

## Common and Uncommon presentation of Childhood Cancers - Neuroblastoma

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### Presenting Features of Neuroblastoma

In the text book "*Hutchison & Cockburn, Practical Paediatric Problems, 6th Edition, 1986*" we can read two passages of vivid description of this condition: "*The child with neuroblastoma is likely to be ill, miserable and fractious, anorexic, to lose weight and anaemic.....*" & "*Another mode of onset is with swelling of the abdomen due to an adrenal tumour..... The neuroblastoma feels hard but its irregular craggy surface contrasts with the smoothness of the renal tumour....*" However, this presenting pattern is only typical for those patients with metastatic neuroblastoma which accounts for >60% of cases. Localized neuroblastoma can be quite asymptomatic and rarely, if ever, progresses to metastatic disease.

**Features** in order of frequency for metastatic neuroblastoma:

- *fever*
- *abdominal mass*
- *cytopenias*
- *lymphadenopathy*
- *bone pain,*
- *hepatosplenomegaly*
- *proptosis*

The first symptoms of metastatic neuroblastoma are often vague and include:

- *fatigue,*
- *loss of appetite*
- *fever*

Later symptoms depend on tumor locations: it may cause distension & constipation (the tumour in the abdomen [respiratory distress (thorax), paraplegia (in the paraspinal area), bone pain and limping (lesions in the legs and hips), and proptosis with periorbital ecchymosis **Raccoon eye sign** (in periorbital metastasis).

Common presenting features of **Localized Neuroblastoma** include isolated abdominal distension, cervical or supraclavicular mass with or without Horner's syndrome, but a significant number of patients are asymptomatic with an incidentally detected mediastinal or abdominal tumour only.

### Uncommon Presentations

- **Lower limb paresis** - intraspinal epidural extension of a primary paraspinal tumour (4%)
- **Severe diarrhoea** - vasoactive intestinal peptide (VIP) - (4%)

- **Acute cerebellar encephalopathy** - cerebellar ataxia, rapid and random eye movements (opsoclonus), and myoclonic jerks - (2.8%)
- **Horner syndrome** - in patients with lesions in the cervical /upper thoracic sympathetic ganglia (1.7%)
- **Hypertension, flushing, and periods of excessive sweating** - increased catecholamines (0.2%)

#### **VIP & Neuroblastoma**

- WDHA (watery diarrhea, hypokalemia, achlorhydria) Syndrome (“Vipoma”)
- Nearly 7% of neuroblastomas secrete vasoactive intestinal peptide (VIP)
- VIP induces growth inhibition & morphological differentiation of cultured human neuroblastoma cell lines
- It is hypothesized that VIP may be operative in the autocrine regulation of neuroblastic growth and differentiation
- VIP secreting NB are more mature and usually have a better prognosis
- Elevated serum ferritin (>142 ng/mL) NSE (>100 ng/mL) are associated with a bad prognosis
- 25% of VIP can occur after initiation of treatment

#### **Opsoclonus Myoclonus Ataxia Syndrome**

- Involuntary, arrhythmic, chaotic and multi-directional saccades of eye movement
- With horizontal, vertical and torsional components
- Presents during fixation, convergence, or even during eye lid closure and sleep
- Large amplitude and high frequency (10 to 15Hz)
- Associated with:
  - Myoclonic jerks involving head, trunk and limbs
  - Cerebellar ataxia with dysarthria and truncal ataxia
  - Impairment of conscious state
  - Cognitive and psychiatric manifestations

**Risk-directed Approach** – different treatment regimen according to the risk stratification is called for;

- Low risk- Surgery alone
- Immediate risk- Multimodality = Surgery + chemotherapy
- High risk- Intensive multimodality - intense chemotherapy + surgery + local radiation therapy + immunotherapy ± bone marrow transplant + differentiating agents (ie. Retinoic acid)

**"Wait and see"** strategy for Stage 4S or localized neuroblastoma in infants

- With increase frequency of USG which led to an increase of localized neuroblastoma detected in pre- and post-natal period
- Localized neuroblastomas in infants may regress spontaneously & a "wait and see" strategy has been adopted for tumours found by urinary mass screening
- Metastatic neuroblastoma in infancy not involving bone (stage 4S, can involve bone marrow, skin, lymph nodes and liver) can also regress spontaneously but

low intensity treatment may be needed if there is nerve compression or rapid enlarging liver.

### **Conclusions**

- Neuroblastoma is a heterogenous group of disease with a diverse presenting features
- They also have different outcome and requires different treatment approaches
- More defined biological markers and genetic profiling can help us to apply risk stratified approach more accurately
- The overall outcome of neuroblastoma improved significantly over the past 2 decades