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Case reports

Child neglect followed by marked thymic involution and fatal systemic pseudomonas infection

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Summary. The case of a 9-month-old baby girl who failed to develop normally due to nutritional neglect and secondary immunodeficiency characterized by marked thymic involution is reported. The child died of systemic *Pseudomonas aeruginosa (P. aeruginosa)* infection manifested in pneumonia, lung abscesses, bacterial endocarditis and ecthyma gangrenosum. At autopsy the child was 64 cm in height (normal for a 4- to 5-month-old child) and 5.1 kg in weight (normal for a 2- to 3-month-old child). Multiple gangrenous ecthymas, consisting of deep ulcers, induration and inflammation, were observed in the skin over the entire body. The lungs showed hemorrhagic pneumonia, multiple lung abscesses, and necrotizing arteritis in the abscesses and surrounding areas. The thymus weighed 2.3 g and showed marked involution. Histological examination showed so-called nutritional thymectomy characterized by servere cortical atrophy and clustering, cystic dilation and amorphous changes of the Hassall's corpuscles. In the heart, dark brown verrucae were present at the attachment sites of the tendinous cords of the papillary muscle in the anterior and posterior cusps of the mitral valve, suggesting infectious endocarditis. Bacteriological examination demonstrated *P. aeruginosa* in the ecthymas, lung abscesses and blood. As primary immunodeficiency was considered unlikely, immunodeficiency secondary to thymic involution following malnutrition seemed to have led to a fatal systemic infection with *P. aeruginosa,* whose virulence is generally weak. This suggests a close association of the development of such infection and immunodeficiency with child neglect.

Key words: Child neglect – Malnutrition – Thymic involution – Secondary immunodeficiency – Pseudomonas aeruginosa infection

Zusammenfassung. Beschreibung eines 9-Monate alten weiblichen Säuglings, welcher sich wegen Mangelernährung verzögert entwickelte. Die Entwicklungsstörung führte zu einer Immundefizienz, welche durch eine ausgeprägte Thymus-Involution charakterisiert war. Das Kind starb an einer systemischen Infektion durch Pseudomonas aeruginosa mit Manifestation einer Pneumonia, Lungenabszessen, bakterieller Endokarditis und Ecthyma gangraenosum. Bei der Obduktion war das Kind 64 cm lang – entsprechend einem Alter von 4–5 Monaten – und wog 5,1 kg – entsprechend einem Lebensalter von 2–3 Monaten. Die Haut des gesamten Körpers wies multiple gangränöse Ecthyme auf, welche aus tiefen Geschwüren, Verhärtung und Entzündung bestanden. Die Lungen zeigten eine hämorrhagische Pneumonie, zahlreiche Abszesse und eine nekrotisierende Arteriitis in den Abszessen und in den umgebenden Geweben. Der Thymus wog 2,3 g und zeigte eine ausgeprägte Involution. Die Histologie zeigte eine sog. „ernährungsbedingte Thymektomie", welche durch schwere kortikale Atrophie charakterisiert war und durch Anhäufung, zystische Erweiterung und amorphe Veränderungen der Hassall'schen Körperchen. Im Herzen waren tiefbraune Warzen vorhanden. An den Anheftungsseiten der Sehnenfäden der Papillarmuskeln im vorderen und hinteren Segel der Mitralklappe, wie bei infektiöser Endokarditis. Die bakterielle Untersuchung wies Pseudomonas aeruginosa in den Ecthymen, den Lungenabszessen und im Blut nach. Da eine primäre Immundefizienz als unwahrscheinlich erachtet wurde, wurde eine sekundäre Immundefizienz aufgrund einer Thymusinvolution, bedingt durch Nahrungsmangel, für ursächlich für die Pseudomonas aeruginosa-Infektion gehalten, ein Keim, welcher generell wenig virulent ist. Dieser Umstand legt eine enge Assoziation zwischen der Entstehung dieser Infektion und der Immundefizienz durch Kindesvernachlässigung nahe.

Schlüsselwörter: Kindesvernachlässigung – Mangelernährung – Thymusinvolution – Sekundäre Immundefizienz – Pseudomonas aeruginosa-Infektion

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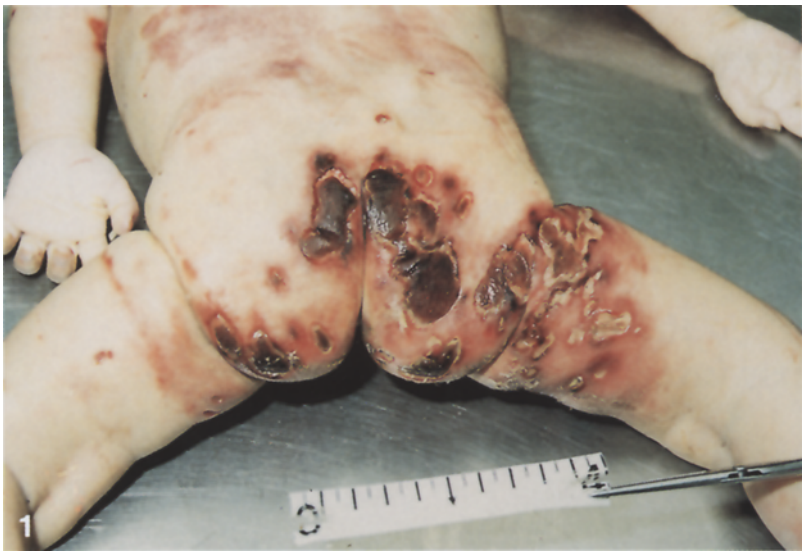

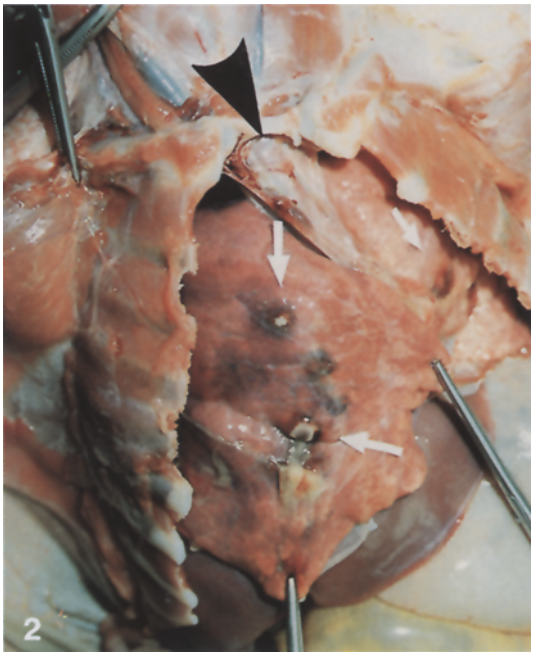

Fig. 1. Multiple ecthyma gangrenosum in the lumbogluteal region. Deep ulcers varying in size and surrounding induration and inflammation are observed

Fig. 2. Markedly involuted thymus in the mediastinum between the right and left lungs *(arrow head)* and multiple abscesses in both lungs *(arrows)*. The entire lungs show hemorrhagic pneumonia and attachment of fibrin, exudated to the bilateral lower lobes due to pleuritis

Introduction

The diagnosis of child abuse represented by the battered child syndrome is based on various old and new injuries resulting from being beaten. Intracranial damage due to violence frequently causes death [1] but on the other hand, some children die of malnutrition as a result of neglect [2].

The case of a 9-month-old baby girl is reported, who was born at term with no abnormalities, developed immunodeficiency secondary to negligent malnutrition and died of systemic *Pseudomonas aeruginosa (P. aeruginosa)* infection. In addition, the relationship between malnutrition due to child abuse and neglect and infection is discussed.

Case report

1. Case profile

A woman living with a man disappeared, also leaving her 9-month-old baby daughter and her son of 2 years 3 months. The 9-month-old child had been born at term with no abnormalities, but had suffered from malnutrition since birth. The man did not provide the female infant with adequate nutrition; she developed fever and skin eruption on December 23 but was not taken to hospital. She was found dead in the bedroom at about 3:00 p.m. on January 1. Approximately 18 h later, a judicial autopsy was performed on the grounds of suspected abandonment by the protector resulting in death.

2. Physical findings

The child was 64 cm in height, weighed 5.1 kg and appeared malnourished. Mild greenish putrefactive discoloration was observed in the abdomen. The scalp and the skin of the scapular region, the upper and lower extremities (especially the medial femur), the lumbogluteal region and the external genitalia emitted a specific foul odor and showed ulcerative lesions of various sizes. These lesions had sharp margins with a deep ulcer in the center, partly covered with crusts containing dark red-brown blood and accompanied by induration and inflammation in the surrounding area (Fig. 1). In addition, there were multiple indurations with a red halo, blisters and pustules with various degrees of central ulceration. These skin lesions were macroscopically diagnosed as ecthyma gangrenosum (or ecthyma cachecticorum or ecthyma gangrenosum cachecticorum) [3, 4], which was confirmed by histopathological examination of the skin.

There was some bleeding (1–4 cm diameter) in the subcutaneous soft tissue of the right cheek anterior to the right auricle and in the right auricle. In each latero-abdominal region, there was an old rectangular skin scar with a slightly pale central area surrounded by light brown pigmentation.

3. Autopsy findings

In both lungs, multiple abscesses (about 1 cm in diameter) surrounded by hemorrhagic necrosis were present. Inflammation extended throughout the lungs with inflammatory pleural adhesions on the anterior and posterior surfaces of the bilateral lower lobes and pleurisy on the visceral and parietal sides. The thymus showed marked involution and weighed only 2.3 g (Fig. 2).

In the heart, dark brown verrucae were observed at the attachment site of the papillary muscle at the an-

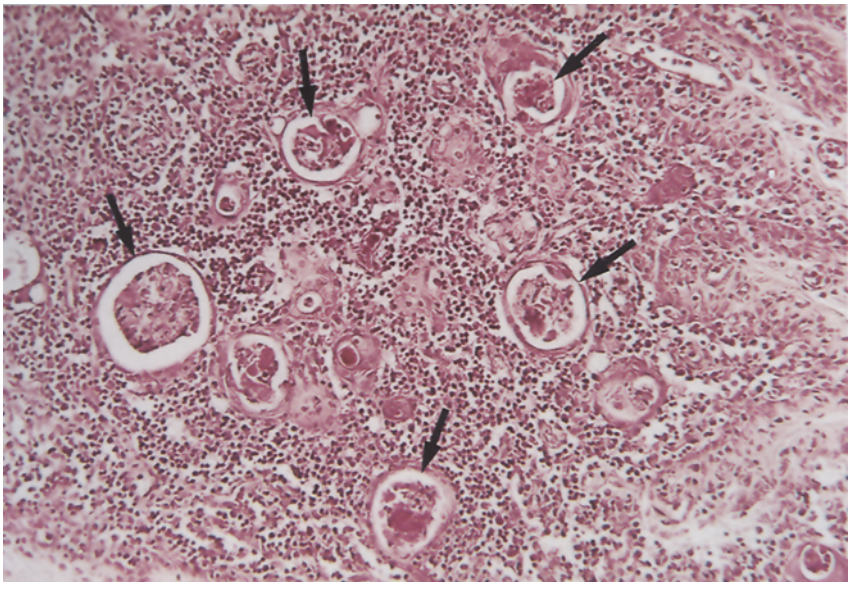

Fig. 3. In the thymus, the cortex is markedly involuted and interlobular connective tissue is clearly seen. Clustering of Hassall's corpuscles due to cortical involution, cystic dilation *(arrows)* and amorphous changes are observed. H & E; × 100

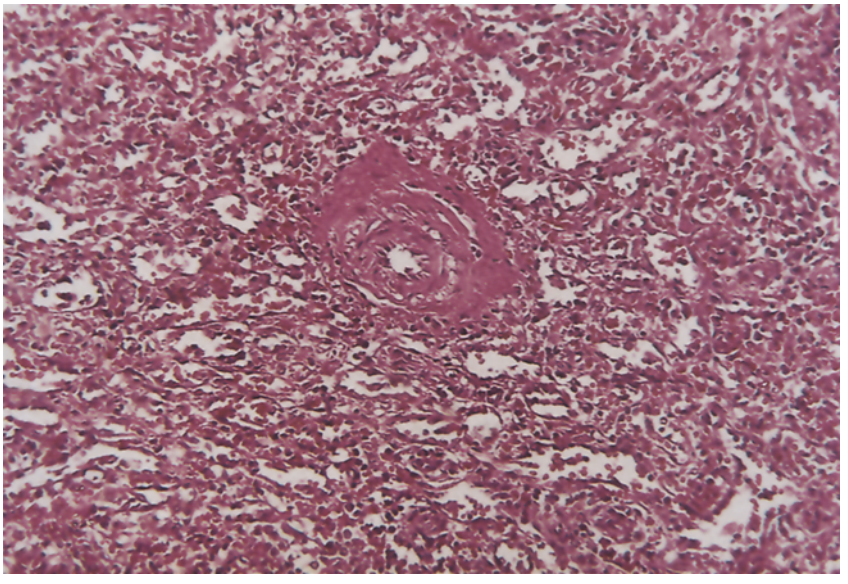

Fig. 4. In the spleen, lymphocytes in the thymus-dependent area around the splenic arteriole are markedly depleted. H & E; × 100

terior and posterior cusps of the mitral valve. There were, however, no congenital abnormalities in the heart or major vessels, and the fenestra of the oval foramen was closed.

The stomach contained slightly milky-white fluid (26 g), which consisted primarily of transparent mucus and contained a few minute brown seaweed-like fragments. The mucosa of the gastric body showed punctate erosion.

The spleen weighed approximately 22 g with a slightly cloudy pulp. The cerebral surface was congested and edematous, but the cerebrospinal fluid showed no marked changes.

4. Histopathological findings

a) Skin lesions. In the ulcerative lesion in the center of the ecthymas, the epidermis was defective and the dermis was exposed. Bleeding was observed in the dermis and subcutaneous tissue but infiltration of inflammatory cells such as polymorphonuclear leukocytes and lymphocytes was relatively slight. These findings were consistent with the characteristics of ecthyma gangrenosum.

b) Pulmonary lesions. In the bilateral lungs, many leukocytes, erythrocytes, and inflammatory exudate were present in most alveoli, suggesting hemorrhagic pneumonia. In addition, there were multiple abscesses consisting of necrotic pulmonary tissue and numerous inflammatory cells. In the large and small arteries inside the abscesses and their surrounding areas, purulent lysis of the arterial wall and hemorrhage per rhexis were observed, showing necrotizing arteritis.

c) Thymus. The cortex of the thymus showed marked involution and the interlobular connective tissues were

compressed. Cortical involution resulted in clustering of Hassall's corpuscles, which were dilated in a cystic pattern and frequently contained amorphous structures (Fig. 3).

d) Lymph nodes and spleen. The number of lymphocytes was markedly decreased due to depletion of the paracortex of the lymph nodes and around the splenic arteriole (Fig. 4) corresponding to the thymus-dependent area.

5. *Bacteriological findings*

Gram staining of smear specimens from the skin lesions on the medial side of the right femur and those of necrotic tissue of the abscess in the right lung showed many gram-negative bacilli and gram-positive cocci in the former specimens, and only 5–10 gram-negative bacilli per visual field in the latter.

A culture of the blood from the heart showed *P. aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis* (endogenous bacteria in the skin), glucose non-fermentative gram-negative bacilli and G group β streptococci (each + 1).

The findings of the bacteriological examination and the properties of the cutaneous and pulmonary lesions suggested a systemic infection caused by *P. aeruginosa.*

6. *Other information*

Subsequent investigation revealed that in December the brother had also been hit or kicked several times in the face, back, abdomen, gluteal region and external genitalia by the man suspected of neglect of the baby girl. The brother was taken to hospital at the end of December after an alleged fall in the bathroom and was admitted with a diagnosis of bruises to the head, laceration of the forehead and subcutaneous bleeding in the face, head, trunk and perineum. After being discharged, he was left in the care of a relative of his mother.

Discussion

Child abuse most frequently becomes manifest in various traumatic lesions [1], but sometimes in infection. Some children with polymicrobial sepsis secondary to abuse after intravenous injection of contaminated material have been reported. However, a long time elapsed in each before the sepsis was correctly diagnosed, as an initial diagnosis of fever of unknown cause was first recorded or the children were transferred from hospital to hospital or immunodeficiency was first suspected [5–8].

In children with infection resulting from abuse or neglect, psychological and physical stress have been reported and also thymic involution, i.e., decreased cellular immunity, resulting from nutritional disturbance [9].

Immunodeficiency secondary to malnutrition is characterized by more severe impairment of cellular immunity than of humoral immunity [10]. Smythe et al. [11] reported that infants with protein-calorie malnutrition showed tonsillar atrophy, marked impairment of both delayed hypersensitivity and lymphocyte response to phytohemagglutinin (PHA) and autopsy findings auch as marked thymic atrophy, wasting of peripheral lymphoid tissue, paracortical lymphocyte depletion and loss of germinal centers. This marked thymic atrophy has been termed "nutritional thymectomy", and it has been suggested that this induces gram-negative bacillus sepsis, disseminated herpes simplex infection, anergic response to infection, and gangrene rather than suppuration [11].

In the present case, the 9-month-old female infant was only 64 cm in height and weighed 5.1 kg at autopsy. A survey on the physical growth of infants in 1970 showed a normal height range 67.8–70.5 cm (mean, 69.1 cm) and a weight range 7.8–8.7 kg (mean, 8.2 kg) in female babies aged 8–9 months [12].

In addition, the thymus weight was markedly reduced (to 2.3 g) and the histopathological findings in the thymus were consistent with malnutrition, as reported by Linder [13]. Even if thymic involution associated with acute systemic infection was taken into consideration [14], chronic malnutrition seemed to be the primary cause of the thymic involution. Lymphocyte depletion was marked in T-cell areas (thymus-dependent areas) [15], such as the paracortex of lymph nodes and the area around the splenic arteriole, suggesting decreased cellular immunity.

The cause of death in this case seems to have been systemic infection with *P. aeruginosa* associated with decreased cellular immunity resulting from malnutrition. T-cells play a primary role in the biological defense against such gram-negative bacilli as *P. aeruginosa* and *Escherichia coli.* The pathogenic importance of *P. aeruginosa* has increased of late, because it causes so-called opportunistic infection in patients with malignant tumors or immunodeficiency and those treated with immunosuppressants [16, 17].

P. aeruginosa infection frequently occurs in the form of respiratory tract infection, such as pneumonia, and less frequently in the form of cutaneous phlegmonous inflammation, i.e. local necrosis due to proteolytic enzymes produced by *P. aeruginosa*, sepsis, meningitis, and urinary tract infection [16, 17].

Multiple ecthyma gangrenosum, as observed in this case, occurs in the lumbogluteal region in infants suffering from malnutrition. The prognosis is poor, with deep ulceration and rapid progression of the condition. The causative agents are *P. aeruginosa*, which is the most common, *Staphylococcus aureus* and group A streptococci [3, 4]. In this case, gram-negative bacilli were detected both in the gangrenous lesion on the medial femur and in the lung abscesses, and *P. aeruginosa* was found in the blood culture. These findings, together with the characteristic and specific foul odor in the cutaneous lesions, suggest *P. aeruginosa* infection.

P. aeruginosa sepsis seemed to be present. Dissemination of this organism over the entire body may have induced ecthyma gangrenosum, pneumonia, pulmonary abscesses, and bacterial endocarditis, resulting in death.

Copeland [18] reported a 15-month-old male infant who developed panhypogammaglobulinemia, a decrease in complement factors C_3 and C_4, and thymic involution secondary to child abuse and died of multiple pulmonary abscesses and gangrene in the facial skin. In this case, *P. aeruginosa* was detected in the oral cavity and lung abscesses. Copeland also considered the possible involvement of genetic factors in the development of the immune abnormality. However, at autopsy, this 15-month-old male infant was only 72.5 cm in height, which is average for 9 months after birth, and weighed 5.45 kg, which is average for 3 months after birth and less than the lower limit for 6 months after birth [19]. The apparent underdevelopment, malnutrition and markedly decreased weight, which were also observed in our case, indicate that immunodeficiency occurred secondary to malnutrition and may have been complicated by physical and psychological stress due to abuse and neglect, as suggested by Fukunaga [20].

This secondary immunodeficiency should be differentiated from primary severe combined immunodeficiency [21] and DiGeorge syndrome [22]. In severe combined immunodeficiency, which develops about 1 month after birth, the weight of the thymus is normally less than 1.5 g and the condition frequently leads to death in 3–6 months. In most cases [21], no pulp differentiation or formation of Hassall's corpuscles is observed. In the present case, the thymus weighed 2.3 g, the patient died at the age of 9 months and Hassall's corpuscles were present. These findings excluded primary severe combined immunodeficiency. On the other hand, DiGeorge syndrome is characterized by thymic aplasia and hypoplasia, abnormalities of the heart or major vessels, aplasia or hypoplasia of the parathyroid glands and abnormal calcium metabolism [22]. In our case, no abnormalities of the heart and major vessels, and no diseases suggestive of decreased parathyroid function, such as tetany, were observed at birth, which excludes this syndrome.

We have reported on a 9-month-old female baby who failed to develop normally due to negligent chronic malnutrition and secondary immunodeficiency accompanied by severe thymic involution. The cause of death was systemic infection with *P. aeruginosa* manifested in pneumonia, lung abscesses, bacterial endocarditis and ecthyma gangrenosum. Attention should be paid to cases of immunodeficiency resulting from child abuse and neglect and should be differentiated from primary immunodeficiency before deciding whether legal action should be taken.

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References

1. Wecht CH, Larkin GM (1984) The battered child syndrome (1). In: Carmi A, Zimrin H (eds) Child abuse. Springer, Berlin Heidelberg NewYork, pp 157–182
2. Schmitt BD, Krugman RD (1987) Abuse and neglect of children. In: Behrman RE, Vaughan VC III (eds) Nelson textbook of pediatrics, 13th edn. Saunders, Philadelphia, pp 79–84
3. Weinberg AN, Swartz MN (1987) Infections due to pseudomonas aeruginosa. In: Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF (eds) Dermatology in general medicine, 3rd edn. McGraw-Hill, NewYork, pp 2125–2128
4. Lever WF (1975) Histopathology of the skin, 5th edn. Lippincott, Philadelphia, p 275
5. Kohl S, Pickering LK, Dupree E (1978) Child abuse presenting as immunodeficiency disease. J Pediatr 93:466–468
6. Halsey NA, Frentz JM, Tucker TW, Sproles T, Redding J, Daum RS (1983) Recurrent nosocomial polymicrobial sepsis secondary to child abuse. Lancet II:558–560
7. Rubin LG, Angelides A, Davidson M, Lanzkowsky P (1986) Recurrent sepsis and gastrointestinal ulceration due to child abuse. Arch Dis Child 61:903–905
8. Koch C, Høiby N (1988) Severe child abuse presenting as polymicrobial bacteremia. Acta Paediatr Scand 77:940–943
9. Dourov N (1986) Thymic atrophy and immune deficiency in malnutrition. Curr Top Pathol 75:127–150
10. Purtilo DT, Connor DH (1975) Fatal infections in protein-calorie malnourished children with thymolymphatic atrophy. Arch Dis Child 50:149–152
11. Smythe PM, Schonland M, Brereton-Stiles GG, Coovadia HM, Grace HJ, Loening WEK, Mafoyane A, Parent MA, Vos GH (1971) Thymolymphatic deficiency and depression of cell-mediated immunity in protein-calorie malnutrition. Lancet II:939–943
12. Nakajima H, Sasaki N (1979) Evaluation and diagnosis of physical growth abnormalities. In: Suwa S (ed) Pediatric Department MOOK, no. 6, Growth disturbance in children (in Japanese). Kanehara Shuppan, Tokyo, pp 16–34
13. Linder J (1987) The thymus gland in secondary immunodeficiency. Arch Pathol Lab Med 111:1118–1122
14. Baarlen J van, Schuurman H-J, Huber J (1988) Acute thymus involution in infancy and childhood: a reliable marker for duration of acute illness. Hum Pathol 19:1155–1160
15. Roitt IM (1977) Essential immunology, 3rd edn. Blackwell Scientific Publications, Oxford, pp 70–76
16. Jawetz E, Melnick JL, Adelberg EA, Brooks GF, Butel JS, Ornston LN (1989) Medical microbiology, 18th edn. Prentice-Hall, London
17. Zwadyk P (1980) Pseudomonas. In: Joklik WK, Willett HP, Amos DB (eds) Zinsser microbiology, 17th edn. Appleton-Century-Crofts, NewYork, pp 760–766
18. Copeland AR (1988) A case of panhypogammaglobulinemia masquerading as child abuse. J Forensic Sci 33:1493–1496
19. Vaughan VC III, Lift IF (1987) Growth and development: The first year. The second year. In: Behrman RE, Vaughan VC III (eds) Nelson textbook of pediatrics, 13th edn. Saunders, Philadelphia, pp 10–16
20. Fukunaga T, Yamamoto Y, Yamada M, Tatsuno Y, Imabayashi T, Mizoi Y (1990) Thymus of abused/neglected children. Jpn J Leg Med (Suppl) 44:162
21. Gosseye S, Diebold N, Griscelli C, Nezelof C (1983) Severe combined immunodeficiency disease; a pathological analysis of 26 cases. Clin Immunol Immunopathol 29:58–77
22. Conley ME, Beckwith JB, Mancer JFK, Tenckhoff L (1979) The spectrum of the DiGeorge syndrome. J Pediatr 94:883–890