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A Study of Digestive Absorption in Four Cases of Down's Syndrome. Down's Syndrome, Malnutrition, Malabsorption, and Alzheimer's Disease

F. ABALAN, A. JOUAN, M. T. WEERTS, C. SOLLES, J. BRUS, and M. F. SAUNERON*

*C. H. S. C. Perrens, 121 rue de la Béchade, 33076 Bordeaux Cédex, France. *Departement d'Immunologie et Maladies Parasitaires, Université de Bordeaux II, 33076 Bordeaux Cédex, France. (Reprint requests to FA)*

Abstract — Many data suggest that patients with Down's syndrome (DS) suffer from digestive malabsorption. A fecal test of absorption (search for undigested meat fibers following the ingestion of a measured diet) was conducted in 4 patients with DS. The results point to malabsorption in these patients and support the hypothesis of malabsorption in DS. The etiology of probable malabsorption in DS is discussed. Data are presented suggesting that chronic malnutrition caused by malabsorption could be the cause of the neuropathologic signs of Alzheimer's disease occurring at or slightly before the fourth decade in all patients with DS.

Introduction

The hypothesis that patients with Down's Syndrome (DS) suffer from digestive malabsorption was proposed by Matin et al. (1) to explain blood values for vitamin B1, nicotinic acid, and ascorbic acid in the deficient range, despite a dietary intake previously assessed as adequate and containing a daily 50 mg supplement of ascorbic acid. This hypothesis is supported by the description in DS of impaired digestive absorption of vitamin A (2, 3), low blood levels of vitamin B1 despite adequate dietary intake and vitamin B1 supplements (4, 5), and xylose excretion below normal after oral administration of a xylose load (6). This hypothesis could also explain the other signs of malnutrition (7) observed in DS: red-cell folate values in the deficient range (8), unusual susceptibility to infections (9, 10), depressed reactivity to skin-tests antigens (11), impaired neutrophil bactericidal capacity (12), decreased responsiveness of lymphocytes to mitogens (9, 13, 14), and decreased capability of peripheral blood T lymphocytes to form rosettes with sheep red blood cells (9, 13). It could also possibly explain why patients with DS have low calcium and copper hair concentrations (15) and low platelet calcium levels (16).

We report here the results of a simple and reliable fecal malabsorption test in 4 cases of DS. Data are presented suggesting a possible link between malnutrition and malabsorption in DS and the development of the neuropathologic signs of Alzheimer's disease (AD) in all patients with DS (17).

Patients and methods

We studied the 4 patients with DS who were in our psychiatric hospital. Sex and age of patients were respectively 2 males (29 and 39) and 2 females (both 46). In all cases, the diagnosis of Trisomy 21 had been confirmed by chromosome analysis.

The digestive malabsorption test used was the microscopic examination of stools for undigested meat fibers after a measured diet. Patients were fed according to the method of Moore et al. (18) modified slightly: minced meat was used to avoid the appearance in the stools of undigested meat fibers owing to the insufficient dental mastication of such patients. Each patient was fed for seven days (days 1 to 7 included) a daily diet containing 100 g of fat and at least two meat meals (250 to 300 g of meat). After the equilibration period (days 1 to 3 included) the patients received on day 4 a carmine marker with lunch. Four days later, a second carmine marker was given at lunch.

Every stool was collected from the appearance of the first marker and up to, but not including, the appearance of the second marker. These patients being incontinent, the stools were collected in diapers. Care was taken not to collect urine.

The stools were kept at +4°C in a plastic container, and sent each morning to the laboratory where microscopic examination was performed within the six hours following their arrival. Patient identification was unknown to the tester. The stools of each container were homogenized and a small piece of the stools (approximately 5 mm × 3 mm) was taken at random from each container. This small piece was then mixed thoroughly with a 0.8% saline solution in order to obtain a satisfactory thin smear covering the entire area under the coverslip. The entire coverslip was examined and only rectangular meat fibers with clearly evident cross-striations (undigested meat fibers) were counted. Their number per coverslip (18) and per 5 minute search under high magnification (×400) (19) was counted.

Results

The number of undigested meat fibers was over 150 per coverslip and over 50 per 5 minute search in all the patients.

Discussion

More than 10 undigested meat fibers per coverslip or per 5 minute search under high magnification (×400) indicate a malabsorption syndrome (18, 19, 20, 21, 22, 23). Our results indicate digestive malabsorption in our four patients with DS.

The malabsorption test we used is often neglected. It was chosen because it is safe and reliable (18). The quantitative fecal fat determination which is often recommended was not used because the fecal incontinence did not allow an absolutely complete collection of stools and because false negatives have been reported with the latter test (24, 25). It was impossible to perform other tests such as the secretin test, breath tests, etc. This was due to the mental state of the patients and for ethical reasons.

Our results strongly support the hypothesis (1) that patients with DS have a malabsorption syndrome. The malabsorption test used does not make it possible to determine whether malabsorption is the consequence of pancreatic insufficiency, of reduced intestinal absorptive capacity, or of another cause (18, 19, 20, 21, 22). Malabsorption in DS could be caused by cystic fibrosis and/or celiac disease: abnormally high sweat osmolality and cases of cystic fibrosis (26, 27, 28) as well as cases of celiac disease (29, 30, 31, 32) have been reported in DS. The description in DS of a case of cystic fibrosis in a neonate (27), of cases of cystic fibrosis and of celiac disease in babies and children (26, 28, 30, 32), of impaired vitamin A absorption in children (2, 3), and of nutritional deficiencies in babies and children (4, 8, 13), all suggest that malabsorption and nutritional deficiencies are early events in the life of patients with DS. Malabsorption could be genetic in origin.

Data suggest that chronic malnutrition caused by malabsorption could be the cause (33) of neuropathologic signs of AD in all patients with DS at or slightly before their fourth decade (17):

the Parkinsonism-dementia complex on Guam Island which is characterized neuropathologically by two (neurofibrillary degeneration and granulovacuolar degeneration) of the three main cerebral lesions of AD (34) is probably caused by chronic nutritional deficiency in calcium and magnesium (35, 36); neurofibrillary degeneration is the consequence of malnutrition (review of the literature prior to 1925 by Jackson) (37), of cholera, intestinal tuberculosis and bacillary dysentery (38); dementia is a consequence of malabsorption syndromes (39), and dementia, memory disorders, and intellectual deterioration are the consequences of chronic malnutrition (40, 41, 42, 43, 44).

Conclusion

This work strongly supports the hypothesis of malabsorption in DS. It suggests further studies in DS to confirm our findings, and to determine the cause(s) of this probable malabsorption. It also suggests work examining the possible relationship between chronic malnutrition due to malabsorption in DS and the development of the neuropathologic signs of AD in DS. Such studies would greatly contribute to the knowledge of such a devastating illness as AD.

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References

1. Matin M A, Sylvester P E, Edwards D, Dickerson J W T. Vitamin and zinc status in Down's syndrome. Journal of Mental Deficiency Research 25: 121, 1981.
2. Sobel A E, Strazzula M, Sherman B S, Elkan B, Morgenstern S W, Marius N, Meisel A. Vitamin A absorption and other blood composition studies in mongolism. American Journal of Mental Deficiency Research 62: 642, 1958.
3. Auld R M, Pommer A M, Houck J C, Burke F. Vitamin A absorption in mongoloid children. A preliminary report. American Journal of Mental Deficiency Research 63: 1010, 1959.
4. Schmid F Von, Christeller S, Rehm W. Untersuchungen zum Status von Vitamin B1, B2 und B6 beim Down Syndrom. Fortschritte Der Medizin 93: 1170, 1975.
5. Reading C M, Mc Leay A, Nobile S. Down's syndrome and thiamine deficiency. Journal of Orthomolecular Psychiatry 8: 4, 1979.
6. Williams C A, Quinn H, Wright E C, Sylvester P E, Gosling P J H, Dickerson J W T. Xylose absorption in Down's syndrome. Journal of Mental Deficiency Researcy 29: 173, 1985.
7. Chandra R K. Immunocompetence as a functional index of nutritional status. British Medical Bulletin 37: 89, 1981.
8. Gericke G S, Hesseling P B, Brink S, Tiedt F C. Leucocyte ultrastructure and folate metabolism in Down's syndrome. South African Medical Journal 51: 369, 1977.
9. Franceshi C, Licastro F, Paolucci P, Masi M, Cavicchi S, Zannotti M. T and B lymphocyte subpopulations in Down's syndrome. A study on non-institutionalised subjects. Journal of Mental Deficiency Research 22: 179, 1978.
10. Thase M E. Longevity and mortality in Down's syndrome. Journal of Mental Deficiency Research 26: 117, 1982.
11. Sutnick A I, London W T, Blumberg B S, Gertsley B J. Susceptibility to leukemia: immunologic factors in Down's syndrome. Journal of the National Cancer Institute 47: 923, 1971.
12. Barkin R M, Weston W L, Humbert J R, Sunada K. Phagocytic function in Down syndrome. II. Bactericidal activity and phagocytosis. Journal of Mental Deficiency Research 24: 251, 1980.
13. Burgio G R, Ugazio A G, Nespoli L, Marcioni A F, Bottelli A M, Pasquali F. Derangements of immunoglobulin levels, phytohemagglutinin responsiveness and T and B cell markers in Down's syndrome at different ages. European Journal of Immunology 5: 600, 1975.
14. Gershwin M E, Crinella F M, Castles J J, Trent J K T. Immunologic characteristics of Down's syndrome. Journal of Mental Deficiency Research 21: 237, 1977.
15. Barlow P J, Sylvester P E, Dickerson J W T. Hair trace metals in Down's syndrome patients. Journal of Mental Deficiency Research 25: 161, 1981.
16. Mc Coy E E, Sneddon J M. Decreased calcium content and 45Ca2+ uptake in Down's syndrome blood platelets. Pediatric Research 18: 914, 1984.
17. Burger P C, Vogel F S. The development of the pathologic changes of Alzheimer's disease and senile dementia in patients with Down's syndrome. American Journal of Pathology 73: 457, 1973.
18. Moore J G, Englert E, Bigler A M, Clark R W. Simple fecal tests of absorption. A prospective study and critique. American Journal of Digestive Diseases 16: 97, 1971.
19. Page L B, Culver P J. A syllabus of laboratory examinations in clinical diagnosis. Revised ed., pp 374–380 Harvard University Press, Cambridge Ma., 1961.
20. Gradwohl R B H. Clinical laboratory methods and diagnosis. 5th ed., Vol. 2, pp 1261–1304. The C. V. Mosby Cy. St Louis, 1956.
21. Rothman M M, Katz A B. Analysis of feces, p 694 in Gastroenterology, 2nd ed., Vol. 2. (H L Bockus, ed) W B Saunders Cy. Philadelphia, 1964.
22. Goiffon B. Coprologie fonctionnelle. Encyclopedie Médico-chirurgicale. Estomac-Intestin 90–10: A–10 and A–20, 4–1977.
23. Greenberger N J, Toskes P P. Approche d'un patient porteur d'une maladie pancréatique. p 1607 in Harrison-Principes de médecine interne. 3éme éd. française, Vol. 2. (Isselbacher et al., eds) Flammarion, Paris, 1982.

24. Montogomery R D, Haeney M R, Ross I N, Sammons H G, Barford A V, Balakrishnan S, Mayer P P, Culank L S, Field J, Gosling F. The ageing gut: a study of intestinal absorption in the elderly. Quarterly Journal of Medicine 47: 197, 1978.
25. Toskes P P, Deren J J, Fruitterman J, Conrad M E. Specificity of the correction of vitamin B12 malabsorption by pancreatic extract and its clinical significance. Gastroenterology 65: 199, 1973.
26. Milunsky A. Cystic fibrosis and Down's syndrome. Pediatrics 42: 501, 1968.
27. Vetrella M, Barthelmai W, Matsuda H. Kongenitale amegakarycytäre Thrombocytopenie mit finaler Pancytopenic bei Trisomie 21 mit cystischer Pankreasfibrose. Zeitschrift Fur Kinderheilk 107: 210, 1969.
28. Symon D N K, Stewart L, Russel G. Abnormally high sweat osmolality in children with Down's syndrome. Journal of Mental Deficiency Research 29: 257, 1985.
29. Levo Y, Green P. Down's syndrome and autoimmunity. The American Journal of the Medical Sciences 273: 95, 1977.
30. Bentley D. A case of Down's syndrome complicated by retinoblastoma and celiac disease. Pediatrics 56: 131, 1975.
31. Howell S J L, Foster K J, Rechless J. Protracted survival in patients with Down's syndrome. British Medical Journal 287: 1429, 1983.
32. Nowak T V, Gjishan F K, Schulze-Delrieu K. Celiac sprue in Down's syndrome: considerations on a pathogenic link. American Journal of Gastroenterology 78: 280, 1983.
33. Abalan F. Alzheimer's disease and malnutrition: a new etiological hypothesis. Medical Hypotheses 15: 385, 1984.
34. Corsellis J A N. Ageing and the dementias. p. 796 in Greenfield's neuropathology. 3rd ed. (Blackwood W et al. eds) Edward Arnold. London, 1976.
35. Garruto R M, Yanagihara R, Gajdusek D C. Disappearance of high incidence amyotrophic lateral sclerosis and parkinsonism-dementia on Guam. Neurology 35: 193, 1985.
36. Reed D, Labarthe D, Chen K M, Stallones R. A cohort study of amyotrophic lateral sclerosis and parkinsonism-dementia on Guam and Rota. American Journal of Epidemiology 125: 92, 1987.
37. Jackson C M. The effects of inanition and malnutrition upon growth and structure. pp 173–190. Churchill, London, 1925.
38. Alexander L, Wu T T. Cerebral changes in gastrointestinal infections with terminal cachexia. Archieves of Neurology and Psychiatry 33: 72, 1935.
39. Cooke W T. Neurologic manifestations of malabsorption. p 225 in Handbook of Clinical Neurology. Vol. 28 (Vinken P J et al, eds) Elsevier, Amsterdam, 1976.
40. Leyton G B. Effects of slow starvation. Lancet 2: 73, 1946.
41. Kral V A. Psychiatric observations under severe chronic stress. American Journal of Psychiatry 108: 185, 1951.
42. Thygesen P, Hermann K, Willanger R. Concentration camp survivors in Denmark. Persecution, disease, disability, compensation. Danish Medical Bulletin 17: 65, 1970.
43. Ström A. Norwegian concentration camp survivors. Universitetsforlaget. Oslo, 1968.
44. Abalan F. Malnutrition and Alzheimer's dementia. The British Journal of Psychiatry 147: 320, 1985.