Systemic disease and the upper airway

The upper airway plays an important role in the clinical manifestations of numerous systemic diseases. A comprehensive and detailed overview is given of the systemic diseases and their specific symptoms in each part of the upper airway.

Systemic diseases can affect the upper airway in a very significant way. The effects are increased when the medicines used to treat the systemic diseases are also brought into consideration. This issue of CME covers many different diseases and the effects of medicine on the upper airway. Therefore, to avoid repetition, only systemic diseases causing specific upper airway symptoms are given in tabular form.

These will be mentioned under the following headings:
- the nose, paranasal sinuses and nasopharynx
- the oropharynx
- the laryngopharynx and larynx.

Nose, paranasal sinuses and nasopharynx

Pain

The differential diagnosis of rhinogenic pain can be extremely challenging because systems in the head and face are functionally and structurally interdependent and because patients often give vague descriptions of the pain. A precise history is therefore vital to make a presumptive diagnosis so that appropriate special investigations can be selected. The possible systemic diseases in the differential diagnosis of rhinogenic pain are summarised in Table I (p. 744).

Rhinorrhoea

Spontaneous drainage of fluid from the nose can be a sign of disease if the quantity, colour, odour and consistency differ from that of the normal nasal discharge. It can be watery, mucoid, purulent or blood-tined, uni- or bilateral and constant or intermittent. Systemic diseases giving rise to nasal discharge are listed in Table II (p. 744).

Epistaxis

Nosebleeds may be symptomatic of an underlying disorder (sometimes a life-
Table I. Pain: nose, paranasal sinuses and nasopharynx

<table>
<thead>
<tr>
<th>Inflammatory lesions</th>
<th>Tumours causing local or referred pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic rhinosinusitis</td>
<td>Benign tumours</td>
</tr>
<tr>
<td>TB</td>
<td>Paget's disease</td>
</tr>
<tr>
<td>leprosy</td>
<td>histiocytoma</td>
</tr>
<tr>
<td>lues</td>
<td>Systemic neoplasias</td>
</tr>
<tr>
<td>parasitic and fungal infestation</td>
<td>eosinophilic granuloma</td>
</tr>
<tr>
<td>Allergic rhinosinusitis</td>
<td>plasmacytoma</td>
</tr>
<tr>
<td>Polyposis associated with asthma and salicylate hypersensitivity mucoviscidoses</td>
<td>(extramedullary) lymphoma</td>
</tr>
<tr>
<td>Secondary atrophic rhinitis (ozaena)</td>
<td>Distant metastases (e.g. metastases involving cranial nerve V)</td>
</tr>
<tr>
<td>syphilis</td>
<td>hypernephroma</td>
</tr>
<tr>
<td>lues</td>
<td>osteogenic sarcoma</td>
</tr>
<tr>
<td>Wegener's disease</td>
<td>haemangiendothelioma</td>
</tr>
<tr>
<td>Rhinitis sicca anterior</td>
<td>seminoma</td>
</tr>
<tr>
<td>lupus erythematosus</td>
<td>breast carcinoma</td>
</tr>
<tr>
<td>Granulomatous lesions</td>
<td>Pseudotumours</td>
</tr>
<tr>
<td>Wegener's disease</td>
<td>plasma cell granuloma</td>
</tr>
<tr>
<td>Midline granuloma</td>
<td>fibrous dysplasia</td>
</tr>
</tbody>
</table>

Table II. Nasal discharges caused by systemic diseases

<table>
<thead>
<tr>
<th>Watery</th>
<th>Mucoid</th>
<th>Discoloured</th>
<th>Bloody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coryza</td>
<td>Toxic rhinitis</td>
<td>Fungal infection</td>
<td>Wegener's granulomatosis</td>
</tr>
<tr>
<td>Gonorrhoeal</td>
<td>Occupational rhinitis</td>
<td>Mucormycoses in diabetics or immuno-compromised</td>
<td>Midline granuloma</td>
</tr>
<tr>
<td>Diphtheric</td>
<td>Rhinitis of pregnancy</td>
<td>Infections</td>
<td>(angiocentric T-cell</td>
</tr>
<tr>
<td>Allergic</td>
<td>Cystic fibrosis</td>
<td>Diphtheria</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Food intolerance</td>
<td>(mucoviscidosis)</td>
<td>Tuberculosis</td>
<td>Syphilis</td>
</tr>
<tr>
<td>Inhalants</td>
<td></td>
<td></td>
<td>Leprosy</td>
</tr>
<tr>
<td>Rhinitis medicamentosa</td>
<td></td>
<td></td>
<td>Malleus</td>
</tr>
<tr>
<td>CSF leak*</td>
<td>Pituitary adenoma</td>
<td></td>
<td>Leishmaniasis etc.</td>
</tr>
</tbody>
</table>

* Coupled CSF leak with + glucose on dipstick and R- transferrin measurements.

threatening disease) extrinsic to the nasal region. Essential hypertension is responsible for most of these epistaxes. In more than 80% of cases the nose bleeds from the Kiesselbach plexus sited on the anterior part of the septum. In some cases the bleeding site cannot be localised. The epistaxis is then managed by either blind packing of the nasal cavity and/or ligation or embolisation of the supplying vessels. Table III (p. 745) gives a synopsis of systemic causes of epistaxis.

Once a patient with life-threatening epistaxis has been stabilised, a thorough evaluation is required. Table IV (p. 745) illustrates the management of epistaxis.

Nasal obstruction

The obstruction may be uni- or bilateral, transient or permanent, partial or complete and based on a functional or structural cause. Systemic causes are listed in Table V (p. 746).

sleep disturbance
snoring-obstructive sleep apnoea
headaches
hyposmia or anosmia
increased susceptibility to upper airway infection and paranasal sinus disease

Nasal fetor

The secondary causes of atrophic rhinitis and all chronic specific infectious diseases are included in the differential diagnosis for nasal fetor.

Dry nose

A dry nose may be due to exogenous or endogenous influences. Exogenous influences include environmental factors, previous radiation to the head, bacterial, fungal or parasitic chronic inflammation and drug action, e.g. atropine. Endocrine diseases such as Basedow disease, cretinism and adenocortical hyperfunction, as well as Sjögren's disease, constitute endogenous influences.
Morphological change

Some of the diseases associated with this symptom have been mentioned under the previous headings.

Inflammatory conditions such as lupus erythematosus, TB, syphilis, sarcoidosis, and granulomas and granulomatoses cause morphological changes. Tumours (Table 1) also fall in this category.

Pharynx/mouth

The oro- and hypopharynx are part of both the upper respiratory and digestive tracts. It is therefore convenient to consider the entire pharynx and oral cavity as a single unit.

Pain

The disorders listed in this section have pain as their main symptom. Table VI (p. 746) gives a summary of the systemic diseases associated with oropharyngeal pain.

Dysphagia

Dysphagia is a symptom which encompasses functional or physical difficulties in swallowing. It may be associated with odynophagia and has numerous causes (Table VII, p. 748).

Mucosal lesions

Some of the diseases affecting the mucosa of the mouth and pharynx are listed in Table VIII (p. 748).

Tumours

Some systemic diseases manifest as pseudotumours in the oropharyngeal region:

- fibrous dysplasia
- plasma-cell granuloma
- gouty tophi
- sarcoidosis
- Wegener's granulomatosis
- midline granuloma
- Paget's disease.
- Kaposi's sarcoma and malignant

lymphoma may manifest in the oropharyngeal region as part of a systemic involvement.

Oropharyngeal fetor

Bad breath can have many causes (Table IX, p. 749).

Blood in sputum

It is important to differentiate between haemoptysis (blood from lungs), haematemesis (blood from gastro-intestinal system) and ENT haemorrhage. Systemic conditions that can cause blood in the sputum through ENT haemorrhage include the following:

- fracture of skull base with cavernous sinus and carotid artery involvement
- Osler-Rendu-Weber disease
- haemorrhagic diathesis
- bleeding from a hypopharyngeal diverticulum.

Table III. Causes of epistaxis

<table>
<thead>
<tr>
<th>Systemic disorders</th>
<th>Pseudo-epistaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>Pulmonary haemoptysis</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>e.g. bronchietasis</td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>pulmonary oedema</td>
</tr>
<tr>
<td>Epistaxis in pregnancy</td>
<td>Injury of ICA</td>
</tr>
<tr>
<td>(hormone based)</td>
<td>Haematemesis, e.g. bleeding</td>
</tr>
<tr>
<td>Endocrine causes</td>
<td>oesophageal varices</td>
</tr>
<tr>
<td>Bleeding disorders - platelet,</td>
<td></td>
</tr>
<tr>
<td>coagulation factor or vascular</td>
<td></td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
</tr>
<tr>
<td>Uraemia</td>
<td></td>
</tr>
<tr>
<td>Hepatic insufficiency</td>
<td></td>
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<tr>
<td>Hereditary</td>
<td></td>
</tr>
<tr>
<td>haemorrhagic telangiectasia</td>
<td></td>
</tr>
<tr>
<td>(Osler-Rendu-Weber disease)</td>
<td></td>
</tr>
</tbody>
</table>

Table IV. Management of epistaxis

- Stabilise patient — cardiovascular assessment
- History — to distinguish between local and systemic causes (e.g. systemic diseases, medications taken, family history, etc.)
- Localisation of the bleeding site/causes
  Anterior — local trauma, infectious diseases
  Posterior or midnasal — hypertension, tumours
  Diffuse — bleeding disorders
- Bleeding and coagulation analysis
  Bleeding time — 2 - 6 min
  Clotting time — 4 - 10 min
  Partial thromboplastin time — 25 - 35 s
  Prothrombin index — 70 - 120%
  Platelet count — 150 000 - 300 000/ mm³
  With suspected consumption coagulopathy
    fibrinogen — 150 - 300 mg/dl
    fibrin breakdown products — up to 10 µg/ml
- Radiography in selected cases
Table V. Systemic causes of a blocked nose

<table>
<thead>
<tr>
<th>NOSAL PARANASAL SINUSES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinitis sicca anterior</td>
<td></td>
</tr>
<tr>
<td>Septal perforation with crusting</td>
<td></td>
</tr>
<tr>
<td>Nasal polyposis</td>
<td></td>
</tr>
<tr>
<td>Atrophic rhinitis</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td></td>
</tr>
<tr>
<td>Specific inflammatory conditions</td>
<td></td>
</tr>
<tr>
<td>TB, leprosy, tertiary syphilis, rhinoscleroma</td>
<td></td>
</tr>
<tr>
<td>Lupus, sarcoidosis</td>
<td></td>
</tr>
<tr>
<td>Rare tropical infections</td>
<td></td>
</tr>
<tr>
<td>Blastomycosis, leishmaniasis</td>
<td></td>
</tr>
<tr>
<td>Fungal infections</td>
<td></td>
</tr>
<tr>
<td>Granulating mucosal diseases</td>
<td></td>
</tr>
<tr>
<td>Wegener's granulomatosis</td>
<td></td>
</tr>
<tr>
<td>Stewart's (midline) granuloma</td>
<td></td>
</tr>
<tr>
<td>Chronic rhinopathy</td>
<td></td>
</tr>
<tr>
<td>Exogenous factors</td>
<td></td>
</tr>
<tr>
<td>Inflammatory conditions</td>
<td></td>
</tr>
<tr>
<td>Rhinitis medicamentosa</td>
<td></td>
</tr>
<tr>
<td>Occupational rhinopathy</td>
<td></td>
</tr>
<tr>
<td>Endogenous factors</td>
<td></td>
</tr>
<tr>
<td>Immunopathies — IgA deficiency, agammaglobulinaemia</td>
<td></td>
</tr>
<tr>
<td>Functional deficits — sick cilia syndrome (Katagren)</td>
<td></td>
</tr>
<tr>
<td>Endocrine dysfunctions — cystic fibrosis</td>
<td></td>
</tr>
<tr>
<td>Disturbed neuro-autonomic regulation — diabetes mellitus</td>
<td></td>
</tr>
</tbody>
</table>

Table VI. Systemic diseases associated with throat pain

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsillitis in</td>
<td></td>
</tr>
<tr>
<td>Diphtheria, infective mononucleosis (IMN), scarlet fever</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
</tr>
<tr>
<td>Leukaemia</td>
<td></td>
</tr>
<tr>
<td>Chronic pharyngitis</td>
<td></td>
</tr>
<tr>
<td>Sjögren's disease</td>
<td></td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td></td>
</tr>
<tr>
<td>Functional deficiencies — hypothyroidism, diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>Specific and nonspecific infections — TB, leues, Candida, diphtheria, etc.</td>
<td></td>
</tr>
<tr>
<td>Pharyngitis associated with Zenker diverticulum or reflux oesophagitis</td>
<td></td>
</tr>
<tr>
<td>Pharyngo-oesophagitis (Plummer-Vinson*)</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal pain associated with neuralgia of V, IX, X</td>
<td></td>
</tr>
</tbody>
</table>

* Plummer-Vinson syndrome affects mostly women over 40 years of age. An iron deficiency is probably the underlying cause. The clinical picture includes pale, dry skin, spoon nails, dry hair and sometimes a mucosal web of the oesophageal inlet. It can be a precursor of oesophageal carcinoma.

True haemoptysis can be caused by:
- bronchitis
- pulmonary infarction
- pneumonia
- bronchiectasis
- fungal aspergiloma
- congested lung
- ruptured aortic aneurysm, etc.

Haematemesis can be caused by diseases such as:
- oesophageal varices, malignancy
- oesophagitis
- peptic or duodenal ulcer, etc.

Larynx

Pain

Laryngeal pain is the main symptom in these systemic diseases:
- acute laryngitis, e.g. diphtheria
- chronic laryngitis with perichondritis, e.g. TB
- cricoarytenoid arthritis
- superior laryngeal neuralgia.

Cough

Cough is a warning sign of disease in many parts of the respiratory tract. The differential diagnosis includes systemic diseases of pulmonological, cardiological and miscellaneous (e.g. mediastinal tumours, aortic aneurysm, gastro-oesophageal reflux, etc.) causes. The character of the cough may signify a specific diagnosis, e.g. nocturnal cough may signify congestive heart failure, while cough during or after meals may indicate hypopharyngeal diverticulum, hiatus hernia or neurogenic dysphagia (Table X, p. 749).

Morphological change and hoarseness

Hoarseness often co-exists with morphological change in the larynx. Causes of these symptoms are summarised in Table XI (p. 749).

Stridor

Any disease causing narrowing of the airway to less than a third of its
Table VII. Causes of dysphagia

- Inflammatory — laryngeal tuberculosis, syphilis, etc.
- Non-inflammatory — sicca syndrome (Sjögren's disease), sarcoidosis
- Neurological
  - soft-palate palsy in diphtheria
  - central nervous disease
  - bulbar paralysis
  - botulism
  - toxic diphtheria
  - multiple sclerosis
  - cerebral ischaemia
  - polyneuritis
  - diabetic neuropathy, etc.
- Muscular — myasthenia gravis, dermatomyositis, etc.
- Psychogenic — globus hystericus
- Cervical spine — osteoarthritis, etc.
- Dermatological — scleroderma, SLE, pemphigus, etc.
- General
  - botulism
  - pernicious anaemia
  - agranulocytosis
  - tetany
  - tetanus
  - goitre or thyrotoxicosis
  - hypokalaemia
  - vitamin A, B12, deficiency
  - mitral valve disease
  - aortic aneurysm, etc.

Table VIII. Diseases which affect the mucosa of the mouth and pharynx

- Viral diseases — AIDS, sporadic viropathies (e.g. mononucleosis, varicella)
- Bacterial diseases — TB, syphilis, diphtheria, leprosy, rhinoscleroma, gonorrhea
- Protozoal infections — leishmaniasis
- Fungal infections — candidiasis, actinomycosis
- Drug-related stomatitis
- Aphthous mucosal diseases — Behçet's syndrome, herpangina
- Dermatoses with OF-lesions — pemphigus vulgaris, pemphigoid, erythema multiforme (including Stevens-Johnson syndrome), scleroderma, SLE, etc.
- Granulating diseases — sarcoidosis, histiocytosis X and eosinophilic granuloma, Wegener's granulomatosis, midline granuloma, specific granulomata (TB, hies, fungal)
- Hipovitaminoses B1, B6, B12, niacinamide, C and A
- Manifestations of haemorrhagic disorders — haemophilia A
- Neoplasma — plasmacytoma, metastases

Diameter will produce stridor. The diseases listed in Table XI can also be included in the differential diagnosis of stridor.

Voice disorders

Systemic diseases mainly cause organic abnormalities of the larynx. Thus any disease causing structural or functional interference with the joints, the nerve supply or the muscles of the larynx, will cause dysphonia. See Table XI for differential diagnosis.

Conclusion

The abovementioned lists of systemic illnesses emphasise that multidisciplinary aspects must often be considered in the differential diagnosis of upper airway symptoms. History-taking should be thorough and systematic and should include specific questions on every detail of each symptom, e.g. the precise character, onset, location, underlying or associated diseases and how they are influenced by external factors. A full ENT and general examination should follow. Fundoscopy can, for example, help with the early detection of vasculitis seen in Wegener's granulomatosis. After a presumptive diagnosis has been made, further specific diagnostic investigations can be selected.

FURTHER READING

Table IX. Systemic causes of bad breath (halitosis)

- Oral cavity
  Behcet’s disease
  Erythema multiforme

- Oropharynx
  Acute infections: IMN, diphtheria, etc.
  Chronic infections: lues, TB, etc.

- Respiratory tract
  Ozaena
  Bronchitis
  Bronchiectasis
  Pneumonia
  Lung abscess
  Tumours

- Digestive tract
  Zenker’s diverticulum
  Hiatus hernia with oesophagitis

- Other causes
  Diabetes mellitus
  Vitamin B preparations

Table X. Systemic diseases associated with cough

<table>
<thead>
<tr>
<th>Dry cough</th>
<th>Wet cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otolaryngological chronic laryngotracheitis</td>
<td>Otolaryngological aspiration tracheobronchitis</td>
</tr>
<tr>
<td>environmental and/or occupational influences</td>
<td>tracheo-oesophageal fistula</td>
</tr>
<tr>
<td>fungal infection</td>
<td></td>
</tr>
<tr>
<td>endolaryngotracheal goitre</td>
<td></td>
</tr>
<tr>
<td>tracheal compression</td>
<td></td>
</tr>
<tr>
<td>recurrent nerve palsy</td>
<td></td>
</tr>
<tr>
<td>vagus nerve irritation</td>
<td></td>
</tr>
</tbody>
</table>

- Pulmonological bronchial asthma
- Pulmonological sarcoidosis
- Pulmonological bronchopulmonary neoplasms

- Cardiovascular left heart failure
- aortic aneurysm
- CNS diseases with dysphagia

Table XI. Causes of morphological change and hoarseness

- Chronic laryngitis
  Chronic hyperplastic laryngitis
  exogenous noxious agents — thermal, mechanical, chemical, smoking
  Reinke oedema
  inflammatory processes, etc.

- Atrophic laryngitis
  environmental/occupational insult
  endocrine factors (e.g. laryngopathy of pregnancy)
  metabolic influences (e.g. nephroses)
  auto-immune factors (e.g. Sjogren’s disease)

- Fungal infection (Candida, histoplasmosis, etc.)
- Laryngeal oedema
  Inflammatory oedema (e.g. perichondritis caused by TB, radiation)
  Non-inflammatory oedema associated with cardiac, renal or hepatic insufficiency
  myxoedema
  drug intolerance

- Arthritis of crico-arytenoid joint
  Osteo-arthritis
  Rheumatoid arthritis
- Specific inflammatory conditions
  Tuberculosis
  infiltrating (reddish submucous nodules)
  ulcerating (necrosis, perichondritis)
  tuberculoma (granular mass)
  mucosal lisp (diffuse)
  Sarcoïdosis (small, firm nodular infiltrates)

- Syphilis
  secondary (ulcers)
  tertiary (gummas — pseudotumour, ulceration, destruction)
  Leprosy (nODULES, ulcers, scarring)
  Leishmaniasis (plaques or ulcers)
  (Rhino) scleroma (granulomas)
  Granulomatoses
  Hand-Schüller-Christian’s disease
  Wegener’s disease

- Various dermatoses
  Herpes simplex, zoster
  Pemphigus
  Erythema multiforme

- Storage diseases
  Amyloidosis
  Lipoproteinosis
  Gout

- Neurogenic morphological changes
  Allergic — serum prophylaxis (tetanus antitoxic)
  Bronchial carcinoma
  Diabetic neuropathy
  CNS diseases — bulbar, pseudobulbar paralysis, multiple sclerosis
  Cardiac diseases — dilatation of left atrium in mitral stenosis,
  aortic aneurysms, etc.
  Toxic-infectious — rheumatic fever, IMN, diphtheria
  Goitre

- Tumours
  Malignant — lymphoma, plasmacytoma
  Metastases — hyperneoplasia

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