Heerfordt's Syndrome

Synonyms: Heerfordt syndrome (USA form), Heerfordt's disease, Heerfordt-Mylius syndrome, Heerfordt-Waldenstrom syndrome, Waldenstrom's uveoparotitis, uveoparotid fever, febris uveoparotideae, neuro-uveoparotitis syndrome, uveoparotic paralysis, uveomeningitic syndrome

See also the separate Sarcoidosis article.

Definition

Heerfordt's syndrome is an acute syndromal presentation of sarcoidosis, presenting with the following features:
- Fever.
- Uveitis.
- Swelling of parotid ± other salivary/lacrimal glands.

Facial nerve palsy may be a feature but is not thought necessary to confirm the syndrome by all authors.

Several physicians were involved in its discovery and characterisation. Hence, it has a plethora of eponymous names. It forms a small proportion (<5%) of sarcoidosis cases, with variation in its incidence across different ethnic groups.

Involvement of the eyes, nervous system and salivary glands in isolation occurs frequently in sarcoidosis. Strictly, to fit the criteria of this syndrome, they must all present in combination, along with episodes of fever.

Other features of sarcoidosis may co-exist with the syndrome, such as skin lesions and evidence of thoracic involvement. It represents a form of neurosarcoidosis, so there may be other neurological involvement such as meningism, or other cranial nerve lesions leading to ophthalmoplegia, pupillary reflex dysfunction or other abnormalities.

Epidemiology

Heerfordt's syndrome is relatively rare. In one series of 1,000 sarcoidosis patients, 83 had symptoms of Heerfordt's syndrome. Parotid gland involvement has a documented incidence of 6%. [4, 5]

Risk factors
- Young adulthood - more frequent in those aged between 20-40 years. [6]
- More common presentation in women than in men. [6]

Presentation

Additional features of sarcoidosis may appear alongside the core syndrome.

Fever and constitutional upset
- The patient may have experienced paroxysmal episodes of fever or night sweats.
- Other symptoms such as headache and weight loss may occur.
Eye symptoms

- Acute uveitis presents with:
  - Eye discomfort
  - Photophobia
  - Blurred vision
  - Seeing 'floaters'
  - Red eye

- The lacrimal glands may be involved, causing puffy eyelids.

Parotid swelling

- May be unilateral or bilateral - bilateral in 73% of cases of parotid sarcoidosis.[3]
- Diffuse, painless swelling of the parotid ± other salivary glands/lacrimal glands.
- May cause a dry mouth.

Cranial nerve palsy

- Strictly speaking, it must affect the facial nerve (CN VII).
- There is abrupt onset within a short period of the parotid swelling.
- The nerve is thought to be entrapped/infiltrated by granulomatous inflammation in the parotid gland or facial canal but the exact site remains uncertain.
- There may be accompanying disturbance of taste (chorda tympani dysfunction - supporting presumed site of lesion).
- Other cranial nerves can be involved. Symptoms of other cranial neuropathies commonly involved in neurosarcoidosis include:
  - Disturbance of smell.
  - Blurred vision/diplopia/sight impairment.
  - Speech or swallowing difficulty.
  - Vertigo/deafness/tinnitus.
  - Weakness of trapezius/neck muscles.
  - Tongue deviation or atrophy.

Signs

General

These may include:

- Pyrexia.
- Evidence of recent weight loss.
- Facial swelling around the cheeks.
- Swollen eyelids.
- Inflamed eyes, squinting in light.
- Visible facial nerve palsy with drooping of features on one side (NB: if bilateral, facial symmetry may be preserved).[7]

Cranial nerve palsy

- Lower motor neurone CN VII lesion - affects the whole face including the forehead and eyelids.
- Bell's phenomenon may be seen - upward, outward turning of the eyeball as the patient attempts to close the eyelids.
- Examine other cranial nerves, as other palsies may be present.
- If an alternative cranial nerve palsy is found in place of facial nerve paralysis, most would still define the syndrome as Heerfordt's, provided all other classical features of the syndrome are present.
- Bilateral lower motor neurone facial nerve palsy of abrupt onset in young adults is virtually always due to sarcoidosis.
- There may be accompanying signs of meningism.

Eyes

- Anterior uveitis is painful and presents with:
  - Miosis.
  - Pupillary irregularity.
  - Injected conjunctivae next to the cornea (so-called perilimbal flush).

- Fundoscopy may show retinal detachment or vasculitis and papilloedema if there is posterior uveitis.
- Severe cases may show hypopyon - a collection of yellowish inflammatory exudate and cells at the bottom of the anterior chamber.
- Slit-lamp examination may reveal cells, flare and precipitates in the anterior chamber/vitreous humour.

Salivary/lacrimal glands
Diffuse, firm swelling which is not tender to palpation.

Thoroughly examine the heart, chest, skin, eyes, joints, abdomen, lymph fields, nervous system, salivary glands and upper respiratory tract in all patients presenting with suspected sarcoidosis in order to detect the full extent of the disease.

Differential diagnosis

The syndrome is a fairly distinct clinical entity and once recognised is not likely to be confused with illnesses other than sarcoidosis, being virtually pathognomonic for the disease.

Sarcoidosis has a vast differential diagnosis, depending on its mode of presentation. See also the separate Uveitis and Facial Nerve Palsy articles.

For more information about other causes of parotid enlargement, see the separate Salivary Gland Disorders article.

Investigations

- Serum angiotensin-converting enzyme (ACE) - which is usually elevated.
- Hypercalciuria occurs in about 30% of patients and hypercalcaemia in about 10%.
- Gallium scanning of the parotid gland may be helpful.
- Biopsy of the parotid gland and other sites of the disease may be required in some cases and may reveal the classic non-caseating epithelioid granulomata.
- Optic nerve involvement may be detected by imaging - MRI is of more assistance than CT in this situation.

Additional investigations may include:

- CXR - to look for evidence of hilar adenopathy or pulmonary involvement.
- Basic screening bloods such as ESR, FBC, U&E/LFTs, which are usually performed as baseline investigations but are fairly nonspecific.
- Autoantibodies if there is any suspicion of a connective tissue disease.
- Lumbar puncture, which may be needed where there is suspicion of meningitis - in sarcoidosis, it shows a sterile pleomorphic inflammatory picture.

Management[1, 8]

Sarcoidosis tends to undergo spontaneous remission in 50-60% of cases and does not always require active management. The disease course is very variable and difficult to predict.
Medical

- The most troublesome aspect of the syndrome to manage is uveitis which may be sight-threatening and requires expert ophthalmological assessment and monitoring. Topical or systemic corticosteroids are the mainstays of management of ocular sarcoidosis. Other immunomodulatory drugs may be used as steroid-sparing or disease-modifying agents.
- Systemic steroids are used to treat the facial nerve palsy if it is troublesome enough and does not resolve - usually successfully.

Surgical

Surgical intervention may be used to treat the complications of cataracts or vitreous opacification, once active disease has been controlled. Uveitis increases the risk of glaucoma, so a significant proportion of patients may require trabeculectomy or other glaucoma drainage devices.

Complications

Ocular sarcoidosis

- Ocular sicca syndrome.
- Band keratopathy.
- Cataracts.
- Glaucoma.
- Vitreous haemorrhage.
- Retinal detachment.
- Cystoid macular oedema.
- Sight impairment due to macular disease.
- Diplopia.
- Optic atrophy.

Neurosarcoidosis

- Seizures.
- Hydrocephalus.
- Deafness.
- Spinal cord lesions causing motor/sensory paresis.
- Pituitary dysfunction.
- Sterile meningitis.

Parotid sarcoidosis

- Xerostomia.
- Oral infections/dental caries due to reduced saliva secretion.

Prognosis

Prognosis is very variable:

- Of the acute presentations of sarcoidosis, it carries a relatively poorer outlook in terms of severity of disease; however, permanent complications can be avoided or ameliorated by adequate management in many cases.
- Facial paralysis tends to recover or respond to steroids.
- Heerfordt’s syndrome is not thought to relapse once it has remitted or responded to therapy; however, other patterns of sarcoidosis may follow it.
- The degree of involvement of sarcoidosis at other sites will influence the overall prognosis.
- One American study reported that of all deaths reported in the period 1988-2007, 0.05% listed sarcoidosis as the primary cause on the death certificate. [9]
Prevention

The cause of sarcoidosis is not really understood so primary preventative strategies do not exist. Patients with sarcoidosis are prone to relapse and may benefit from long-term specialist follow-up. Patients should be advised to seek early help if they experience symptoms potentially attributable to sarcoidosis.

Further reading & references

- SILA; The Sarcoidosis Charity
- Dua A; Heerfordt's disease or syndrome; whonamedit.com

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