Introduction

Despite the clinical picture being extremely characteristic, cluster headache (CH) has been underestimated in the past. In most of the cases, the patients were diagnosed as being affected by other painful conditions such as trigeminal neuralgia, sinusitis and dental diseases.

The prevalence of cluster headache is still a controversial matter, both because the existing epidemiological studies had not been carried out on homogeneous population, and because the inclusion criteria and the personnel devoted to collecting clinical data and to recording methodology differed [1–4].

Only after the introduction of the classification of the International Headache Society (IHS) in 1988 [5] have more precise clinical criteria been available for this primary headache and more detailed epidemiological data have been obtained [6–10].
ber of new headache patients under 18 years of age attending for a period of 12 months. This was accompanied by an additional sheet in which the clinical history of the patients, the characteristics of the headache, the results of general and neurological examinations and the complementary investigations needed for the differential diagnosis were recorded. This sheet was structured to include any clinical characteristics which would allow the diagnosis of cluster headache to be made according to the IHS classification [5] and was completed when a case of CH was suspected.

Two semesters of recording were chosen: the first period lasted from 1 November 2000 to 30 April 2001; the second period was from 1 May 2001 to 31 October 2001. After these two periods of recording, the sheets for the recording of all examined patients and, in the case of suspicion of cluster headache, the clinical sheets of the patients were sent to the Reference Center of Perugia, where the diagnosis was reconfirmed according to the 1988 IHS criteria [5].

Results

We examined 6629 subjects under 18 years of age suffering from headache and attending for the first time one of the 27 headache centers. Of these, 3102 (46.8%) were boys and 3527 (53.2%) were girls.

Three boys were suspected as having CH on the basis of the clinical characteristics: two were examined in the first period of the study while the other was examined in the second period. One case was excluded because the cluster-like symptoms were due to chronic inflammation of the paranasal sinuses; the headache receded after adequate anti-inflammatory and antibiotic treatments.

Only two cases were, therefore, diagnosed as having cluster headache on the basis of the clinical characteristics: two were examined in the first period of the study while the other was examined in the second period. One case was excluded because the cluster-like symptoms were due to chronic inflammation of the paranasal sinuses; the headache receded after adequate anti-inflammatory and antibiotic treatments.

The prevalence of cluster headache in the 6629 children and adolescents examined affected by a headache disorder was calculated to be 0.03%.

Case 1

The patient is a 17-year-old boy who experienced the first and only cluster headache episode when he was 16 years old. The attacks were of severe intensity, with unilateral, orbital and supraorbital locations on the right side, lasting 15 minutes; the frequency was 2–3 attacks per day with onset at different times of the day. Headache was associated with conjunctival injection, nasal congestion, rhinorrhea, miosis, ptosis and eyelid edema. Other autonomic symptoms included pallor and palpitations. The clinical history and the general and neurological examinations excluded secondary headache disorders listed in groups 5–11 of the 1988 IHS classification. To treat the attacks, the patient used sumatriptan nasal spray (one puff per nostril), and this was moderately effective, reducing the intensity of the attacks or stopping them in a few minutes. He was preventively treated with verapamil per os at the dosage of 120 mg for two months with satisfactory results. No family history emerged for CH or for other primary headache disorders.

Case 2

This 9-year-old boy had his first cluster headache episode when he was 7.5 years old. He presented attacks of severe intensity of unilateral pain on the right side, with an orbital location. The cluster period lasted 7 days with a frequency of one attack per day. The duration of the attacks varied from 30 to 60 minutes and he was treated with 500 mg acetylsalicylic acid per os with no efficacy. The time of onset for all episodes was around 10:30 in the morning. The attacks were associated with the following symptoms: conjunctival injection, nasal congestion and rhinorrhea. Pallor was also present. Even in this case, the clinical history and the general and neurological examinations excluded secondary headache disorders listed in groups 5–11 of the 1988 IHS classification. Up to 31 October 2001, the child had a total of three cluster headache periods. Family history was not remarkable.

Table 1 Patients attending the 27 headache centers and clinics in the one-year study period

| Headache centers and clinics | All patients, n | Boys, n | Girls, n |
|-----------------------------|----------------|--------|--------|
| Alessandria                 | 167            | 87     | 80     |
| Ancona                      | 143            | 62     | 81     |
| Bari                        | 93             | 30     | 63     |
| Bergamo                     | 169            | 93     | 76     |
| Biella                      | 101            | 55 (1 case) | 46 |
| Chieti                      | 120            | 55 (1 case) | 65 |
| Fano                        | 97             | 53     | 44     |

Cont. →
Discussion

Several studies have investigated the prevalence of cluster headache in the general population and in out-patients attending centers and clinics devoted to headache disorders.

A lifetime prevalence between 0.07% and 0.14% emerged in population-based studies [6–10] with a clear male preponderance which seems to decrease in the last decades [8, 9]. This was attributed to changes in lifestyle factors over the years (such as employment rate and smoking habits), but this finding was not recently confirmed [22].

Typically, the mean age at onset of cluster headache is around 28–30 years, even if CH is believed to begin at any age up to around 70 years.

With regards to the onset of headache in childhood, Lance and Anthony [14] reported one patient that had isolated episodes of retro-orbital pain and lacrimation at the age of 8 years which recurred twice each year until typical bouts occurred in his second decade.

Ekborn et al. [2], identified well-defined cases of cluster headache in young Swedish 18-year-old males, and already in 1970 the same authors described 8 cases of cluster headache in a total of 105 patients affected by the same disorder who presented their first episode at an age ranging from 10 to 15 years [3].

Kudrow [16] described in detail, in his monograph Cluster headache. Mechanisms and management, a “three-year, two month old girl having a history of headache since age one. The major characteristics of her headache disorder were consistent with the diagnosis of cluster headache and, more specifically, with primary chronic cluster headache.

A study carried out by Swanson et al. [13] confirmed the onset of cluster headache before age 40 years and identified this primary headache disorder in only two boys aged 15 and 19 years, respectively, whereas they did not find cluster headache in patients under the age of 15 years. A recent study including 554 patients with episodic and chronic cluster headache examined between 1963 and 1997 showed 125 cases with an age at onset of CH from 10 to 19 years, with a clear prevalence in males (male-to-female ratio, 3.6:1) [22]. Furthermore, Garrido et al. [23] reported a 5-year-old child with cluster headache starting at age 3 years. There are also additional reports in the literature of onset in early childhood with the youngest patients being 3 and 4 years old [24, 25].

Based on these findings, the present one-year study was aimed at verifying the occurrence of this primary disorder in

---

Cont. Table 1

| Headache centers and clinics | All patients, n | Boys, n | Girls, n |
|-----------------------------|----------------|---------|---------|
| Florence                    | 446            | 225     | 221     |
| San Giovanni Rotondo (FG)   | 231            | 111     | 120     |
| Foggia                      | 540            | 232     | 308     |
| Genoa                       | 205            | 77      | 128     |
| Ivrea                       | 140            | 59      | 81      |
| L’Aquila                    | 307            | 165     | 142     |
| Mestre (VE)                 | 37             | 16      | 21      |
| Milan                       | 81             | 35      | 46      |
| Naples                      | 97             | 36      | 61      |
| Padua                       | 677            | 336     | 341     |
| Palermo: Aiuto Materno Hospital | 561    | 270     | 291     |
| Palermo: Ingrassia Hospital | 201            | 122 (1 case) | 79 |
| Pavia                       | 720            | 306     | 414     |
| Perugia                     | 64             | 31      | 33      |
| Rome: La Cattolica          | 76             | 37      | 39      |
| Rome: S. Carlo Hospital     | 337            | 157     | 180     |
| Sassari                     | 192            | 81      | 111     |
| Turin: Molinette Hospital   | 59             | 25      | 34      |
| Turin: S. Anna Hospital     | 97             | 33      | 64      |
| Trieste                     | 671            | 313     | 358     |
| Total                       | 6629           | 3102    | 3527    |

a Cluster headache with undetermined periodicity (3.1.1)
b Episodic cluster headache (3.1.2)
c Excluded because the cluster-like clinical symptoms were secondary to at paranasal sinusitis
children and adolescents with compelling headache and attending headache centers in Italy. Among the 6629 outpatients with headache under 18 years of age, two cases of CH were diagnosed: boys aged 9 and 17 years with ages of CH onset of 7 and 16 years, respectively. For both patients the diagnostic criteria for single CH attacks were fulfilled. They were diagnosed, on the basis of the presentation of the cluster periods over time, as having episodic CH and CH with undetermined periodicity, respectively.

In the older patient some doubt can be expressed regarding the efficacy of sumatriptan for cluster attacks because of the brief duration of the attacks (15 minutes) and the formulation used (intrasalinal, which is certainly not the first choice treatment and not as fast as subcutaneous injection). This observation makes the hypothesis of spontaneous recovery from the attack plausible. On the other hand the efficacy of verapamil as prophylactic treatment seems to support the diagnosis, although a spontaneous relief of cluster period cannot be excluded.

For the younger patient, treatment had some limitations because both sumatriptan and verapamil were contraindicated. In any case, the use of the latter prophylactic drug was not taken into consideration independently of age, due to the shorter duration of the cluster periods. In this patient, the inefficacy of acetylsalicylic acid for cluster attacks should be emphasised, in agreement with a previous report of two cases of childhood cluster headache [18]. One of the few treatment options in this case could be oxygen, which sufficiency controlled CH attacks in an affected child [24]. The younger CH patient identified in our study did not use oxygen, and therefore its efficacy could not be verified.

Indomethacin, a first choice treatment for chronic paroxysmal migraine in adults, has been demonstrated to be effective in relieving attacks in 2 cases of childhood headache [26]. Indomethacin should be mentioned as an alternative treatment.

No family history emerged for either patient, although a genetic risk for cluster headache has been described [27, 28].

On the basis of our results, the one-year prevalence of cluster headache in our out-patients affected by headache under age 18 years attending specialized centers and clinics was 0.03%. This value is smaller than that derived in the general population of all ages, and this finding further confirms the rarity of early diagnosis of this primary disorder in childhood and adolescence, at least as previously reported [3, 4].

The more brief duration of the attacks (as observed in both patients identified in our study) can partially explain the rarity of childhood cluster headache diagnosis, particularly among young patients selected from headache centers. It is also possible that childhood-onset cases may not be referred to a specialized tertiary headache or neuropsychiatric center due to the brief duration and low frequency per year of the cluster periods with spontaneous recovery [16].

Cases of CH with onset in childhood and adolescence should, in any case, be carefully followed to observe the course of the disease and the effects of therapeutic approaches. Finally, considering the rarity of cluster headache in childhood and adolescence and the frequent atypical clinical pattern in children and adolescents compared to adults (less and shorter duration of attacks, sometimes very short cluster periods), it is recommendable that appropriate neuroimaging examinations be carried out in young cluster headache patients to exclude organic disorders responsible for cluster-like attacks, such as arteriovenous malformations, endosellar or cervical spinal cord tumors, and paranasal sinus diseases, as suggested by previous studies [29, 30].

References

1. Kunkle EC, Pfeiffer JR, Withot WM, Hamrich LW (1952) Recurrent brief headache in “cluster” pattern. Trans Am Neurol Assoc 77:240–243
2. Ekbom K, Ahlborg B, Schele R (1978) Prevalence of migraine and cluster headache in Swedish men of 18. Headache 18:9–19
3. Ekbom K (1970) A clinical comparison of cluster headache and migraine. Acta Neurol Scand 46( Suppl):41
4. D’Alessandro R, Gamberini G, Benassi G, Morganti G, Cortelli P, Lugasere E (1986) Cluster headache in the Republic of San Marino. Cephalalgia 6:159–162
5. – (1988) Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. Cephalalgia 8(Suppl 7):1–96
6. Rasmussen BK, Jensen R, Schroll M, Olesen J (1991) Epidemiology of headache in a general population – a prevalence study. J Clin Epidemiol 44:1147–1157
7. Monteiro-Pereira JM, Maio R, Calheiros JM (1999) Cluster headache prevalence in a general population. In: Olesen J, Goadsby PJ (eds) Cluster headache and related conditions. Oxford University, Oxford, pp 57–60
8. Manzoni GC (1998) Gender ratio of cluster headache over the years: a possible role of changes in lifestyle. Cephalalgia 18:138–142
9. Manzoni GC (1999) Cluster headache and lifestyle: remarks on a population of 374 male patients. Cephalalgia 19:88–94
10. Ekbom K (1999) A clinical and pathophysiological overview. In: Olesen J, Goadsby PJ (eds) Cluster headache and related conditions. Oxford University, Oxford, pp 13–22
The Ad Hoc Committee for Cluster Headache in Childhood and Adolescence comprises the following researchers:

- **Alessandria.** P. Rasmini, D. Besana, Division of Neuropsychiatry of Childhood and Adolescence, Hospital of Alessandria

- **Ancona.** M.A. Tavoni, C. Cardinali, Division of Neuropsychiatry of Childhood and Adolescence, Salesi Hospital

- **Bari.** F.M. Puca, M.P. Prudenzano, First Neurologic Clinic, Policlinico of Bari

- **Bergamo.** S. Conte, Division of Neuropsychiatry of Childhood and Adolescence, Ospedali Riuniti di Bergamo

- **Biella.** A. Graziano, Service of Neuropsychiatry of Childhood and Adolescence, ASL di Biella

- **Chieti.** P. Tamburro, G. Di Meo, Center for the Study of Headache and Cervico cranial and Facial Pain, Institute of Medical Semeiotics, University of Chieti

- **Fano.** M. Burroni, V. Stoppioni, P. Geronzi, C. Ngradi, L. Boltri, Division of Neuropsychiatry of Childhood and Adolescence, ASL 3 Fano

- **Florenc.** C. Zammarrano Bogliolo, L. Calistrri, S. Caldas, Headache Center, First Pediatric Clinic, Ospedale Meyer Azienda Ospedaliera Anna Meyer

- **Foggia.** A. Spinu, L. Zizzo, Center for the Study of Headache, Unit of Neuropsychiatry of Childhood and Adolescence, Ospedali Riuniti di Foggia

- **San Giovanni Rotondo (FG).** M. Crisetti, M.I. Iussi, N. Germano, Service of Neuropsychiatry of Childhood and Adolescence, Casa Solliove della Sofferenza Hospital

- **Genoa.** E. Veneselli, M.E. Celle, S. Rolando, L. Saccomani, Division of Neuropsychiatry of Childhood and Adolescence, Gaslini Institute

- **Ivrea.** M. Perencio, C. Crotta, A. Martini, Division of Neuropsychiatry of Childhood and Adolescence, ASL 9, Ivrea

- **L’Aquila.** E. Tozzi, Pediatric Clinic, University of L’Aquila

- **Mestre (VE).** L. Perulli, Division of Neuropsychiatry of Childhood and Adolescence, Hospital of Mestre

- **Milan.** D. Riva, C. Pantaleoni, Unit of Developmental Neurology, IRCCS, C. Besta National Neurological Institute

- **Naples.** A. Pascotto, F.M. Ruja, F. Tigliani, Clinic of Neuropsychiatry of Childhood and Adolescence, Second University of Naples

- **Padua.** P.A. Battistella, E. Nodari, M. Gatta, C. Naccarella, F. Benini, Division of Neuropsychiatry of Childhood and Adolescence, Department of Pediatrics, University of Padua

11. Bahra A, May A, Goadsby PJ (1999) Diagnostic pattern in cluster headache. In: Olesen J, Goadsby PJ (eds) Cluster headache and related conditions. Oxford University Oxford, pp 61–65

12. Sjöstrand C, Waldenlind E, Ekborn K (2000) A follow-up study of 60 patients after an assumed first period of cluster headache. Cephalalgia 20:653–657

13. Swanson JW, Yanagihara T, Stang PE, O’Fallon WM, Beard CM, Melton LJ III, Guess HA (1994) Incidence of cluster headaches: a population-based study in Olmsted County, Minnesota. Neurology 44:433–437

14. Lance JW, Anthony M (1971) Cluster headache. Headache 11:275–279

15. Kudrow L (1980) Cluster headache: mechanisms and management. Oxford University, Oxford, pp 10–18

16. Maytal J, Lipton RB, Solomon S, Shinnar S (1992) Childhood onset cluster headaches. Headache 32:275–279

17. McNabb S, Whitehouse W (1999) Cluster headache-like disorder in childhood. Arch Dis Child 81:511–512

18. Curless RG (1982) Cluster headache in children. J Pediatr 101:393–395

19. Trucco M, Badino R (1993) A case of chronic cluster-like headache in a patient with cerebrovascular disease. Funct Neurol 8:423–427

20. Mosek A, Hering-Hanit R, Kuritzky A (2001) New-onset cluster headache in middle-age and elderly women. Cephalalgia 21:198–200

21. Torelli P, Cologna D, Manzoni CG (1999) Gender ratio in cluster headache. In: Olesen J, Goadsby PJ (eds) Cluster headache and related conditions. Oxford University, Oxford, pp 49–52

22. Ekborn K, Svensson DA, Träff H, Waldenlind E (2002) Age at onset and sex ratio in cluster headache: observations over three decades. Cephalalgia 22:94–100

23. Garrido C, Tuna A, Ramons S, Temudo T (2001) Cluster headache in a 3 year old child. Rev Neurol 33(8):732–735

24. Evers S, Frese A, Majewski A, Albrecht O, Husstedt IW (2002) Age of onset in cluster headache: the clinical spectrum (three case reports). Cephalalgia 22:160–162

25. Del Bene E, Poggiomi M (1987) Typical and atypical cluster headache in childhood. Cephalalgia 7(Suppl 6):128–130

26. D’Cruz OF (1994) Cluster headaches in childhood. Clin Pediatr 34:241–242

27. Russell MB, Andersson PG, Thomsen LL (1995) Familial occurrence of cluster headache. J Neurol Neurosurg Psychiatry 58:341–343

28. Leone M, Russell MB, Rigamonti A, Attanasio A, Grazzi L, D’Amico D et al. (2001) Increased familial risk of cluster headache. Neurology 56:1233–1236

29. Masson C, Lohericy S, Guillaume B, Masson M (1995) Cluster-like headache in a patient with a trigeminal neurinoma. Headache 35:48–49

30. Zanchin G, Rossi P, Licandro AM, Fortunato M, Maggioni F (1995) Cluster-like headache. A case of sphenoidal aspergilloma. Headache 35:494–497
- **Palermo.** A. Vecchio, N. D’Japico, L. Parisi, Division of Neuropsychiatry of Childhood and Adolescence, Aiuto Materno Hospital

- **Palermo.** V. Raieli, M. Eliseo, Division of Neuropsychiatry of Childhood and Adolescence, Polo Pediatrico, Casa del Sole, Ingrassia Hospital

- **Pavia.** G. Lanzì, Institute of Neuropsychiatry of Childhood and Mondino Institute, University of Pavia

- **Perugia.** G. Mazzotta, P. Sarchielli, A. Alberti, E. Cittadini, F. Floridi, A. Mattioni, B. Gallai, V. Gallai, Department of Neuroscience, University of Perugia

- **Rome.** P. Mariotti, Institute of Neuropsychiatry of Childhood and Adolescence, Catholic University Sacro Cuore

- **Rome.** D. Moscato, S. Carlo of Nancy Hospital, IDI

- **Sassari.** C. Mastropaolo, F. Zorodda, F. Carboni, Division of Neuropsychiatry of Childhood and Adolescence, University of Sassari

- **Turin.** L. Savi, Headache Center, Department of Neuroscience, Le Molinette Hospital, University of Turin

- **Turin.** B. Bassi, P. Boffi, Institute of Neuropsychiatry of Childhood and Adolescence, OIRM S. Anna, University of Turin

- **Trieste.** G. Reljia, Department of Clinical Medicine and Neurology, University of Trieste