

HEAD AND NECK

Recurrent Bell's palsy: outcomes and correlation with clinical comorbidities

Paralisi di Bell recidivanti: risultati clinici e correlazione con comorbidità

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SUMMARY

Recurrent Bell's palsy (RBP) has been reported to range from 2.6 to 15.2% of primary Bell's palsy (BP) and has been associated with systemic comorbidities such as diabetes and hypertension. A retrospective analysis of patients affected by BP and RBP were performed to define the signs and symptoms associated with recurrence and the outcomes. Clinical and subjective characteristics of 341 patients affected by facial palsy were analysed. Facial function was assessed via House-Brackmann and Sunnybrook grading system. Characteristics of the palsy and systemic comorbidities (diabetes, hypertension, herpetic infections, autoimmunity disorders, audio-vestibular symptoms) were analysed in BP and RBP patients applying Fisher exact and the Mann-Whitney U tests, while time to recovery was explored with univariate and multivariate analysis. Twenty-four patients presented two or more episodes of facial palsy, representing a recurrence rate of 7%. Associated symptoms (e.g. retroauricular pain, taste disorder, dry eye etc.) were similar between BP and RBP patients. RBP occurred at older age than primary episode ($p = 0.03$). Recurrence was a risk factor for delayed recovery ($p = 0.02$), although final facial function was similar between the two groups. In conclusion, no significant differences were found between primary BP patients and RBP patients in terms of symptoms, palsy severity and presence of comorbidities. Delayed facial nerve function recovery in RBP did not affect the final outcome. Treatment of facial nerve recurrences must be the same of the primary episode, although the presence of prodromal symptoms may alert the patient and early corticosteroid treatment may be commenced even before the onset of paresis.

KEY WORDS: Recurrent • Alternating • Bell's palsy • Facial paralysis • Outcomes

RIASSUNTO

Dati di letteratura riportano che una recidiva di paralisi di Bell (RBP) si presenta nel 2,6-15,2% dei pazienti che hanno già sviluppato in precedenza una paralisi di Bell (BP); la RBP è stata associata a comorbidità come diabete e ipertensione. Questo studio riporta un'analisi retrospettiva dei pazienti affetti da BP e RBP per definire i segni e i sintomi associati alla recidiva e i risultati clinici a lungo termine. Sono state analizzate le caratteristiche cliniche e soggettive di 341 pazienti affetti da paralisi facciale. La funzione facciale è stata valutata tramite il sistema di classificazione House-Brackmann e Sunnybrook. Le caratteristiche della paralisi e delle comorbidità sistemiche (diabete, ipertensione, infezioni erpetiche, disordini autoimmuni, sintomi audio-vestibolari) sono state analizzate nei pazienti con BP e RBP con i test di Fisher Exact e Mann-Whitney U, mentre il tempo di recupero è stato esplorato tramite analisi statistica univariata e multivariata. Ventiquattro pazienti (7%) hanno presentato una paralisi recidivante. La prevalenza e tipologia dei sintomi associati (ad esempio dolore retroauricolare, disturbi del gusto, secchezza oculare ecc.) erano simili tra i pazienti con BP e RBP. I pazienti con recidiva di paresi risultavano più anziani dei pazienti con paralisi primaria ($p = 0,03$), mentre i due gruppi non differivano in termini di sesso, gravità della paralisi e presenza di comorbidità. La recidiva è risultata essere un fattore di rischio per un recupero tardivo ($p = 0,02$), sebbene la funzione facciale finale fosse simile tra i due gruppi. In conclusione, non sono state riscontrate differenze significative tra i pazienti con BP primaria e quelli con BP recidivante in termini di sintomi, gravità della paralisi e presenza di comorbidità. Il recupero ritardato della funzione del nervo facciale in RBP non influenzava l'esito finale. Il trattamento delle recidive del nervo facciale deve essere trattato con le stesse modalità dell'episodio primario, tuttavia la presenza di sintomi prodromici può allertare il paziente e un trattamento precoce con corticosteroidi può essere iniziato anche prima dell'esordio della paresi.

PAROLE CHIAVE: Ricorrente • Recidivante • Paralisi di Bell • Paralisi facciale • Risultati

Introduction

The sudden onset of facial palsy is most commonly due to stroke or Bell's palsy (BP). BP is the most frequent form of peripheral palsy of the facial nerve and represents about 60% of all aetiologies, with a diversely reported annual incidence between 8 and 52.8 new cases per 100,000 individuals¹⁻³. It is believed that reactivation of Herpes viruses in the endoneurium of the geniculate ganglion can play a role in the onset of peripheral idiopathic facial nerve palsy⁴⁻⁶, but the aetiology is not yet completely defined. Medical treatment is based on high-dose of corticosteroids and antiviral agents, even if there is limited evidence of the efficacy of the latter^{7,8}.

Recurrent Bell's palsy (RBP), either ipsilateral or contralateral to the side affected in the primary episode, is a relatively rare disease. The incidence of recurrent facial palsy has been reported to range from 2.6 to 15.2 % of patients who already had a primary episode⁹⁻¹⁷. It was first reported to occur by Devriese and Peltz¹⁰, who first identified alternating or recurrent palsies as those recurrences that affect the contralateral or ipsilateral facial nerve.

The data regarding prognosis of RBP, when compared to primary BP, are conflicting, partly because classification of degree of palsy is not uniform across studies. It is, therefore, not clear whether the pathogenetic mechanisms underlying RBP are the same as BP, and consequently if the therapeutic approaches should be different.

In the present study, subjects presenting with recurrent facial palsy were selected from all patients presenting with unilateral idiopathic facial palsy visited in a tertiary referral centre; the clinical characteristics and prognosis of patients with primary and recurrent BP were compared to define the signs and symptoms associated with recurrence and prognosis of outcomes.

Materials and methods

Subjects

This study was designed as a retrospective cohort study on subjects treated at Policlinico Umberto I University Hospital of Rome, between May 2010 and March 2018. The protocol was approved by the ethics committee of the University (authorisation number # 29-05-08/1432) and written informed consent was administered to each patient before commencing any study-related procedure. In order to obtain a homogeneous cohort of subjects, the eligibility criteria were: age 14 to 89 years;

unilateral Bell's Palsy diagnosed by clinical ENT and neurological assessment; treatment within 48 hours after the onset of the initial symptoms of BP; standardised oral pharmacological treatment with prednisone 1 mg/kg for 10 days plus valacyclovir 500 mg TID for 6 days. Exclusions criteria included: pregnancy; palsy due to metabolic, neurological, infective, neoplastic, toxic or iatrogenic disease; traumatic injury to the facial nerve, VZV infection (Ramsay-Hunt syndrome), Melkersson-Rosenthal syndrome.

Study procedures

Two routinely scale systems were used to assess the facial palsy severity in the clinical practice: the House-Brackmann facial grading (HB) scale¹⁸ and the Sunnbrook facial (SB) grading system¹⁹. The HB scale measures the global degree of paresis/paralysis, ranging from grade I (normal function) to VI (complete paralysis). It was chosen for its simplicity of assessment, most frequent use and robustness. Nevertheless, this scale lacks accuracy on synkinesis and regional asymmetry; therefore, the SB scale system, with a score ranging from 0 to 100, was added as it provides regional scores at rest and motion also in addition to accurate information on synkinesis.

Each patient was evaluated at his/her first visit and 10 days - 1, 3, 6 months post onset. Patients were interviewed to gather information on diabetes, hypertension, previous herpetic infections, systemic infections, autoimmunity disorders, audio-vestibular symptoms and family history of facial palsy. For the palsy itself, information about the presence and side of recurrence and time lapse between episodes, and all associated symptoms, were collected.

Patients who at first examination had HB \geq IV or who had no improvements to HB II-III grade after 10 days underwent the following: brain MRI with gadolinium, audiometric and impedance tests, and electrophysiological tests (electromyography, electroneurography and blink reflex). Furthermore, patients with HB grade $>$ IV, who did not show improvement at the second clinical assessment and were negative for secondary palsy, were referred to physical rehabilitation²⁰.

Statistical analysis

Data are presented as proportion and mean \pm standard deviation or median (interval), as appropriate. Differences between patients with BP and RBP were tested by Fisher's exact test and Mann-Whitney U test for categorical and continuous variables, respectively. Time to recovery was explored with univariate (Log-Rank

test) time-to-event analyses. To further verify if the time to recovery was truly different in patients with BP and RBP, we ran a Cox proportional hazards regression model in a stepwise fashion to obtain hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). The main time variable was defined as the period (days) elapsed from palsy onset and the last available visit or outcome reached (i.e. recovery to a HB equal or less than grade II). Demographic and clinical variables were included Aa covariates of interest: sex, age, HB and SB grades (entered as multilevel variable), first BP or RBP episode, familial history and presence or absence and type of comorbidity (hypertension, diabetes, audio-vestibular symptoms, autoimmunity, herpetic infections). Two-tailed p -values < 0.05 were considered as significant, without correction for multiple comparisons considering the exploratory nature of the present study. Data were analysed using the Statistical Package for Social Sciences, version 16.0 (IBM SPSS Inc., Chicago, Ill., USA).

Results

A total of 341 patients (198 men, 143 women, mean age 50.2 ± 17.9 years, range: 14 to 89) attended the Emergency Department due to BP from May 2010 to March 2018.

Of these 341 patients, 30 were lost to follow-up and 22 had incomplete data collection, and we thus analysed the data of 289 patients. The mean HB grade

was 3.7 ± 1.07 , the Sunnybrook score was 40.7 ± 20.8 . Twenty-four patients (7.0%) had a RBP. All patients with RBP were included in the analysis with exception of one patient at his third episode of facial palsy with clinical characteristics of Melkersson-Rosenthal syndrome (oedema of the lips, lingua plicata and relapsing facial palsy). Table I shows the characteristics of patients according to either a first BP episode ($n = 265$) or RBP ($n = 24$). Patients with RBP were older than the other patients ($p = 0.03$). The two groups did not differ in terms of sex, BP severity (HB and SB), or presence of comorbidities.

Eleven patients presented the palsy on their right side, and 13 on their left side. In RBP subjects, the median time from the previous episode was 6 years (interval: 2-33); the paresis involved the ipsilateral and contralateral side in 12 and 7 cases, respectively, while the remaining 5 cases were not able to report the previously affected side. The time elapsed from the previous BP episode and the previously affected side (ipsilateral or contralateral) did not influence the outcome. Interestingly, we found that patients with recurrent BP in the contralateral side were more likely to have hypertension (6 of 7) than those presenting a further ipsilateral BP episode (1 of 12) ($p = 0.02$) in the absence of other significant differences. Nevertheless, we do not think that this finding has a clinical correlation.

Considering the symptoms associated at onset of paresis among patients affected by RBP, 10 presented retroauricular pain, 4 dysgeusia, 4 dry eye, 4 hyperlacrimation and 3 patients had dry mouth; these symptoms were present alone or in combination. All the patients except one were at their second palsy; 15 palsies were ipsilateral and 8 contralateral. The patient affected by Melkersson-Rosenthal syndrome already presented 1 palsy on his left side and 3 on the right side. Five patients reported a family history of BP. Three patients, already treated in our clinic for BP, came to our observation with prodromal symptoms (retroauricular pain, dry eye, dysgeusia) before the onset of paresis that occurred within the next following days²¹.

A total of 224 patients (78%) recovered from BP after a mean time of 63.4 days (interval: 2 to 357), while the remaining 65 (22%) did not completely recover after 6 months of follow-up.

Figure 1 shows the Kaplan-Meier curve displaying time to recovery from BP according to study group (first BP episode versus recurrent BP). Patients with first BP episode recovered faster than those with RBP ($p = 0.04$ by the Log-Rank test). No difference in terms of final facial function was found between the two groups.

Table I. Main characteristics of study sample ($n = 289$) according to the presence of a first BP episode or a recurrent BP.

	First BP episode	Recurrent BP	P-value
N	265	24	-
Gender (female:male)	113:152	10:14	1.00
Age, years	49.4 ± 18.1	57.2 ± 14.0	0.03
HB score	3.95 ± 0.65	3.83 ± 0.92	0.68
SB score	40.7 ± 21	40.4 ± 20.2	0.60
Presence of comorbidity	186	19	0.48
Hypertension	83	11	0.17
Diabetes	28	5	0.17
Autoimmunity disease	18	0	0.38
Infectious disease	5	2	0.11
Audio-vestibular abnormal	37	4	0.76
Herpes virus infection	108	12	0.39
Familial history of BP	27 (10%)	5 (20%)	0.16
Follow-up, days	60 ± 58	70 ± 59	0.34

Values are presented as means \pm SD or N as appropriated. Significant values are in bold. BP: Bell palsy; HB: House-Brackmann.

Table II. Cox regression model (stepwise fashion) showing variables predictive for BP recovery.

	N	HR	95% CIs	p
HB grade				
III	117	1.00	-	-
IV	85	0.61	0.42-0.88	0.01
V or VI	87	0.42	0.29-0.60	< 0.001
First BP episode	265	1.00	-	-
Recurrent BP	24	0.52	0.29-0.91	0.02

HR < 1.0 indicates a greater risk of not recovering from BP. Significant values in bold. BP: Bell palsy; HB: House-Brackmann; HR: hazard ratio; 95% CIs: 95% confidence intervals.

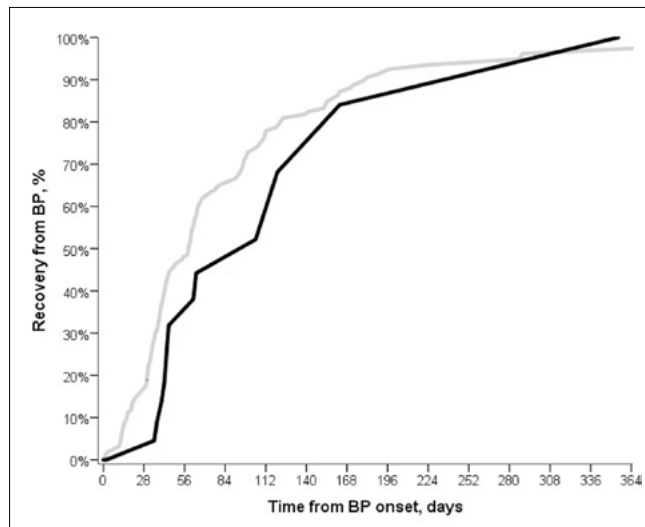


Fig. 1. Kaplan-Meier curve showing the time to Bell's Palsy recovery in patients with a first episode (BP) (n = 265; grey line) and in those with recurrence (RBP) (n = 24; black line).

Findings from the Cox regression model are shown in Table II. As expected, higher HB grades were associated with delayed recovery (HR: 1.00 for grade III, 0.61 for grade IV, 0.42 for grade V or VI; $p < 0.001$). Also, RBP was a risk factor for delayed recovery (HR: 0.52; $p = 0.02$). The remaining clinical variables, including sex, age and comorbidities, did not contribute to fit the model.

Discussion

Recurrence of peripheral facial palsy is well known and has been reported by several studies; physicians and rehabilitation therapists should inform patients presenting with a primary episode that recurrence may occur even after several years. In the present study, 24 of 289 patients (7%) developed a second episode of facial palsy, a percentage that is in accordance with data

present in the literature⁹⁻¹⁷. Although RBP has been associated with systemic comorbidities such as diabetes and hypertension^{9 10 22-25}, our results did not show such a correlation. Findings in the literature are often discordant as far as correlation of comorbidities with severity of outcomes, mainly due to composition and homogeneity of study groups, follow-up times and differences in classification of severity of palsy.

Many studies have addressed the incidence of recurrence with respect to the side, ipsilateral or contralateral. Ralli et al.¹⁴ found an increased incidence in the contralateral side compared to the ipsilateral side, while Navarrete et al.²² found a major incidence on the right side, regardless if ipsilateral or contralateral. Almost all studies agree in judging ipsilateral RBP as being worst in terms of long-term prognosis. Nevertheless, no clear follow-up timing has been established, and clinical evaluation of degree of palsy and systematic statistical approaches have been used. In their study, Ralli et al.¹⁴ evaluated 35 patients with recurrent unilateral BP. The incidence of recurrence was higher in younger patients, with a poorer prognosis for palsies occurring on the same side of the primary episode. Similarly, Navarrete et al.²² found worse recovery in patients where recurrence occurred ipsilaterally to the primary episode. On the contrary, Cirpaciuc and coauthors¹³ did not find differences in the recurrence rate between RBP presenting in the ipsilateral or contralateral side respect to the primary BP. The authors reported a prevalence of incidence in young females (68% of the cases), in subjects with age between 21 and 30 years and with a family history of multiple episodes of RBP. In our study, a family history of BP was present in 5 patients (20%) suggesting a genetic predisposition for this pathology. Indeed, some studies found an association of certain human leukocyte antigens (HLAs) with the palsy, although these findings were not confirmed by other studies^{26 27}.

The association between recurrent facial palsy and diabetes mellitus has been reported with an incidence between 5.6% and 28.6%^{10 11 15 23 25}. However, other authors have found no difference in diabetes incidence between primary and recurrent BP⁹.

The study of Chung et al.⁹ analysed the differences between primary and recurrent BP as far as the role of degree of palsy, side and comorbidities over palsy prognosis. The authors have studied a large population (1,257 subjects) affected by BP correlating the degree of palsy, assessed via House-Brackmann classification, electrophysiologic tests and MRI. In their study, the incidence of RBP was 5.7%. The study group was

homogeneous as far as treatment with steroids and antivirals, and outcomes were evaluated after a minimum of 6 months follow-up. The rate of recovery for BP was significantly higher (88.4%) than RBP (72.2%). Interestingly, while diabetes did not seem to influence incidence of RBP, recurrence was significantly higher in subjects who were pregnant or affected by hypertension, although these factors were no longer significant after logistic regression analysis.

Some studies have shown that the peak of incidence was in a younger age^{10 13 14 23} and described women as most susceptible to recurrence (68%)¹³. In the present study, a higher incidence was found in elderly patients, which is probably was due to a time factor that increased the probability to develop a second episode of paresis. Moreover, in our study, synkinesis did not seem to have higher prevalence in RBP. One possible reason is that synkinesis was found to have a prevalence at a younger age²⁸, due to functional and structural changes related to aging that reduce recovery of the peripheral nervous system after injury.

No difference was found between BP and RBP concerning SB score and HB grade as far as palsy severity, although in the Kaplan-Meier analysis primary BP showed a significant faster recovery.

As far as RBP characteristics are concerned, time elapsed from the previous palsy episode did not differ between ipsilateral and contralateral presentation. Concerning symptoms associated with paresis, their distribution was not significantly different between the two groups. Nevertheless, the previous experience of a primary BP episode led 3 of our patients to attend our facial palsy centre before onset of the paresis when only retroauricular pain and taste disorder were present, which allowed us to begin corticosteroid treatment in the very early stage of the paresis.

In the present study, no significant difference was found between the incidence of RBP in ipsilateral or contralateral recurrence, although there was a mild prevalence for the ipsilateral side.

Recurrence and higher HB grades were risk factors for delayed recovery, confirming the findings of Chung and al.⁹. Patients with primary BP recovered faster than patients with RBP ($p = 0.05$). Nevertheless, despite the delayed recovery in RBP, no difference was found in final facial function. Other studies found different recovery rates between the two groups^{9 10 15}, possibly because of the presence of other confounding factors such as incidence of comorbidities and differences in therapeutic approaches.

Conclusions

In conclusion, no significant difference in terms of symptoms, palsy severity and presence of comorbidities was found between primary BP patients and RBP patients. Final facial nerve function, even if delayed in recurrences, was similar in the two groups. The management of a recurrent facial palsy must be the same as the primary episode; nevertheless, the presence of prodromal symptoms may alert the patient to go to emergency department, allowing the beginning of corticosteroid treatment in the very early stage of the paresis.

Conflict of interest statement

None declared.

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