

**Case Report**

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**Henoch-Schönlein purpura associated with a neuroblastoma: Report of one case and a review of the literature**Qiaoli Dong<sup>1,2</sup>, Shanshan Cao<sup>1,3</sup>, Hongwen Zhang<sup>1,\*</sup>, Hui Geng<sup>1</sup><sup>1</sup>Department of Pediatrics, Peking University First Hospital, Beijing, China;<sup>2</sup>Department of Pediatrics, Affiliated Hospital of Hebei University, Baoding, China;<sup>3</sup>Health Center, Beijing Entry-exit Inspection and Quarantine Bureau, Beijing, China.

**Summary** Malignancies such as solid tumors and hematologic malignancies can often induce or be associated with Henoch-Schönlein purpura (HSP) in older males but not in children. Described here is the case of a 5-year-old boy who clinically presented with HSP. An imaging study of the abdomen revealed a right retroperitoneal neoplasm that histopathology postoperatively confirmed to be a neuroblastoma. Malignancies are sometimes associated with HSP mostly in older males, though children are affected, albeit rarely. Thus, all patients with HSP must be carefully examined to identify or exclude an underlying disease.

**Keywords:** Henoch-Schönlein purpura (HSP), neuroblastoma, malignancy

**1. Introduction**

Henoch-Schönlein purpura (HSP) is the most common vasculitic disease affecting children. HSP is a multisystem immunoglobulin A-mediated vasculitis with a self-limited course that affects the skin, joints, gastrointestinal tract, and kidneys (1,2). HSP has many causes, including infections, drugs, foods, and malignant tumors. Many malignancies, such as solid tumors and hematologic malignancies, are reported to induce or be associated with HSP. Such tumors include carcinoma of the lung, bronchus, esophagus, stomach, intestine, breast, kidney, prostate, and thyroid (3-12) while hematologic malignancies include non-Hodgkin lymphoma, Hodgkin disease, multiple myeloma, myeloproliferative disease, and myelodysplastic syndrome (10,11,13-17).

However, patients with HSP associated with a malignancy are mostly older males with a mean age of 60 years (7,8,10,11). Neuroblastomas are the most common extracranial solid tumors in children, but there are no reports of children with HSP associated with a neuroblastoma as has been reported here.

**2. Case report**

A 5-year-old boy with a weight of 19.5 kg (75 percentile), height of 110.0 cm (50 percentile), and blood pressure of 100/75 mmHg presented with numerous purpuras, bilateral knee joint pain, and abdominal pain without bloody diarrhea at almost the same time. The boy had no upper respiratory tract infections or other precipitating factors prior to the onset of those symptoms. A physical examination on admission found numerous flat or palpable purpuras that were typical of HSP in both lower extremities. There were no signs or abnormal findings upon physical examination of the abdomen. No lymphadenopathy and hepatosplenomegaly was evident. The boy was diagnosed with HSP.

Laboratory results such as urine output, renal function, prothrombin time, complements C3 and C4, anti-double stranded DNA antibodies, antinuclear antibodies, and anti-smooth muscle antibodies, C-reaction protein, and antistreptolysin O were all normal. The boy was treated with vitamin C, calcium gluconate, cimetidine, and dipyridole. Joint pain and abdominal pain improved but purpuras did not change. A routine abdomen ultrasound two weeks after the diagnosis of HSP revealed a right adrenal-occupying lesion (4 cm × 6 cm) and magnetic resonance imaging suggested a neoplasm. Further laboratory tests revealed higher levels of vanillylmandelic acid (VMA) and

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homovanillic acid (HVA) in the urine. Histopathology confirmed the neoplasm to be an adrenal neuroblastoma (stage II, American Children's Oncology Group staging system, CCSG). HSP completely resolved soon after surgery, and continued chemotherapy was given using the OPEC schedule (vincristine [O], cisplatin [P], etoposide [E], and cyclophosphamide [C]). HSP did not recur during a follow-up of 12 months.

### 3. Discussion

The patient experienced purpura and joint and abdominal pain without kidney involvement, fulfilling the diagnostic criteria for HSP (18). Abdominal ultrasound and magnetic resonance imaging revealed a right retroperitoneal neoplasm that histopathology postoperatively confirmed to be a neuroblastoma. HSP was associated with a neuroblastoma in this 5-year-old boy. Moreover, neuroblastoma was an incidental finding diagnosed by the routine abdomen ultrasound; the patient had no abdominal signs or abnormal physical findings on admission.

Malignancies are known to cause vasculitis like HSP. In 2006, Zurada *et al.* (11) reviewed literature on adult malignancy-associated HSP from around the world, and they found a total of 31 cases. Patients were overwhelmingly male (94%) with a mean age of 60 years and presented predominantly with solid tumors (61%) and secondly with hematologic malignancies (39%). The most frequent tumors were lung cancer ( $n = 8$ ), multiple myeloma ( $n = 5$ ), prostate cancer ( $n = 5$ ), and non-Hodgkin lymphoma ( $n = 3$ ). The majority of patients (55%) developed HSP within 1 month of cancer diagnosis or detection of metastases. Their findings were similar to those in a report by Pertuiset *et al.* (8). In 2009, Mitsui *et al.* (10) reported 23 cases of HSP in patients with underlying malignant tumors. HSP was thought to be closely associated with a tumor in nine patients, and seven of the nine exhibited new metastatic lesions or died due to underlying cancer within 1-32 months. Based on these reports, HSP associated with a malignancy is characterized by: *i*) patients who are mainly older males (over 40-60 years: over 85%); *ii*) development within 1-3 months of diagnosis or metastasis of a neoplasm; *iii*) causes are mostly solid tumors (over 60%), and especially carcinoma of the lung, followed by hematologic malignancies (about 40%); and *iv*) development in the absence of a precipitating factor. This suggests that adults, and especially older men who present with unexplained HSP, should be evaluated for an occult neoplasm (5,6), while patients with a known history of malignancy who present with HSP should be evaluated for metastatic disease (11). A skin biopsy is an important way to determine the underlying pathology in adult HSP (17). Malignancies induce or are associated with HSP mostly in older males, but children can also be affected, albeit

rarely. Funato *et al.* (19) reported acute lymphoblastic leukemia mimicking HSP in a 3-year-old boy.

Neuroblastomas are the most common extracranial solid tumors in children, accounting for about 8%-10% of all pediatric tumors (20,21). That said, there are no reports of HSP associated with a neuroblastoma or other malignancy in children. The current case is the world's first case of HSP associated with a neuroblastoma.

Tumors are known to be one of the causes of vasculitis (8,10,22). Vasculitis is reported to occur during the course of malignancies in 2.3%-8% of patients (23). The incidence of vasculitis in cancer is estimated to be 1 in 1,800 for hemopathies and 1 in 80,800 for solid tumors (24). The relationship between vasculitis and malignancy remains unclear: *e.g.* fortuitous association, paraneoplastic syndrome, or neoplasms induced by immunosuppressive drugs prescribed to treat vasculitis, and so on (25). HSP is an allergic vasculitis disease caused by an immunologic mechanism (26-29). Neoplasm antigens such as paraneoplastic antibodies or abnormally produced IgA lead to the formation of immune complexes that induce the lesions of HSP (10).

The development of HSP and a neuroblastoma at the same time in the current patient is curious. Maybe both diseases developed independently or maybe HSP was a paraneoplastic syndrome of the neuroblastoma. However, neuroblastomas are known to induce other forms of vasculitis such as Kawasaki disease (30). In the current patient, HSP was likely to be induced by the neuroblastoma. The first reason for this conjecture is because the neuroblastoma appeared to develop prior to HSP given to the size of the neuroblastoma and the course of HSP. Second, there were no precipitating factors before the onset of HSP and no relapse during 12 months of follow-up. However, genetic studies of the neuroblastoma, *e.g.* studies of the *N-Myc* gene and paraneoplastic antibodies, were not performed, and neither was a skin biopsy.

In conclusion, many malignancies may cause HSP, but in older males HSP is mostly caused by solid tumors. Reported here is the first case of HSP associated with a neuroblastoma in a 5-year-old boy. Epidemiological studies are needed to determine the association between HSP and malignancy in children.

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