^9$ /l (polymorph 78%, lymphocytes 20%, monocytes 2%). The serum album was 37 g/l, globulin 33 g/l and protein electrophoresis was reported as normal. The Rose Waaler test was weakly positive but an immunofluorescent screen for autoantibodies was negative. The immunoglobulins were normal. The patient histocompatibility profile was HLA2, AW32, BW40, B27. Viral complement fixation tests were unremarkable and both the Paul Bunnel test and the VDRL where negative. The serum mucoproteins were raised at 3.25 g/l. The CSF pressure was 230 millimetres of CSF in the recumbent position and the cell count was 5 $x10^6$ leukocytes/litre. The CSF protein was 0.3 g/l and the gamma globulin fraction was 33%. Fluorescein angiography confirmed papilledema. Skull and chest X-rays were normal and an EEG showed a non specific increase in theta activity. Air ventriculography showed minimal dilatation of the right lateral ventricle whilst at operation the dura was noted to be slack and the ventricular pressure normal.

The patient was treated with 16 mg of dexamethasone daily in the initial stages and there was rapid resolution of her papilledema and relief of her symptoms. The recurrent skin and mucosal disturbances were very little improved by a maintenance dose of steroids (5 to 10 mg of Prednisolone per day) though the headaches were kept at bay. In the follow up period (2 years) she had an intermittent arthropathy and developed brisk tendon reflexes and abdominal reflexes.

Consultant report 4 years later:

I have seen her at six monthly intervals over the last two years and she has remained perfectly well during this time. There have been no neurological symptoms at all, and no recurrence of her ulcers. When I last saw her in December, she was taking Imuran 50mg b.d. and Prednisolone 5mg daily. Her GP checks her blood at regular intervals.

Case 2

A 30 yr old wool Winder presented with a one year history of lethargy, malaise and recurrent crops of all ulcers. She had been otherwise well until two weeks before her admission to a local general hospital. She then developed a sore throat, fever and continuous frontal headaches associated with vomiting. She was admitted to hospital as a possible case of meningitis but she improved. It was concluded that she had a respiratory infection and was treated with co-trimoxazole. She was discharged 4 days later though on that day she became aware that her right leg appeared to drag. Within two days it was completely paralysed and the left leg was becoming weak. She was admitted to our neurology unit 3 days later when she was complaining of severe pain between the shoulders, a painful left eye and partial blindness in the right eye. By this time she was

paraplegic and incontinent of urine. On examination, she was pyrexic (39.4°C), had marked next stiffness and a positive Kernig's sign. She had ulcers on the gums and on the dorsum of the tongue. There was a single large genital ulcer. She had bilateral uveitis with an inflammatory vitreous haze on the left. On the right there was a central retinal venous occlusion. The visual acuity with J6 on the left and J14 on the right. The rest of the general examination was normal except for a mild persistent bronchospasm. Neurological examination revealed bilateral first degree horizontal phasic nystagmus. In the left arm there was weakness of the triceps, wrist extensors and small hand muscles. There was a complete flaccid areflexic paraplegia with a dissociated sensory level below D8 on both sides with sacral sparing on the right.

On investigation, an emergency myelogram was normal. The CSF showed a marked pleocytosis with 400 polymorphs and 350 lymphocytes $x10^6$/l. The CSF protein was elevated to 1.3 g/l. Her ESR was 70 mm/hr, haemoglobin 13.3 g/dl and blood white cell count 11.46 $x10^9$ /l . Her serum albumen was 33 g/l, globally 32 g/l and protein electrophoresis was reported as normal. An immunofluorescent screen for auto-antibodies with negative, VDRL negative and viral complement fixation tests showed a raised Mycoplasma pneumoniae antibody titre if 1 in 80. This remained consistent over the first two estimations and fell to 1 in 60 three months after the acute illness. The patient histocompatibility profile was HLA A2, A10, B12, B27. The prothrombin time, fibrinogen level (2,8 g/l) and euglobin lysis time were normal but these were only investigated in the recovery phase of her illness.

Initially, she was treated with 80 mg of Prednisolone per day. This was accompanied by a rapid resolution per eye signs and a much slower improvement of her neurological status. The bronchospasm was initially resistant to this therapy they did disappear within two weeks will stop six months after the acute episode she was able to walk with a frame and was continent of Europe. There has been a patchy return of sensitivity to temperature and pain in her legs. Maintenance therapy with 10 mg of prednisolone/day has been continued and 18 months after the acute episode there had been no relapses.

Consultant report 4 years later:

She has not been seen by any neurologist since 1976, having been followed up by the general physicians. As far as I can tell from the notes, she has slowly deteriorated and has a marked spastic paraparesis. In addition, there is reference to her arms being slightly involved. She has great difficulty walking and uses a tripod stand. The main problem at present appears to be urinary incontinence and she has been under the surgeons care for investigation. More recently, she has been referred to the Urology Department at Newcastle for urodynamic studies and I gather these are still in progress. As far as I can tell from the notes, she is still on a small dose of Prednisone 5 mgs. b.d., and is also on an anti-platelet regime of Anturan and Aspirin.

Discussion

Kalbian and Challis [2] reported three patients with associated BS and benign intra-cranial hypertension; there have been a handful of further cases reported that had features compatible with this association. Case 1, in this report, is a further instance of this association. The cause of benign intracranial hypertension and the pathophysiology of this association is not understood.

In the second case, there was a severe meningo-myelitis with features of a milder diffuse encephalitis. The severe spinal cord disturbance appeared to involve those areas of the court in the supply territory on the anterior spinal artery. The evolution, however, was suggestive of a gradual occlusion of first the right then the left anterior sulcal artery with some spread to involve the circumflex vessel on the right. Suchenwirth et al [3] also reported a patient whose signs suggested an anterior sulcal artery occlusion but this was unilateral. In our case, whilst the clinical features suggested an arterial occlusion, the evolution was unlike a sudden thrombotic or embolic occlusion. Arteritis and arterial occlusions are described in BS [4] and in both the mucosal and ocular manifestations a small vessel arteritis with thrombosis with intimal hyperplasia may be seen though they may be secondary features consequent on the inflammatory process. Similar arteritic changes are described in occasional autopsy reports of neuro-BS within the nervous system though rarely in a situation that could be considered as the primary event and subsequent cause of the multifocal necroses [1]. It is possible that vicious cycle of arteritis and resulting ischaemia exacerbate the primary process and lead to an apparently arterial distribution. In experimental diseases that stimulate the sero-negative spondarthritides

minor local traumata are followed by disease typical local responses and reinforce the plausibility of this suggestion.

I do not believe that a raised Mycoplasma pneumoniae titre has been previously reported in BS; but, a report from Japan has suggested that raised titres to Mycoplasma hominis may be common [5].

References

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