OLGU SUNUMU CASE REPORT

A Case of Paraneoplastic Pemphigus Associated with Pancreatic Carcinoma

Pankreas Karsinomunun Eşlik Ettiği Bir Paraneoplastik Pemfigus Olgusu

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ÖZET Paraneoplastic pemphigus, a rare form of autoimmune blistering diseases, may present with polymorphic cutaneous lesions such as erythema, papulosquamous eruptions, bullae, targetoid lesions or lichenoid eruptions. The disease is usually accompanied by hematologic malignancies, while few cases presenting in association with non-hematologic neoplasms have also been reported. To our knowledge, only one case with pancreatic carcinoma has been reported previously. The diagnosis of pancreatic carcinoma located in the corpus is often delayed because of its asymptomatic course and absence of a specific laboratory marker. Here, we describe a male patient with fatal paraneoplastic pemphigus resistant to conventional therapy and found to be associated with an underlying occult pancreatic carcinoma.

Anahtar Kelimeler: Pemphigus; pancreatic neoplasms

ABSTRACT Paraneoplastik pemfigus, eritem, papüloskuamöz erüpsiyonlar, büller, dairesel lezyonlar ya da likenoid erüpsiyonlarla kendini gösterebilen, otoimmün büllü hastalıkların nadir bir formudur. Az sayıda olguda nonhematolojik neoplazilerle birliktelik bildirilmiş olsa da genellikle hematolojik malignitelere eşlik eder. Bizim bilgilerimize göre literatürde şu ana kadar pankreas karsinomlu tek olgu bildirilmiştir. Korpusta lokalize pankreas karsinomunun tanısı, asemptomatik seyri ve spesifik laboratuvar belirteçlerinin olmamasından dolayı çoğunlukla gecikir. Biz burada, konvansiyonel tedavilere dirençli ve altta yatan pankreas karsinomunun eşlik ettiği, fatal sonlanan paraneoplastik pemfiguslu bir erkek olguyu sunuyoruz.

Key Words: Pemfigus; pankreas kanseri

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Paraneoplastic pemphigus (PNP) is an autoimmune blistering disorder associated with an underlying hematologic or non hematologic malignancy. The disease was initially described by Anhalt *et al.* in 1990.[1] In PNP, severe and intractable stomatitis is usually the first presenting manifestation and is extremely recalcitrant to the therapy. In general, the prognosis of PNP is poor in comparison with classic pemphigus. Usually there is no significant response to the therapies with high dose corticosteroids and other immunosuppressive agents, intravenous immunoglobulins and plasmapheresis. But treatment of underlying tumour often results in a slow resolution of the skin lesions. Here, we present a fatal case of PNP associated with pancreatic carcinoma.

CASE REPORT

A 63-year-old man presented with 1-month duration of widespread erosions in oral mucosa and multiple bullae and erosions of trunk, extremities and scalp was referred to our clinic. Dermatological examination revealed annular, sharply demarcated, coalescing painful erosions partially covered with hemorrhagic crust, intact and ruptured blisters of different sizes on erythematous macules on the anterior, lateral and posterior trunk, periumbilical region, axillar and inguinal areas, upper and lower extremities and scalp (Figure 1 A). There were painful erosions on tongue, hard and soft palate, and hemorrhagic crusts on the lips (Figure 1B). His right hand was amputated 30 years ago following a trauma. Weight loss, malasie, weakness and dysphagie were also noted. The physical examination was unremarkable. On his laboratory investigations, complete blood count was normal except for anemia (Hb: 9.3 g/dl) and the erythrocyte sedimentation rate was 12 mm/h. Biochemical parameters, viral markers, blood, urine and sputum cultures, routine chest X-ray, tumour markers (Carcinoembryogenic antigen, alpha-fetoprotein, carbohydrate antigen 19-9, prostatic specific antigen, free prostatic specific antigen, thyroglobuline) and autoantibodies were either negative or within normal limits. A punch biopsy of the lesional skin on the trunk revealed suprabasillar clefting and acantholysis with the typical tombstone appearance of pemphigus vulgaris and lymphocytic, histiocytic and eosinophilic infiltrate and oedema in the dermis (Figure 2). On direct immunofluorescence (DIF), Immunoglobulin G (IgG) and complement 3c (C3c) deposits were detected at dermo/epidermal junction. Antibodies against PNP could not be tested since the required substrate was not available. Therapy was initiated with methylprednisolone (1 mg/kg/d). On the second week of therapy, toxic hepatitis and sepsis developed, and the therapy was discontinued. Systemic antibiotherapy and supportive therapy were given. Due to progression of the lesions, intravenous immunoglobulins (IvIg; 0.5 g/kg/d, 5 consecutive days), mycophenolate mofetil (2 g/d) and pulse methylprednisolone (20 mg/kg/d, once) were given. Partial and short periods of remission was obtained and new lesions appeared after each of these therapies. On the 74th day of his hospitalization, the patient developed a sudden epigastric pain and abdominal ultrasonography was performed. It revealed an increase of the echogenity in the pancreatic region. An associated malignancy of pancreas was suspected and a mass located in the pancreatic corpus invading the superior mesenteric artery and vein, splenic vein and coeliac truncus compatible with pancreatic carcinoma was detected on the computerized tomography of abdomen and pelvis (Figure 3). On the 77th day of hospitalization the patient's condition suddenly deteriorated and he died of the respiratory failure which was related to sepsis and/or primary malignancy. Permission for autopsy was not granted.

DISCUSSION

Paraneoplastic pemphigus is a recently described term as a new type of pemphigus characterized by particular clinical, histological and immunopathological features, occuring in association with underlying lymphoproliferative neoplasm.[1]

The disease can be defined and identified by the following: (i) painful stomatitis and a polymorphous cutaneous eruption with lesions that may be blistering or may resemble erythema multiforme or a drug eruption; (ii) histological findings that reflect the variability of cutaneous lesions, showing acantholysis, lichenoid or interface change; (iii) DIF demonstrating deposition of IgG and complement in the epidermal intercellular space and basement membrane zone; (iv) serum autoantibodies that bind the cell surface of skin and mucosa in a pattern typical for pemphigus, but in additon bind to simple, columnar and transitional epithelia; (v) the serum autoantibodies identify desmogleins 1 and 3 as well as members of plakin family of epithelial proteins including desmoplakin 1 and 2, envoplakin, periplakin, bullous pemphigoid antigen 1 (BPAg1) and plectin.[2] Because antibodies against PNP could not be tested in our laboratories due to lack of the substrate, the last 2 diagnostic criteria

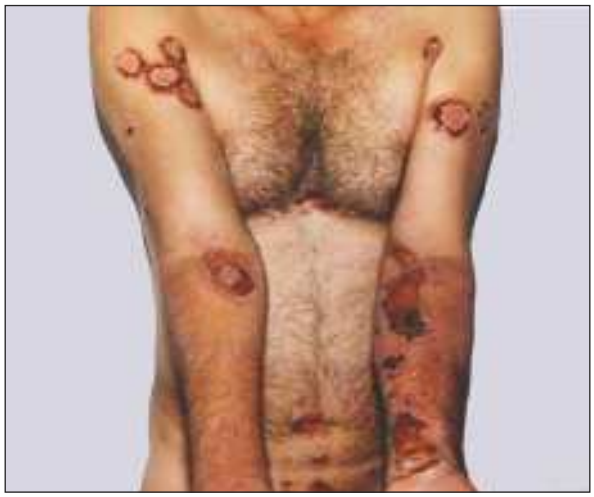

FIGURE 1A: Annular, sharply demarcated erosions of different sizes on the anterior trunk, periumblical region and upper extremities.

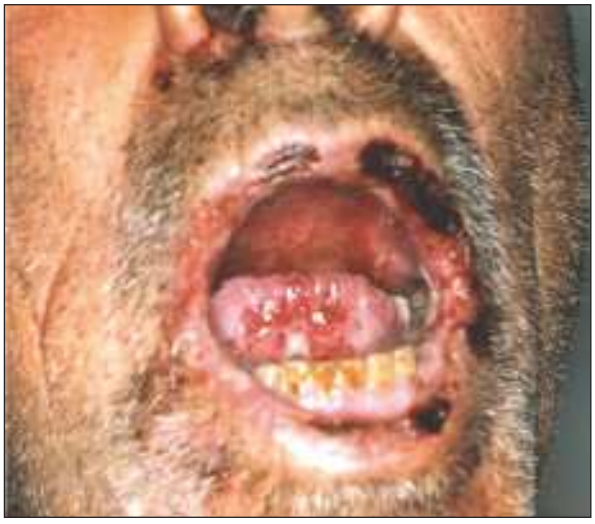

FIGURE 1B: Erosions on tongue, hard and soft palate, and hemorrhagic crusts on the lips.

could not be demonstrated in our case. PNP may display at least 5 different clinical and immunopathological variants (pemphigus-like, pemphigoid-like, erythema multiforme-like, graft-vs-host disease-like and lichen planus like).[3] More recently, a new term 'paraneoplastic autoimmune multiorgan syndrome' in which autoantibodies are thought to target many organs including kidney, muscles, mucous membranes and skin has been proposed.[4] Although not widely accepted yet, the higher mortality rate, the more aggressive and recalcitrant nature in this syndrome rather than classical PNP suggests that it may likely be the case in our patient. However, this hypothesis could not be confirmed since postmortem biopsies and indirect immunofluorescence were not available in our patient.

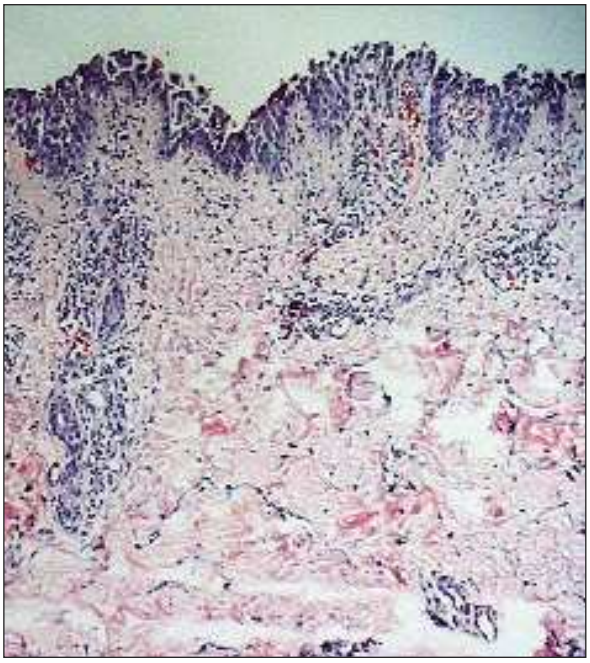

FIGURE 2: Suprabasillar clefting and acantholysis with the typical tombstone appearance of pemphigus vulgaris and lymphocytic, histiocytic and eosinophilic infiltrate and oedema in the dermis (H&E, x40).

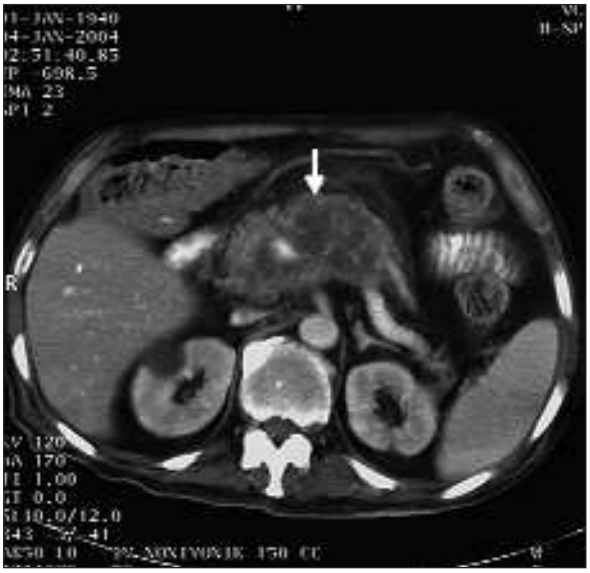

FIGURE 3: Computerized tomography of abdomen and pelvis detecting a mass located in the pancreatic corpus invading the superior mesenteric artery and vein, splenic vein and coeliac truncus compatible with pancreatic carcinoma.

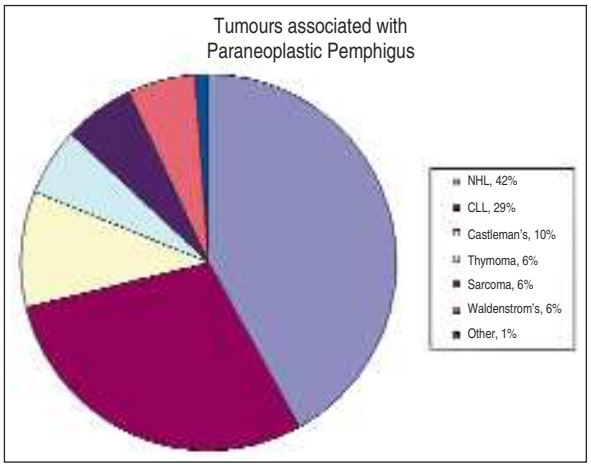

FIGURE 4: The proportion of specific neoplasms associated with paraneoplastic pemphigus shown graphically (From Anhalt GJ. Paraneoplastic Pemphigus. J Investig Dermatol Symp Proc 2004;9:29-33).[1]

Although the most common neoplasms reported to be associated with PNP are non-hodgkin disease, chronic lymphocytic leukemia and Castleman's disease,[2] some other solid organ tumors (retroperitoneal tumours,[5,6] hepatocellular carcinoma,[7] uterine carcinoma,[8] lung carcinoma,[9,10] renal cell carcinoma,[11] tongue cancer,[12] malignant melanoma,[13] pancreatic carcinoma[14]) could also be associated with the disease (Figure 4). To the best of our knowledge, only one case of pancreatic carcinoma has been reported so far.

The mortality rate is about 90%.[3] The exact cause of death in PNP has been attributed to multiple factors including malignancy, side effects of the potent medications, sepsis, gastrointestinal bleeding, multiorgan failure and respiratory failure.[2] In our case, recalcitrant lesions, sepsis and death may have been due to not only side effects of the potent immunsupressive agents used for the treatment, but also due to the underlying malignancy. Since pancreatic carcinoma located in the corpus is an indolent tumor without a significant laboratory marker, the diagnosis is often delayed. This case represents another example of fatal PNP with polymorphic clinical features resistant to therapy and related with pancreatic carcinoma demonstrating the severity and complexity of the pathogenesis.

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