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Paroxysmal Positional Vertigo: The Role of Possible Vascular Factors in Etiology

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OBJECTIVE: The aim of this work is to examine the influence of vascular damage on several clinical aspects of paroxysmal positional vertigo.

MATERIALS AND METHODS: A retrospective study was conducted on 536 consecutive patients with paroxysmal positional vertigo. Various factors associated with vascular risk or clear vascular damage were taken into consideration: hypertension, diabetes, hypercholesterolemia, cerebrovascular disease, and ischemic heart disease. Patients were divided into group A (patients with 2 or more vascular factors) and group B (patients without vascular factors or with only 1 vascular factor). The following clinical parameters of paroxysmal positional vertigo were evaluated: recovery time, nystagmus, relapse, and trend of the active phase. The latter involved a form of paroxysmal positional vertigo characterized by immediate negativization of the objective picture with the first rehabilitative maneuver and a return to positivity at the next follow-up visit. We defined the patients in which the clinical behavior was repeated for at least 3 successive sessions as type 1M (maneuver) _ 3S (sessions) paroxysmal positional vertigo.

RESULTS: A comparison (group A vs group B) showed a statistically significant increase (P = .001) in the recovery time of vascular patients (group A), who had a mean number of 3.81 (± 2.75) maneuvers to negativize the clinical picture, as opposed to the mean of 2.44 (± 1.72) for group B. The incidence of atypical nystagmus was 13.6% in group A and 5.4% in group B. The rate of type 1M _ 3S paroxysmal positional vertigo was 25.4% in group A and 6.2% in group B.

CONCLUSIONS: Because they affect recovery time, the vascular factors discussed here represent negative elements for the prognosis of the disorder. The frequency of atypical oculomotor patterns leads us to consider other pathogenetic mechanisms aside from lithiasis, as well as the possibility of central vestibulo-ocular reflex distress.

Though much is known about the pathogenetic mechanisms that involve the canal and cupula and that come into play in paroxysmal positional vertigo (PPV), the etiology of this disorder continues to be particularly vague, despite the numerous studies reported in the literature. Of all the etiologies that are considered, trauma is unquestionably one of the most frequent (from 10% to 30%).[1-3] In fact, in many cases it is possible to identify a cause-and-effect relationship when there is a plausible timeframe between the trauma and the onset of the symptoms of vertigo. Numerous other theories have been posited, such as degeneration of the utricular macula,[4] vertebrobasilar insufficiency,[5] deficiencies such as a lack of vitamin B12,[6] and inflammatory forms resulting from chronic or viral otitis.[7,8] Regarding the latter, recent studies have found the DNA of the herpes simplex type 1 virus in the vestibular ganglia and nuclei of subjects with acute peripheral disorders of the labyrinth.[9]

Regardless of the fact that some of the clinical cases described in this article could effectively cause or be associated with vascular occlusion, this condition must be strongly suspected in patients older than 50 years with a significant clinical history.[10] Anatomic and pathologic studies demonstrating degeneration of the macula and of Scarpa's ganglion[11] in PPV merely confirm the hypothesis whereby PPV can be symptomatic of vascular occlusion of the anterior vestibular artery.

PPV treatment relies on widely established methods that are effective in most cases. In clinical practice, however, there are often objective pictures whose interpretation is unclear. These cases, characterized by slow recovery time or failure to respond to treatment, are difficult to explain, given the fact that the same treatment techniques are used, with similar procedures and timing. Without calling into question the lithiasic pathogenesis of PPV, this clinical trend can be attributed to different events. First of all, there is the possibility of strong adherence of the otoconial mass to the ampullary crest (cupulolithiasis), making it somewhat resistant to mobilization and removal compared with a primary location in the canal (canalolithiasis). Second, there is the possibility of an atypical location in the canal, which would explain the onset of nystagmus with morphologic characteristics and timing that do not match what would commonly be expected. Moreover, the 2 vertical semicircular canals have numerous anatomic and functional interactions, so that an otoconial mass that moves inside them through the force of gravity may cause complex oculomotor responses that can be ambiguous. Last, it must be noted that there can be anatomic variations regarding the orientation of the semicircular canals, which would thus change the positioning standards for evoking the greatest response. Though there are many morphologic and functional factors that can interfere with the dynamics of the canal and cupula, none of the ones mentioned are documentable and thus ascribable as influencing the clinical picture of PPV. Alongside these factors, general ones must also be taken into account, as they can be involved in tissue or metabolic damage through various mechanisms. Of these, vascular factors unquestionably play a leading role, not only because of their frequency but also because of their potential to damage the organs and systems. Since their presence can be verified clinically, they lend themselves well to a qualitative study of PPV dealing with the etiopathogenesis and prognosis of this disorder.

Therefore, we conducted a retrospective study on a population of consecutive patients diagnosed with PPV and treated with physical therapy. The aim was to evaluate a series of parameters-clinical and objective ones as well as case history-in order to identify possible relationships between vascular damage, above all microangiopathic, and certain clinical aspects of PPV, particularly nystagmus, the trend of the active phase, relapse, and recovery time.

MATERIALS AND METHODS

The study involved a cohort of 536 patients with PPV (195 men, 341 women; mean age, 56.8 years), who were referred to our clinic between Jan 1, 2000, and Dec 31, 2002.

After we diagnosed the nature and site of PPV, we included the patients in a rehabilitation protocol that envisaged using Semont's liberatory maneuver as modified by Toupet,[12, 13] as well as the Epley canalith repositioning maneuver[14] in cases of PPV of the vertical semicircular canals. For forms of PPV of the lateral semicircular canal, Vanucchi's position,[15] Baloh's position,[16] and Gufoni's position[17] were used instead.

We focused on seeking elements in the clinical evaluation and medical history that could potentially be implicated as factors that promote and/or trigger the pathology.

For the purposes of our study, we considered in particular the noxae that can most commonly cause or be associated with vascular damage. These included hypertension treated with antihypertensive therapy; hyperglycemia treated with oral hypoglycemic agents or insulin; dyslipidemia (hypercholesterolemia, in particular), treated and untreated with total cholesterol levels exceeding 250 mg\dL; cerebrovascular disease documented via imaging and positive clinical neurologic findings (stroke, transient ischemic attack); and prior acute or chronic ischemic heart disease. Based on the presence of these factors, we considered 2 types of patients:

1. Group A: patients with 2 or more factors associated with the risk of or clear vascular damage and

2. Group B: patients with only 1 factor associated with the risk of or clear vascular damage, or without any of these factors.

The 2 groups showed no statistically significant differences (P = .1) in age (group A: mean age, 58.01 years ± 7.40; group B: mean age, 56.40 years ± 9.70).

Our study also analyzed numerous objective clinical parameters constituting the oculomotor pattern evoked by diagnostic positioning. Specifically, we evaluated the morphologic characteristics of nystagmus, such as its presence in one or more positionings; its inversion (or failure to invert) when returning from the triggering position; inverted nystagmus with respect to what would commonly be expected; and time-related aspects such as latency, duration, and paroxysmal level. Therefore, we examined PPV with a typical oculomotor pattern (typical morphologic parameters and/or timing) and PPV with atypical oculomotor patterns (atypical morphologic parameters and/or timing).

We evaluated recovery time expressed as the average number of maneuvers required to negativize the clinical picture; the data obtained in the patients of the 2 groups being examined were then compared.

We also evaluated the number of patients in whom the disorder returned starting in the second month after negativization of the clinical picture. Moreover, we decided to distinguish between relapse and recurrence, using "relapse" to refer to return of the disorder in the same location in the canal and "recurrence" to define PPV at a different location from the first treated episode.

Last, the study involved quantitative and qualitative analysis of a particular form of PPV. The active phase is characterized by immediate negativization of the objective picture with the first rehabilitative maneuver and return to positivity at the next follow-up visit, scheduled 2 to 3 days after the previous session. We defined the cases in which this clinical behavior was repeated for at least 3 successive sessions as type 1M (maneuver) x 3S (sessions) PPV.

RESULTS

Of the 536 patients, we observed for PPV, 6 were excluded from our analysis as they never negativized, despite all the therapeutic measures that were undertaken. In one patient, we observed a severe neurologic disorder. Therefore, 530 patients completed the rehabilitation protocol and were thus considered cured.

Among the clinical/laboratory pictures we considered, arterial hypertension (treated) was the most frequent pathology, observed in 191 patients. Hyperglycemia (treated) was found in 46 patients, and 62 patients had hypercholesterolemia. Ischemic heart disease was observed in 39 patients, and 21 patients had cerebrovascular disease. A total of 110 patients were included in group A (20.75%); of these, 20 had 3 or more vascular factors. There were 420 patients in group B (79.25%), 136 of whom had only 1 vascular factor and 284 of whom had no vascular factors whatsoever.

On average, 2.70 (± 2.10) maneuvers were required to negativize the clinical picture. The patients in group A with 2 vascular factors (90) had mean maneuvers of 3.63 (± 1.92); within this group, the patients with 3 or more vascular factors required a mean of 4.65 (± 1.70) maneuvers. A comparison (group A vs group B) showed a statistically significant increase (P = .001) in the recovery time of vascular patients (group A), who required a mean number of 3.81 (± 2.75) maneuvers to negativize the clinical picture, as opposed to the mean of 2.44 (± 1.72) for nonvascular patients (group B; Figure 1). Within group B, there was no statistically significant difference (P > .05) among patients with just 1 vascular factor (mean 2.50) and those without any vascular factors (mean 2.40).

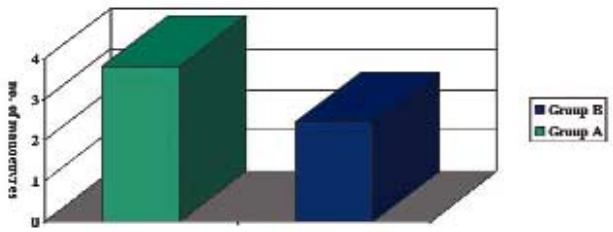

Figure 1: Mean number of maneuvers required to negativize the clinical picture.

PPV presented an atypical oculomotor pattern in 58 of the 530 patients we examined. Atypicality involved only morphologic parameters in 20 patients, but in 8 patients, it involved both the morphologic pattern and timing; in 30 patients with a normal morphologic pattern, timing of nystagmus was altered. Overall, an atypical time pattern was observed in 38 patients, 15 of whom were from group A. Therefore, this group had a 13.6% rate of atypical nystagmus (15\110), whereas the same calculation performed in relation to the patients in group B reflected a rate of 5.4 % (23\420; Figure 2).

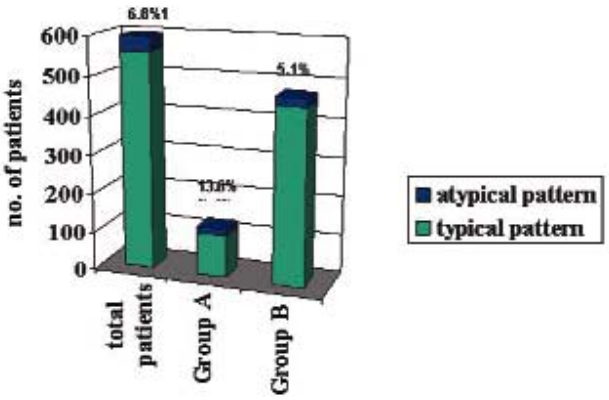

Figure 2: Rate of atypical nystagmus

Thirty-five patients relapsed starting in the second month after negativization of the clinical picture; 2 of these were from group A. Twenty-one patients had recurrence, and 13 of them were from group A. In short, of the 530 patients who took part in the rehabilitation protocol, 56 (10.5%) had a clinical return of the disorder 2 months following recovery, and 15 of them had at least 2 vascular factors. The overall rate was 13.6% (15\110) among patients from group A, as opposed to the rate of 9.7% (41\420) recorded for group B. The rate of relapse and recurrence was respectively 6.6% (35\530) and 3.9% (21\530). In the first case, a comparison between the 2 groups (group A vs group B) showed a rate of relapse of 1.8% (2\110) in group A and of 7.8% (33\420) in group B, whereas the recurrence rates in these groups were respectively 11.8% (13\110) and 1.9% (8\420) respectively (Table).

Type 1M x 3S PPV was observed in 54 (10.2%) of the 530 patients who underwent rehabilitation. Of the 54 patients, more than half (28) came from group A. The rate of type 1Mx 3S PPV in this group of patients was 25.4% (28\110), as opposed to 6.2% (26\420) in group B (Figure 3).

Table. Rate of relapse and recurrence

	Patients (n)	Return of disorder (n)	Relapse (n)	Relapse rate	Recurrence (n)	Recurrence rate
Group A	110	15	2	1.8%	13	11.8%
Group B	420	41	33	7.8%	8	1.9%

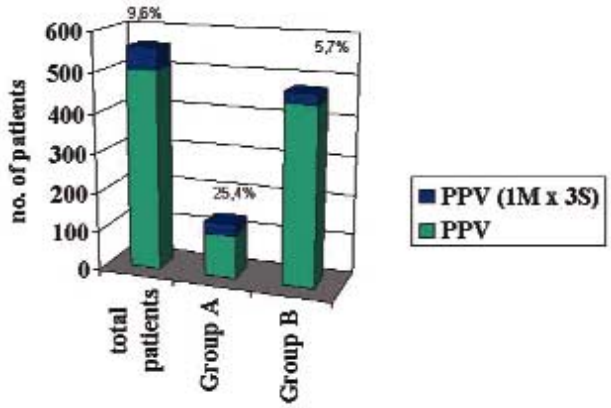

Figure 3: Rate of type 1M ¥ 3S PPV
M = maneuvers; S = sessions; PPV = paroxysmal positional vertigo.

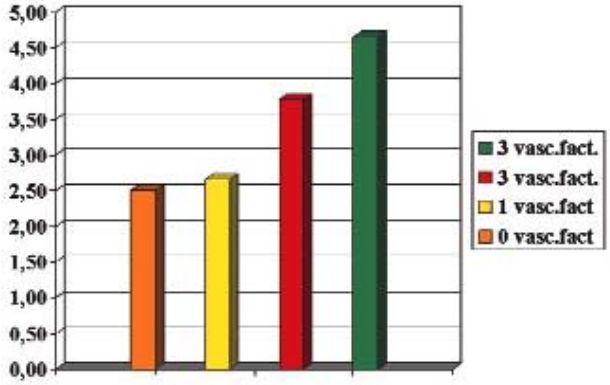

Figure 4: Mean number of maneuvers in relation to the number of vascular factors considered

DISCUSSION

PPV has high recovery rates, regardless of the maneuver used.[18] However, the presence of the vascular factors considered in our study seems to affect not only recovery times but, in some cases, recovery itself. Five of the 6 patients who did not respond to the various treatments were from group A.

The mean number of maneuvers required to negativize the clinical picture was statistically significant when the vascular factors discussed here were present (p=0.001). Moreover, the greater the level of vascular impairment, the more evident this was. In fact, this study shows a close correlation between the extent of hypothesized damage, based on the number of vascular factors and the clinical aspects of the disorder. Specifically, the presence of just 1 vascular factor did not significantly affect recovery time as compared with that of nonvascular patients. Inversely, the mean number of maneuvers required to negativize the clinical picture increased significantly and progressively as the number of vascular factors increased (Figure 4). Therefore, it seems that there must be a combination of several of the factors being examined here in order to trigger-at the anterior vestibular artery-circulatory stress that can cause macular damage extensive enough to influence recovery speed, through the detachment of larger otoconial masses that thus require a growing number of maneuvers in order to remove them.

Another significant element lies in the fact that, among vascular patients, we observed a higher incidence of the type of PPV we defined as type 1Mx 3S, based on the clinical behavior described above. In this case, the active phase of the disorder seems to be affected by persistent macular degeneration, leading to the slow and continuous-albeit not necessarily massive-detachment of otoliths. In turn, this causes build-up of otoconial masses in the canal that can easily be removed with liberating maneuvers. However, they rapidly reform due to continuous macular degeneration.

Understanding the meaning of the evoked oculomotor pattern is far more complex. Atypical morphologic parameters could be due to a different spatial orientation (anatomic variants) of the semicircular canals[19] or, more simply, to the atypical location of otoliths within the canals, particularly the vertical ones (nonampullary arm of the posterior semicircular canal and the ampullary and nonampullary arm of the anterior semicircular canal, common crus).[20] The transformation of PPV with these characteristics into typical form, or the negativization of the objective picture that has occurred in various cases after the triggering maneuver has been repeated, confirms this theory and can be explained by the mobilization of otoconial masses following movement of the head. Atypical patterns that also take the timing parameters of nystagmus into account can be noted in vestibular dysfunctions in various phases of compensation, in the postcritical phase of endolymphatic hydrops, and in

various types of brainstem disorders.[21] As a result, the observance of a higher rate of atypical timing in patients with several vascular risk factors may stem from the frequent association, documented in these cases, between PPV and pictures of vestibular hyporeflexia or areflexia. Likewise, imaging has shown ischemic foci in critical areas of the brainstem and cerebellum in many of our vascular patients, and this may explain the onset of atypical nystagmus.

We feel that, in all these cases, it is essential to consider the possibility of peripheral pathogenetic mechanisms other than lithiasis or of central mechanisms that can cause vestibulo-ocular reflex distress. Likewise, the indication for further neurologic exams is also valid for atypical oculomotor patterns, above all in relation to timing. In our study, an magnetic resonance imaging brain scan performed on a patient with these objective traits who had no vascular factors and did not respond to physical therapy revealed a brainstem tumor (astrocytoma) with cerebellar compression.

Last, this study demonstrated that PPV is a disorder with a high relapse rate, an observation that agrees with the literature.[22,23] In our experience, among patients with several vascular factors, we did not observe a significant increase in the overall return of disease with respect to the rest of the population. However, the study showed that, as opposed to relapse, recurrence increased significantly among the patients from group A. A possible explanation is that in relapse, the return of the disorder in the same location could be attributable to intrinsic morphologic problems in one of the semicircular canals (narrowing, dilatation, and dehiscence). This would lead to build-up of the otoconial mass in a specific part of the canal or to functional problems if an unassociated macular/canal dysfunction is responsible for a selective response of the inferior vestibular nerve (Lindsay-Hemenway syndrome).[24] Inversely, in recurrent PPV distinguished by different locations, the role of factors favoring a given canal seems conceptually less decisive from a pathogenetic standpoint. In this case, we can legitimately posit the influence of general factors such as vascular ones that through persistent ischemic states in the vertebrobasilar area lead to secondary distress of the neuroepithelial structures of the macula, which can be followed by detachments of the otoconial membrane. If the anatomic and functional factors already mentioned are not present, then the ensuing canalolithiasis is more likely to affect different canals. Moreover-and again, due to the presence of systemic factors-over time it can also affect the canals of the contralateral labyrinth.

To summarize, the etiology of PPV is still uncertain. PPV with a vascular etiology can be hypothesized, as has been observed with sudden hypacusia or acute vestibular dysfunction (vestibular neuronitis). In all these cases, the presence of the risk factors noted here represent negative elements for the prognosis of this disorder, which-in patients like these-can be considered expressions of problems involving the microcirculation of the labyrinth.

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