Observations on Melkersson's syndrome

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Summary

The findings in nine cases of Melkersson's syndrome are presented. It is suggested that this condition is less uncommon than is generally realized. A careful personal and family history should be taken in all cases of Bell's palsy, and the tongue examined, if this syndrome is to be recognized. Observations are made on the possible aetiology and on treatment.

Introduction

'Bell's palsy' is commonly visualized as an intrinsic lower motor neurone paralysis of the facial nerve unaccompanied by other manifestations. In consequence it tends to be accepted by many as an 'idiopathic accident'. This concept is not always adequate, and if rigidly adhered to must result in failure to recognize various interesting and unusual associations that accompany some such paralyses. The opportunity is taken to reiterate that recurrent palsy of this nerve is only one of a triad of signs in Melkersson's syndrome (Melkersson, 1928). The others are explosive and repetitive episodes of facial swelling and, in a significant proportion, a deeply fissured tongue ('lingua plicata'), with a scrotal pattern of its surface (Rosenthal, 1930), having familial characteristics (Cockayne, 1933). If the affinity between these apparently diverse signs is not appreciated, then the diagnosis in an individual case is likely to be 'simple Bell's palsy', 'cellulitis' of the face, or even 'angioneurotic oedema' depending upon the interpretation placed upon the dominant presenting sign. That this relationship has escaped the notice of many observers is reflected in the few meagre case reports that have infrequently appeared in our literature. It has been stated (Kunstadter, 1965) that this apparently rare disease did not appear in paediatric records until 1962 (Ehmann & Stickl, 1962), which is surprising in view of the fact that a large number of these cases are to be found in the second decade (Ekbom, 1950), and even earlier. The findings in nine of these patients are presented in Table 1, which tends to show that this syndrome is not uncommon.

Cases 5 and 6 are dealt with in more detail below, with the investigations common to all, because they exhibit a feature not yet described.

Case reports

Case 5

On 15 February 1966 an 8-year-old boy presented with a well-developed lower motor neurone lesion of the facial nerve, which followed a sharp pyrexial illness with particularly severe migrainous headaches. History revealed that 2 years previously he had had a transient weakness of the opposite nerve, which had quickly resolved. On this occasion recovery was slow, the patient appeared 'ill', and was unusually 'shaken' in contrast to what one would expect in that which is usually termed 'Bell's palsy'.

Investigations. The peripheral blood picture was normal, serum proteins 7.2 g/100 ml with serum albumin 66.5%; electrophoretic patterns showed a raised α -globulin, reduced β - and γ -globulins; the CSF was normal in cytology with a protein content of 30 mg/100 ml and negative Lange curve; virus studies on faeces, spinal fluid and blood were negative on monkey tissue culture; urine on routine examination was normal, but an amino-acid chromatogram showed an oversecretion of leucine and taurine, and again when repeated 2 months later there was very gross taurinuria with some oversecretion of leucine. The possibility of hepatic dysfunction was tentatively suggested; liver function tests: bilirubin (direct) nil, total less than 1 mg/100 ml, alkaline phosphatase 18.5 K.A. units, thymol turbidity 1 unit, zinc turbidity 5 units, pseudocholinesterase 50 units, SGOT 46 units and SGPT 14 units. Chromosome studies revealed a normal male chromosome constitution of 46 XY.

Case 6

A well-developed 16-year-old girl, P.W., a half-sister of the above patient was examined and seen to have a marked right facial paralysis. Again there was a history of a pyrexial illness 3 weeks previously, with vertigo and severe

TABLE 1

	Facial paralysis	Lingua plicata	Oedema of the face and other manifestations
9 September 1951	(1) Female aged 15 years. R. facial paralysis, eight attacks involving both sides, with complete bilateral degeneration seven years after initial palsy.	Present	Sudden recurring episodes lymphoedema of R. upper lip with pyrexia and prostrating attacks of hemicrania with premenstrual exacerbation. Progressive thickening of lip led to permanent disfiguration. Erythrocyanosis crurum and troublesome chilblains. Large dentigerous cyst removed from right upper jaw. Death at 27 years from fulminating carcinoma of the vulva.
8 October 1951	(2) Male aged 10 years. Transient right facial weakness after 'Influenza' which recurred 5 months later. A year later a left-sided lesion appeared.	Present	Painless enlargement of submandibular salivary glands, with definite residual thickening 6 months later. Kveim test negative.
6 March 1952	(3) Female aged 12 years. R. facial paresis with uneventful recovery.	Present	
	The above three patients were siblings; their mother had a scrotal tongue.		
7 November 1958	(4) Male, aged 62 years, had L. facial contracture for 25 years due to lower motor neurone lesion seventh nerve. Had first of several attacks of facial palsy when 10 years old.	Present	History of suddenly recurring swellings of the same side of the face which ceased with advent of complete paralysis.
15 February 1966	(5) Male, aged 8 years, left facial paralysis, similar lesion right side 2 years previously.	Present	Pyrexia preceded severe headaches that accompanied the paralysis, and continued for 2 months. Astigmatism. Heavy taurinuria.
15 February 1962	(6) Half-sister of the above patient, aged 16 years. Right facial paralysis.	Present	Severe pyrexial illness, 3 weeks after onset, when back at work, developed a severe right facial paralysis. Severe headaches a feature. Taurinuria. Large transient interscapular swellings. Astigmatism.
	The mother was the parent common to the above two patients.		
5 September 1966	(7) Female aged 52 years. R. facial paralysis. Two years previously had a similar attack with complete recovery.	Absent	Left unilateral attacks of brawny painless swellings of the face, four episodes, the first 15 years earlier.
9 April 1967	(8) Female aged 56 years. Right facial paralysis. 35 years previously had had a similar attack same side, forgotten as recovery spontaneous.	Present	Paralysis on this occasion was preceded by pyrexial illness.
10 October 1967	(9) Male aged 28 years. Paralysis right facial nerve recovered quickly.	Present	The nerve lesion followed a sharp 'influenzal' illness.

hemicrania. The tongue pattern was again that of 'lingua plicata'. The patient looked ill, and in the 4th week unexplained large painless swellings appeared in the interscapular region which disappeared in a few days.

Investigations: CSF clear, not under raised pressure; there was no increase in cells, protein was 50 mg/100 ml, sugar 92 mg, Lange curve negative; serological tests did not indicate infection with influenza A, B or C, parainfluenza, respiratory syncytial adenoviruses, psittacosis, lymphogranulomas, Q fever, Mycoplasma pneumonia, or other infective agents; urine on routine examination was normal, but a chromatogram showed general aminoaciduria with a par-

ticular oversecretion of taurine and some oversecretion of leucine. The pattern showed in a more marked degree the changes seen in the urine of the half-brother above. The test repeated after 2 months showed a similar pattern, serum proteins totalled 6.48 mg/100 ml, serum albumin 68.3% of the total with a reduced γ -globulin on electrophoresis; liver function tests, bilirubin (direct) nil, total 1 mg/100 ml, thymol turbidity 0 units, zinc turbidity 6 units, alkaline phosphatase 6.6 K.A. units, pseudocholinesterase 54 units, SGOT 19 units, SGPT 11 units. There was no anomaly in chromosomal studies, 46 XX.

In both these patients some residual facial

FIG. 1. Tongue of 28-year-old male with first attack of facial paralysis, showing marked central and peripheral fissuring.

FIG. 2. Tongue of 8-year-old boy with a second facial paresis. The tongue is large and beefy with peripheral and median fissuring and a symptomless median glossitis.

weakness is demonstrable some years after the onset of the neurological lesion. Recently both complained of dimness of vision, and the girl was found to have severe astigmatism, and the boy was similarly affected but in moderate degree.

The mother was the parent common to both patients.

The possibility of future recurrent facial pareses and/or attacks of facial oedema will have to be borne in mind in their case.

The components of Melkersson's Syndrome

The main components of Melkersson's syndrome described to date are as follows:

(1) *Facial paralysis*

A lower motor neurone lesion of the seventh cranial nerve is the first sign to appear. It is usually a moderate initial paresis occurring most commonly during the second decade of life, but ranging from the 8th to the 25th year (Ekbohm, 1950). Recurrences of the palsy affecting the same or opposite side are a distinctive feature of this disease, and occasionally paralysis can be complete and permanent. The sequence of events

is well illustrated in one family (Scott, 1964), three members of which developed facial paralysis in the first instance at the ages of 15, 12 and 10 years, respectively. In the following 7 years they shared between them eleven further episodes of facial palsy. For the eldest girl these attacks ceased when both nerves were irreparably paralysed. Presumably for the others the prospect of further attacks still remains. All three of these patients possessed scrotal tongues, so it is difficult to dissociate the apparent vulnerability of the cranial nerve from the congenital abnormality. In a young person presenting with a facial paresis optimism in prognosis should be tempered with caution especially if a plicated tongue is also present, and family history, always important, is particularly so in such cases.

(2) *Lingua plicata*

The lingual abnormality is said to be the least constant sign of the syndrome, occurring in a quarter of the cases (Aukland, 1958) as compared with 0.25% in the general population (Prinz & Greenbaum, 1935). In the largest series collected (Schuppner, 1956) lingua plicata was found in seven out of twenty-one, with some degree of

furrowing in all. Of nine cases seen by the writer seven exhibited typical scrotal tongues marked in degree. In addition the mother of three of these possessed similar plication, though without accompanying stigma, so the figure of 0.25% above may possibly include formes frustes of this syndrome. The tongue is usually beefy in appearance, rough, sometimes scalloped and deeply fissured. The organ is physically normal so demands direct inspection if the peculiar pattern is not to be overlooked. Should such a tongue be noted in the absence of a neurological lesion specific enquiry should be made about previous seventh nerve palsies, as long past or transient lesions may not have occasioned lasting attention. It is equally important to enquire about similar lesions and episodes of facial oedema in the patient's siblings. If palsy and/or facial oedema has not yet occurred in the presence of a scrotal tongue, such possibilities are to be entertained in the future.

(3) *Facial oedema*

As a rule facial paresis precedes the first attack of oedema by a few months, but the latter may be delayed, rarely up to 25 years (Klaus & Brunsting, 1959), and an even longer period has been recorded (Evans, 1965) when 50 years elapsed between the first of several facial pareses and an attack of lymphoedema which affected the lower lip of a 63-year-old female. These swellings are remarkable for two things, a tendency to recur and the rapidity of their development. The tumescence may reach a maximum in a matter of hours. The patient can awaken with a markedly swollen lip that has developed during sleep. Each succeeding attack leaves the affected part thicker than previously, leading to eventual disfiguration. The swelling is said to limit itself to the facial tissues, lips, cheeks and scalp. It may be accompanied by pyrexia and constitutional symptoms of varying degree of severity. A significant proportion suffer from migrainous headaches during these 'explosions' (Cairns, 1961; Rossolimo, 1901; Stevens, 1965), and premenstrual exacerbation of the headaches has been described (New & Kirch, 1933; Scott, 1964); in one girl the right upper lip regularly became swollen prior to menses, at which times the hemicrania was so intense that recumbency for several days was unavoidable. Her symptoms and the pyrexia were relieved by a broad-spectrum antibiotic, so it was tempting to think of the presence of an infective agent or an infective overlay. The pathology on tissue biopsy is a non-specific inflammatory reaction with round-cell infiltration. Again an unexplained

brawny swelling of facial tissues, particularly in a young person, should prompt an examination of the tongue for plication, with specific enquiry about previous facial palsies in the patient or his siblings. Awareness of such a link is necessary for the diagnosis.

Discussion

The causative agent is usually apparent when the facial nerve is damaged by trauma or neoplasm, and if involved by an inflammatory process or a virus infection such as poliomyelitis or herpes zoster, associated findings facilitate the diagnosis. Toxic injury, e.g. lead poisoning, alcohol, or diphtheria, is now uncommon; even then distinguishing features are seldom absent. In leprosy facial palsy is so frequently a concomitant that it suggests the diagnosis in an endemic area. In fifty-nine cases of leprosy motor facial paralysis was noted in forty-two (Monrad-Krohn, 1923). When sarcoidosis involves the nervous system the facial nerve is often involved, and has been described in fifty-eight out of 115 such cases (Colover, 1948), but again attention is unlikely to be distracted from the parent multi-system disease. Similarly, little difficulty is experienced where facial paralysis is an early manifestation of disseminated sclerosis. However, it remains to be admitted that these and other instances where the cause is known, are numerically scanty compared with that large group of so-called 'idiopathic' facial paralyses described by Bell (1844) and named after him, about which a voluminous literature has accumulated since the mid-nineteenth century with little appreciable clarification of the aetiological background. It would appear that cases of Melkersson's syndrome which occur in this country are being included in this group because it is not realized that the facial paralysis of that entity is but one of several facets of a more generalized disorder.

In the absence of precise knowledge about the precipitating cause of 'Bell's palsy' theories about the causation abound, e.g. 'autonomic dysfunction' (Hilger, 1949; Kettel, 1959), 'selective tissue hypersensitivity' (Symonds, 1958) 'primary vascular ischaemia' (Cairns, 1961). The last is in doubt because of the complex intrinsic and extrinsic vascular arrangements which exist in and around the nerve (Blunt, 1954). The sheath of the facial nerve begins below the geniculate ganglion and is continuous with the periosteum of the canal on the one hand and the perineurium on the other. As it descends the aqueduct it increases in thickness and strength which reaches a maximum in density and tough-

ness as it approaches the stylomastoid foramen. When the Fallopian canal is explored for compression and the facial sheath slit, the nerve laterally herniates through the incision (Ballance & Duel, 1932; Morris, 1938; Cawthorne, 1951; Kettel, 1947; Sullivan & Smith, 1950), and is seen to be markedly congested and swollen to twice its normal size (Hall, 1951). This process is particularly marked in the lower third of the canal. This tough sheath envelops not only the nerve but also the rich arterial arcade from which its blood supply is derived. It would appear that the role of the Fallopian canal in facial paralysis is a secondary mechanical one, superimposing adverse pressure effects with consequent ischaemia upon an already existing neurological injury, only when the nerve swells to a size that can no longer be accommodated comfortably in such a restricted and unresilient channel. The bone around the stylomastoid foramen, and that of the mastoid itself, share in the pathological changes, and at operation softening is seen in this area, which particularly affects the tip of the mastoid process and its air cells (Kettel, 1947; Flodgren, 1946; Hall, 1951). This softening is likely to be a bony necrosis due to ischaemia, since a stem vessel from the stylomastoid artery enters the foramen, and branches from it pass through the posterior wall to supply the air cells of the mastoid process. These branches will suffer compression if the nerve is swollen. The nerve as well as the sheath is involved in an inflammatory reaction as it passes the bony portion of the Fallopian aqueduct (Rothlander, 1953; Hall, 1951), and in severe cases peripheral atrophy occurs. The actual agent which causes the nerve to swell and initiate the above chain of events is yet a matter for conjecture.

It is an accepted fact that pulmonary damage can be caused by precipitins formed when antigens enter an apparently normal respiratory tract, as in farmer's lung and various asthmatic states, and the likelihood is enhanced in the presence of congenital abnormalities in the lung structure. It is suspected that disease processes may be similarly caused by the transit of antigens through an apparently normal alimentary wall, and ulcerative colitis may be an example of an autoimmune process. Perhaps it is significant that the chorda tympani conveys taste fibres from the ipsilateral half of the tongue, and also secreto-motor fibres to the submandibular and sublingual glands, which were markedly enlarged in one case seen. The cell bodies of these afferent fibres lie in the geniculate ganglion of the facial nerve in the medial wall of the attic

in the middle ear. In the series of cases of Melkersson's syndrome described here lingua plicata of marked degree was a feature in eight of the nine instances. In the presence of such a tongue the facial nerve is at risk, not only singly but bilaterally, and there is a high incidence of recurrent palsy as well. There is a possibility that the neurological lesion may be an ascending one; whether the affection be due to a 'toxic, infective, antigenic, or autoimmune' process, remains to be elucidated, and to this end it must help if more of these cases were discovered and their associations recorded.

Virus studies in Melkersson's syndrome have produced negative results, but such investigations continue to be necessary, as some cases of facial palsy have been attributed to infection by the ECHO virus (Dick, 1958). The significance of the aminoaciduria in the two cases described has yet to be fully assessed. It may be a casual coincident finding suggesting further congenital weakness, but due to the ever-widening field of manifestations associated with the aminoacidurias (Soupart, 1962), screening will be necessary when further cases present.

Treatment with systemic steroids did not influence the course or the severity of the paralysis or the facial oedema in those cases of the syndrome in which it was tried. Good results have been claimed for cortisone in six out of seven cases of 'Bell's palsy' (Rothlander, 1953), but this is a small series in a condition which has such a high spontaneous recovery rate, although the impression given was that the return to normality was greatly accelerated when the steroid was given early. Others have not found cortisone of proven value (Taverner, 1959). Recently encouraging results have been recorded (Taverner, Kemble & Cohen, 1967) when ACTH gel was employed, which is in peculiar contradistinction to the doubtful benefits obtained by the use of cortisone. The cases selected for treatment followed assessment of their threshold to anodal galvanic stimulation by electrogustometry. This eliminated neurapraxic cases likely to recover spontaneously, and selected those palsies which were at denervation risk only. The results suggest that the hormone is of definite value given early in 'Bell's palsy'.

The exact type of onset in the three elder patients in this series (Table 1) was obscure due to the passage of time. In the six younger patients it is reasonably certain that the presenting signs and symptoms were the initial manifestations of the syndrome. It is interesting to note that the illness began with a sharp pyrexial episode, which subsided, and that a latent period of up

to 2 or 3 weeks elapsed before facial paresis became apparent, while the other associations described indicate that the neurological lesion is only part of a more general affection. It is perhaps an oversimplification to state as many textbooks do, that Melkersson's syndrome is an infrequent variant of Bell's palsy, although the pathological lesion in the nerve is similar in both (Bailey, 1960).

Conclusion

The salient features of Melkersson's syndrome are presented together with some original associations. There is reason to believe that the incidence of this entity is not less here than in those European countries where there has been a recorded interest in it for a long time (Melkersson, 1928; Kettel, 1947; Ekbom, 1950; Schupner, 1956). Awareness of its existence and correlation of the features mentioned will increase the incidence of observation, which will be enhanced if all facial pareses, particularly in the younger age-groups, are considered as potential examples of the syndrome, and only designated as 'Bell's palsy' after inspection of the tongue, and careful investigation of the personal history and that of the siblings. It is again stressed that unexplained swelling of the face should initiate the same train of thought as would a facial paralysis or a scrotal tongue.

Figs. 1 and 2 are typical examples of lingua plicata.

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