Vanishing syndromes

ABSTRACT—Certain syndromes develop because of regression or shrinkage of essential pathways. This account draws attention to six conditions in which different mechanisms and pathways give rise to a scorched-earth policy and to strange clinical syndromes.

Shrinking lung syndrome

Systemic lupus erythematosus (SLE) often affects the lungs, pleura or diaphragm, and it may on rare occasions give rise to loss of lung volume, small clear lung fields on X-ray, and reduction in carbon monoxide diffusing capacity. Is it due to pulmonary vasculitis, fibrosing alveolitis, pleurisy, pneumonitis, immobility of the chest wall or pleura, or functional restriction due to chest pain? All these possible factors have had their supporters since Hoffbrand and Beck's pioneer article in 1965 on unexplained dyspnoea and shrinking lungs in SLE [1].

Diaphragmatic fatigue may sometimes contribute but this is controversial. Larocher et al [2] reported an elegant study of diaphragm strength and conclude that it is unlikely to be due to a primary abnormality of the diaphragm. Fine-cut CT scans ruled out pleural thickening or any significant degree of atelectasis, and also ruled out interstitial fibrosis. The clinical and pathological features of lung involvement in SLE have been well reviewed by Quismorio [3].

This syndrome has also been observed in sarcoidosis, affecting both the lungs and the biliary system in different ways.

Disappearing bile ducts

The bile ducts have a rich blood supply from the hepatic artery. Interference leads to ischaemic necrosis of the bile ducts, both extra- and intra-hepatic, and to their ultimate disappearance [4]. Vascular cholangitis may follow surgical trauma during cholecystectomy or complicate hepatic transplantation. Intimal thickening of hepatic arterioles is a rare feature of chronic allograft rejection in man. Circulating lupus anticoagulant interferes with phospholipid-dependent coagulation and may give rise to hepatic arterial microthrombi and to biliary necrosis in association with primary sclerosing cholangitis. Drugs may also cause biliary necrosis and bile-duct shrinkage and disappearance. They include 5-fluorodeoxyuridine (5-FUDR) when administered directly into the hepatic artery, and formaldehyde which, when injected into hydatid cysts, may leak into the biliary system causing biliary strictures. Fibrosis of the biliary system may also lead to the disappearance of bile ducts. Biliary tract fibrosis with chronic cholestasis due to sarcoidosis is most likely to occur in middle-aged black men, in whom the relentless progression from granuloma formation to fibrosis is most often witnessed (Fig. 1) [5, 6]. Bile-duct damage is the principal feature of primary biliary cirrhosis, and fibrosis leads to disappearing bile ducts [4]. This distortion sometimes makes it difficult to distinguish sarcoidosis from primary biliary cirrhosis (Table 1). Disappearing bile ducts due to biliary fibrosis may, rarely, complicate histiocytosis X [7].

Sjögren's syndrome of disappearing exocrine glands

Henrik Sjögren (1899–1989) was a Swedish ophthalmologist who described his syndrome in 1933 [8]. Sjögren's syndrome is a chronic inflammatory autoimmune disorder which mainly affects women approaching the menopause. Lymphocyte-mediated destruction of exocrine glands leads to diminished or absent glandular secretions and to mucosal dryness. Biopsy of a minor salivary gland is a simple outpatient technique for obtaining histological confirmation of focal lymphocytic infiltrates, acinar destruction and

Fig. 1. Cholestatic sarcoidosis. Liver histology shows a portal zone with a fibrotic healed granuloma and an injured disappearing bile duct. Stained H and E x 80 (Courtesy of Dame Sheila Sherlock)
atrophy, and hypertrophy of ductal epithelial and myoepithelial cells (epimyoepithelial islands). The activated T-lymphocyte population has a high CD4:CD8 ratio as seen in the lymphocytic alveolitis of sarcoidosis. This aggressive immunohistologic pattern is presumably responsible for the oesophageal and pulmonary dysfunction, chronic gastritis with its endoscopic cobblestone appearance, small intestinal malabsorption, pancreatic insufficiency, liver dysfunction, and destruction of the lacrimal and salivary glands (Fig. 2). There is a well-known affinity with HLA-D3; and autoantibodies include SS-A(Ro), SS-B(La), ANA, salivary duct and thyroid antibodies and rheumatoid factor. Excessive CD4 helper activity and a significant reduction in circulating CD8 cells promote chronic B-cell stimulation, which eventually leads to neoplastic B-cell clones and to B-cell lymphomas [9].

There is a close association between primary biliary cirrhosis and the type of Sjögren’s syndrome associated with rheumatoid arthritis [10]. In one series of 38 patients with primary biliary cirrhosis, symptoms of Sjögren’s syndrome were present in nearly one-half but were only severe enough to warrant therapy in 10% of patients.

### Vanishing hypothyroidism

Hypothyroidism in some patients with autoimmune thyroiditis may be due to thyrotropin-blocking antibodies. Their production may subside, leading to remission of hypothyroidism. Chronic autoimmune thyroiditis may therefore cause transient hypothyroidism [11]. This has also been termed vanishing hypothyroidism [12]. Takasu et al [11] found thyrotropin-inhibitory antibodies in 10% of patients with goitrous autoimmune thyroiditis and in 25% with atrophic autoimmune thyroiditis. Some of these patients remained euthyroid after thyroxine therapy had been discontinued.

How is one to assess when thyroxine treatment needs to be continued or when to discontinue it if it is no longer necessary? Utiger [12] suggests that the simplest and most practical way to judge this change of management is by reducing or discontinuing thyroxine therapy. It is certainly a less cumbersome option than repeated tests of thyrotropin-inhibitory antibodies or assessing the response to thyrotropin-releasing hormone.

### Vanishing testis

The testicular regression syndrome is characterised by a rudimentary epididymis and spermatic cord with absence of testicular tissue [13]. It presents clinically as the differential diagnosis of cryptorchidism in boys about four years old (but ranging from two months to 16 years) with impalpable testes. Surgical exploration confirms complete absence of testes. The external genitalia are normal and there is normal internal duct development. Just the testis has vanished; the vanishing testis is usually left-sided or, rarely, bilateral. The testis can be assumed to be absent if vas and epididymis are found within the scrotum but the testis is not in the inguinal canal. This assumption is made because of the intimate relationship between epididymal and testicular development. The histological findings are the presence of vas deferens, epididymis, calcification, haemosiderin pigmentation, and a richly vascular stroma [13].

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**Table 1. Cholestatic sarcoidosis compared with primary biliary cirrhosis**

|                | Sarcoidosis | Primary biliary cirrhosis |
|----------------|-------------|----------------------------|
| Sex            | Equal       | 80% female                 |
| Age            | Young       | Middle age                 |
| Pruritus       | Yes         | Yes                        |
| Jaundice       | Yes         | Yes                        |
| Respiratory complaints | Yes       | No                         |
| Hepato-splenomegaly | Yes      | Yes                        |
| Serum alkaline phosphatase | Raised   | Raised                     |
| Hilar lymphadenopathy | Usual    | Rare                       |
| Hepatic granulomas | Discrete  | Poorly formed              |
|                | Clustered   | Surrounded mixed cells      |
| Serum angiotensin-converting enzyme | Raised    | Raised                     |
| Mitochondrial antibody | No        | Yes (98%)                  |
| Kveim-Siltzbach test | Positive  | Negative                    |
| Broncho-alveolar lavage | Lymphocytosis | Present                   |
| Activated macrophages | Present | Present                    |

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**Fig. 2. Sjögren’s syndrome.** Parotid gland showing dense lymphocytic infiltrate replacing normal structure with scanty remaining atrophic tubules. Stained H and E × 80 (Courtesy of Professor W. Jones Williams)
Koro—the vanishing penis

Koro is a psychiatric disorder manifesting as acute anxiety with the fear of genital retraction into the abdomen [14]. Ancient Chinese texts suggest that complete disappearance of the penis into the abdomen will result in death. This old Chinese wives’ tale has led to bizarre behaviour, including holding the penis or attaching devices to the penis to prevent its retraction. It is most commonly found in the Chinese of South-East Asia, but it also occurs in Hindu and Muslim communities of India and, rarely, in Europe.

The term ‘koro’ includes not only penile shrinkage but also the rare complaint of labial and breast hyperinvolution. There is a folk belief in some communities that ghosts of the dead, who do not have penises, disguise themselves to steal penises from the living [15]. Single cases are rare, but it is not difficult to understand that in primitive communities firmly held beliefs of this kind rapidly swell single cases into large epidemics.

There is a much commoner physical cause for penile shrinkage than the essentially psychiatric koro. Morbid obesity allows the penis to subside into a large fatty pubic pad. Unlike koro, this occurs all over the world, is not a culture-specific disorder, and is not associated with epidemic hysteria.

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